
Guidelines of care for the primary prevention of atopic dermatitis and awareness of comorbid conditions in pediatric atopic dermatitis



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Background: Pediatric atopic dermatitis (AD) is a common, chronic inflammatory skin disorder that significantly impacts the quality of life of affected children and their families. In addition to skin-related symptoms, AD in pediatric patients may be associated with a range of comorbid conditions.

Objective: To provide evidence-based recommendations on primary prevention of AD and to appraise evidence of the association between AD and comorbidities among pediatric patients.

Methods: A multidisciplinary workgroup conducted a systematic review and applied the Grading of Recommendations, Assessment, Development, and Evaluation approach for assessing the certainty of evidence and formulating and grading recommendations.

Results: The workgroup developed 14 evidence-based recommendations on primary prevention of AD and 29 statements on the association between pediatric AD and comorbid conditions.

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[†]Died July 11, 2025.

Funding sources: This study was funded in total by internal funds from the American Academy of Dermatology.

Patient consent: Not applicable.

IRB approval status: Not applicable.

Statement on prior presentation: Contents have not been previously presented.

Editorial Note: Robert Sidbury, MD, MPH, passed away unexpectedly on July 11, 2025, after this manuscript was finalized for submission to the journal. The JAAD editor has confirmed that Dr Sidbury's contributions meet JAAD and ICMJE authorship criteria and that, to the best of the journal's knowledge, his disclosed conflicts are accurately represented.

Disclaimer: Adherence to these guidelines will not ensure successful treatment in every situation. Furthermore, these guidelines should not be interpreted as setting a standard of care or be deemed inclusive of all proper methods of care, nor exclusive of other methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding the propriety of any specific therapy must be made by the physician and the patient in light of all the circumstances presented by the individual patient, and the known variability and biologic behavior of the disease. This guideline reflects the best available data at the time the guideline was prepared. The results of future studies may require revisions to the recommendations in this guideline to reflect new data.

Accepted for publication February 27, 2026.

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Published online April 7, 2026.

0190-9622/\$36.00

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<https://doi.org/10.1016/j.jaad.2026.02.114>

Limitations: This analysis is based on the best available evidence at the time it was conducted. This guideline does not make recommendations for screening or management of comorbidities in children with AD.

Conclusions: We make a conditional recommendation for moisturizing skin care to reduce the occurrence of AD and conditional recommendations against early food introduction, human milk consumption, and probiotic or vitamin D supplementation for the primary prevention of AD. Clinicians should be aware of comorbidities associated with pediatric AD, but further research is needed to optimize screening and/or management of comorbidities. (J Am Acad Dermatol 2026;95:124.e1-e19.)

Key words: allergies; atopic dermatitis; cardiovascular disease; comorbidities; dermatology; diabetes; guidelines; mental health; metabolic syndrome; obesity; osteoporosis; prevention; skin infection.

SCOPE AND OBJECTIVES

Atopic dermatitis (AD) is a chronic inflammatory skin condition affecting 10% to 20% of children worldwide.¹⁻⁴ It often begins in infancy and is associated with appreciable morbidity and healthcare burden. In addition to skin-related symptoms, AD in pediatric patients may be associated with a range of comorbidities, including allergic rhinitis, asthma, food allergies, and mental health disorders. The objective of these guidelines is twofold: (1) to provide evidence-based recommendations for the primary prevention of AD, and (2) to present evidence-informed statements on the associations between AD and pediatric comorbidities. These guidelines aim to support healthcare professionals, caregivers, and policymakers in implementing preventive measures and in understanding the broader health implications of pediatric AD. Children under 18 years of age with AD of any severity in any healthcare setting or context are the target population of these guidelines. Importantly, these guidelines do not make recommendations for screening or management of comorbidities in children with AD.

METHODS

A multidisciplinary workgroup developed these guidelines using a systematic evidence review process, which included (1) identifying and prioritizing clinical questions and outcomes (Table I), (2) systematic retrieval and assessment of evidence, and (3) assessment of the certainty of the evidence and formulation of recommendations or statements of association

using GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) (Tables II and III).

CAPSULE SUMMARY

- The guidelines provide evidence-based recommendations on primary prevention of atopic dermatitis (AD) and appraise evidence of the association between AD and comorbidities among pediatric patients.
- Conditional recommendations are made in favor of moisturizing skin care to reduce the occurrence of AD and against early food introduction, human milk consumption, and probiotic or vitamin D supplementation for the primary prevention of AD.
- Clinicians should be aware of comorbidities associated with pediatric AD, but further research is needed to optimize screening and/or management of comorbidities.

Specific to the clinical question addressing the association between pediatric AD and comorbid conditions, the GRADE for prognosis approach was used to assess the overall certainty of the evidence for each outcome.^{8,9} The GRADEPro Guideline Development Tool was used to create evidence profiles that categorized the overall quality of the body of evidence for each outcome into 1 of 4 categories: high, moderate, low, or very low. Each category represents the confidence in the estimate of effect for an outcome (Table III).

For detailed methodology, see Supplementary

Appendix 1, available via Mendeley at <https://data.mendeley.com/datasets/zjfknbhdd/1>.

DEFINITION

AD, also known as atopic eczema, is a chronic, pruritic inflammatory skin disease that occurs with highest prevalence in children. It follows a relapsing course. AD is often associated with a personal or family history of atopy.

PRIMARY PREVENTION

A range of interventions from skin care to nutritional modifications were explored for their potential for primary prevention of AD. This section of the guideline evaluates the data on infant-focused primary AD prevention interventions to support

Abbreviations used:

AA:	alopecia areata
AAD:	American Academy of Dermatology
AC:	allergic conjunctivitis
AD:	atopic dermatitis
ADHD:	attention deficit hyperactivity disorder
AE:	adverse event
AR:	allergic rhinitis
ASD:	Autism spectrum disorder
CDLQI:	children's dermatology life quality index
CI:	confidence interval
EASI:	eczema area and severity index
EoE:	eosinophilic esophagitis
FA:	food allergies
FDA:	Food and Drug Administration
HR:	hazard ratio
IGA:	investigator global assessment
MD:	mean difference
OR:	odds ratio
POEM:	patient oriented eczema measure
QoL:	quality of life
RCT:	randomized controlled trial
RR:	risk ratio
SAE:	serious adverse event
SCORAD:	scoring of atopic dermatitis

evidence-based clinical practice recommendations (Table IV).

Skin care interventions

Regular use of moisturizing skin care before 2 years of age in children at risk for AD may reduce the development of AD,^{10-12,14-19,21-23} (Supplementary Table I, available via Mendeley at <https://data.mendeley.com/datasets/zjfknbhdd/1>). There is great heterogeneity among applicable studies, in terms of age at intervention, duration of intervention, washout periods, age at assessment, intervention composition timing and frequency, and comparator group. The evidence does not support a protective benefit with the use of moisturizing skin care in the general population.^{13,20} However, providers should educate caregivers about the potential for exposure to allergens in personal care products, though adverse events (AEs) with regular moisturizing skin care appears rare and comparable to standard care.^{12-14,19,22}

Environmental interventions

There is insufficient evidence to recommend dust mite avoidance interventions before the age of 2 years in children at risk of developing AD (Supplementary Table II, available via Mendeley at <https://data.mendeley.com/datasets/zjfknbhdd/1>).²⁴ Due to the underpowered sample in the study by Jabbar-Lopez et al, there is also insufficient evidence to recommend water softening

interventions before the age of 2 years in children at risk of developing AD (Supplementary Table III, available via Mendeley at <https://data.mendeley.com/datasets/zjfknbhdd/1>).²⁶

Dietary interventions

Available evidence suggests no benefit to early complementary feeding for the prevention of AD (Supplementary Table IV, available via Mendeley at <https://data.mendeley.com/datasets/zjfknbhdd/1>).^{20,27} Although early food introduction may reduce the risk of food allergy, it does not alter the occurrence or severity of AD.^{59,60}

Available evidence suggests no benefit from human milk consumption,²⁸ probiotic supplementation,^{29,31-33,35-37} or vitamin D supplementation³⁸ for the prevention of AD (Supplementary Tables V-VII, available via Mendeley at <https://data.mendeley.com/datasets/zjfknbhdd/1>). Furthermore, due to limited, underpowered data, there is insufficient evidence to recommend prebiotic supplementation,^{39,40,42} synbiotic (combined probiotic and prebiotic) supplementation,⁴³ goat milk consumption (note, it may cause gastrointestinal distress and iron-deficiency anemia),^{44,45} fatty acid supplementation,^{25,46-48} enriched formula,⁴⁹ partially hydrolyzed whey formula,⁵⁰⁻⁵⁸ short-term early consumption of hydrolyzed formula,⁵³ or soy formula^{51,54} for the prevention of AD (Supplementary Tables VIII-XV, available via Mendeley at <https://data.mendeley.com/datasets/zjfknbhdd/1>).

COMORBIDITIES

AD detrimentally impacts quality of life (QoL) and overall health, increasing health care utilization.^{61,62} Comorbidities further increase the individual- and population-level burdens of AD, and AD in children is associated with a wide variety of systemic comorbidities, particularly atopic and allergic conditions (Table V). This section of the guidelines appraises the evidence of the association between pediatric AD and comorbid conditions to increase awareness and understanding of AD and its potential associations with the aim of helping providers deliver more holistic care and prevent long-term health consequences and reductions in QoL for these patients.

Allergic conditions

Allergic conjunctivitis.

The association between AD in children and allergic conjunctivitis (AC) is uncertain, due to the absence of consistent evidence, with estimates varying widely across the available studies (Supplementary Table XVI, available via Mendeley at <https://data.mendeley.com/datasets/zjfknbhdd/1>). Pooled

Table I. Clinical questions and scope

Clinical questions	
1. How do infant-focused skin care, dietary, microbiome, environmental, and other interventions affect the risk of developing AD, and do primary AD prevention interventions cause undesirable effects? 2. Are the following comorbidities associated with AD in children and adolescents: mental and behavioral health disorders, allergic conditions, skin infections, asthma, lifestyle choices, alopecia areata, bone fractures, osteoporosis, cardiovascular disease, metabolic syndrome?	
Outcomes of interest	
Primary prevention	Incidence, occurrence, or rate of AD at 6 months to 3 years of age Serious adverse events (as defined by studies) Adverse events of interest (specific to each intervention defined a priori)
Comorbidities	Incidence of select comorbid conditions Prevalence of select comorbid conditions
Scope for prevention	
Characteristic	Inclusion criteria
Population	Healthy full-term (≤ 37 wk gestation) infants ≤ 12 mo without preexisting atopic dermatitis from high risk or general populations
Intervention	Infant-directed interventions intended to prevent development of AD. Including skincare, environmental, dietary, microbiome, and other interventions
Study design	Published RCTs
Scope for comorbidities	
Characteristic	Inclusion criteria
Population	Children and adolescents (< 18 y old) with clinically diagnosed AD of any severity
Exposure	Diagnosis of atopic dermatitis
Study Design	Non-randomized studies (cohort, case-control, cross-sectional)

prevalence of AC in children with AD over 3 studies ($n = 41,169$) was 10.2% (0, 22.0),⁶³⁻⁶⁵ and 1 study found higher adjusted odds of AC in children with AD compared to those without AD (adjusted odds ratio [aOR]: 1.99 [95% confidence interval (95%CI): 1.59-2.49]).⁶⁵

Allergic rhinitis. Allergic rhinitis is a recognized common comorbidity of AD, and our systematic review found moderate certainty evidence that AD in children is associated with AR (Supplementary Table XVII, available via Mendeley at <https://data.mendeley.com/datasets/zjfknbhdd/1>). It is important to note that several studies used in the analysis had high risk for bias and relied on unvalidated exposure and/or outcome assessments. In a pooled analysis of 5 studies,^{66,68,69,71,74} children with AD, compared to those without AD, had a high aOR of AR (3.59 [95%CI: 2.19-5.88]). Furthermore, the association and prevalence of AR may be higher in children with more severe AD.^{67,89} Additionally, in a pooled analysis of 8 studies,^{76,77,80,81,84-86,88,90} children with AD, compared to those without AD, had higher odds of a subsequent diagnosis of AR (aOR: 2.20 [95% CI: 1.88-2.59]).

Eosinophilic esophagitis. The available evidence suggests AD in children is associated with

eosinophilic esophagitis (EoE) (Supplementary Table XVIII, available via Mendeley at <https://data.mendeley.com/datasets/zjfknbhdd/1>). Evaluating 6 studies, the pooled prevalence of AD in children with EoE was 21.8% (95% CI: 7.8-35.8).^{64,93-95,97,98} A retrospective analysis of health care claims data suggested higher odds of EoE in children with AD compared to those without AD,⁶⁹ while 2 other studies demonstrated an increased risk of EoE in children with AD.^{84,96}

Food allergies. Most studies in our systematic review used strict definitions of IgE-mediated food allergies (FA) (including symptoms plus evidence of allergic sensitization and/or oral food challenge) to distinguish food allergy from allergic sensitization to food. With moderate certainty, we concluded that AD in children is associated with FA (Supplementary Table XIX, available via Mendeley at <https://data.mendeley.com/datasets/zjfknbhdd/1>). Including 18 studies ($n = 682,736$), of both caregiver-reported and clinically-confirmed FA, the pooled prevalence of FA in children with AD is 23.6% (95% CI: 21.7-25.4).^{64,79,82,87,103,109,112,115,117-119,121,124-126,128,130,131} Furthermore, 5 studies described increasing FA prevalence with increasing AD severity,^{79,87,119,126,135} while 2 did not.^{125,128}

Table II. Strength of recommendation and certainty of evidence for primary prevention recommendations

Strength of recommendation	Wording	Implication ⁵⁻⁷
<i>Strong recommendation for the use of an intervention</i>	"We recommend..."	Benefits clearly outweigh risks and burdens; recommendation applies to most patients in most circumstances.
<i>Strong recommendation against the use of an intervention</i>	"We recommend against..."	Risk and burden clearly outweigh benefits; the recommendation applies to most patients in most circumstances.
<i>Good Practice Statement</i>	"We recommend..."	Guidance was viewed by the Work Group as imperative to clinical practice and developed when the supporting evidence was considerable but indirect, and the certainty surrounding an intervention's impact was high with the benefits clearly outweighing the harms (or vice versa). Good Practice Statements are strong recommendations as the certainty surrounding the impact of the recommended intervention is high. Implementation of these strong recommendations is considered to clearly result in beneficial outcomes. ⁷
<i>Conditional recommendation for the use of an intervention</i>	"Evidence suggests benefit..."	Benefits are closely balanced with risks and burdens; recommendation applies to most patients, but the most appropriate action may differ depending on the patient or other stakeholder values.
<i>Conditional recommendation against the use of an intervention</i>	"Evidence suggests no benefit..."	Risks and burden closely balanced with benefits; recommendation applies to most patients, but the most appropriate action may differ depending on the patient or other stakeholder values
<i>Insufficient evidence statement</i>	"There is insufficient evidence to recommend..."	The available evidence is inadequate to make a reliable determination about the effectiveness or lack thereof of an intervention
Strength of recommendation	Wording	Implication ⁵⁻⁷
<i>Strong recommendation for the use of an intervention</i>	"We recommend..."	Benefits clearly outweigh risks and burdens; recommendation applies to most patients in most circumstances.
<i>Strong recommendation against the use of an intervention</i>	"We recommend against..."	Risk and burden clearly outweigh benefits; the recommendation applies to most patients in most circumstances.
<i>Good Practice Statement</i>	"We recommend..."	Guidance was viewed by the Work Group as imperative to clinical practice and developed when the supporting evidence was considerable but indirect, and the certainty surrounding an intervention's impact was high with the benefits clearly outweighing the harms (or vice versa). Good Practice Statements are strong recommendations as the certainty surrounding the impact of the recommended intervention is high. Implementation of these strong recommendations is considered to clearly result in beneficial outcomes. ⁷

Continued

Table II. Cont'd

Strength of recommendation	Wording	Implication ^{5,7}
<i>Conditional recommendation for the use of an intervention</i>	"Evidence suggests benefit..."	Benefits are closely balanced with risks and burdens; recommendation applies to most patients, but the most appropriate action may differ depending on the patient or other stakeholder values.
<i>Conditional recommendation against the use of an intervention</i>	"Evidence suggests no benefit..."	Risks and burden closely balanced with benefits; recommendation applies to most patients, but the most appropriate action may differ depending on the patient or other stakeholder values
<i>Insufficient evidence statement</i>	"There is insufficient evidence to recommend..."	The available evidence is inadequate to make a reliable determination about the effectiveness or lack thereof of an intervention
Certainty of Evidence	Wording	Implication ^{5,6}
High	"high certainty evidence"	Very confident that the true effect lies close to that of the estimate of the effect.
Moderate	"moderate certainty evidence"	Moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low	"low certainty evidence"	Confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect
Very Low	"very low certainty evidence"	The estimate of effect is very uncertain; the true effect may be substantially different from the estimate of effect

Examining the association between FA and AD demonstrated similar findings—the pooled analysis of 6 studies found children with AD, compared to those without AD, had higher adjusted odds of FA (aOR 6.53 [95% CI: 3.89-10.96]),^{69,99,100,104,109,112} and Mailhol et al found an association with FA and AD severity in a cohort of 386 children with AD.¹⁰³ The association with AD in children and specific FA (ie, eggs, peanut, cow's milk) is less clear with limited data. Moreover, while studies are limited, children with AD may have higher odds of subsequent diagnosis of FA. While there are many studies examining the link between AD in children and FA, several relied on unvalidated and/or self-reported exposure and/or outcome assessments so are of a high risk of bias.

Asthma. Atopic dermatitis in children is associated with asthma (Supplementary Table XX,

available via Mendeley at <https://data.mendeley.com/datasets/zjfknbhdd/1>). In the pooled adjusted analysis of 9 studies, children with AD had higher odds of asthma (aOR: 3.03 [95% CI: 2.30-4.01]).^{68,69,72,74,140,141,145,150,151} The pooled unadjusted analysis of 5 additional studies demonstrated similar results.^{75,89,147,148,152} Several studies demonstrate children with a prior diagnosis of AD have higher odds and higher risk of a subsequent diagnosis of asthma.^{66,77,81,84,86,88,90,155,158,162,163,169,172}

The pooled prevalence of asthma in children with AD ($n = 955, 098$) is 21.4% (95% CI: 19.6-23.1).^{64,68,74,75,77,79,81-84,87,89,90,116,118,124,131,145,147,148,150,152,154,156,159-161,165-168,170,171} There is evidence that asthma prevalence increases by AD severity. Gerner et al reported increasing asthma prevalence in children with clear/almost clear, mild, moderate and severe AD: 22.9%, 26.5%, 35.7%, and 35.7%,

Table III. Strength of statements of association and supporting evidence: Wording and implications

Statement wording	Overall certainty of supporting evidence	Implication
Is associated	High or moderate	Clear evidence of an important large effect
Is <i>not</i> associated	High or moderate	Clear evidence of no association
Probably associated	High or moderate	Evidence of a moderate effect
Probably <i>not</i> associated	High or moderate	Evidence of small or unimportant effect
May be associated	Low	Evidence of a large, moderate, or small effect based on low quality evidence.
May <i>not</i> be associated	Low	Evidence of no association based on low quality evidence.
Uncertain association	Any quality	Evidence of any magnitude of effect from very low quality evidence or imprecise or inconsistent effect estimates from evidence of any quality.

Strength of evidence	Wording	Implication ^{5,6,8}
High	"high quality evidence"	Very confident that the true magnitude of association lies close to that of the estimate.
Moderate	"moderate quality evidence"	Moderately confident in the estimate of association, but there is a possibility that it is substantially different.
Low	"low quality evidence"	Confidence in the estimate is limited; the true magnitude of association may be substantially different from the estimate.
Very Low	"very low quality evidence"	The estimate is very uncertain; the true magnitude of association may be substantially different from the estimate.

respectively.⁶⁷ Prevalence estimates varied widely across studies, in part related to variability by geography.

Immune-mediated conditions

Alopecia areata. Evidence of the association between AD in children and AA is of low certainty (Supplementary Table XXI, available via Mendeley at <https://data.mendeley.com/datasets/zjfknbhdd/1>). In the pooled analysis of 2 studies, children with AD, compared to those without, have higher unadjusted odds of AA (OR: 3.17 [95% CI: 1.71-5.86]).^{69,75} There are few studies examining this association, which generally rely on unvalidated or self-reported exposure and outcome assessments, with high risk of bias.

Urticaria. AD in children is associated with urticaria (Supplementary Table XXII, available via Mendeley at <https://data.mendeley.com/datasets/zjfknbhdd/1>). The pooled prevalence of urticaria in children with AD ($n = 54,360$) is 9.5% (95% CI: 7.2-11.8),^{65,67,74,75,79,181} and a pooled analysis of 3 studies suggests higher adjusted odds of urticaria in children with AD compared to those without (aOR: 2.98 [95% CI: 2.84-3.14]).^{65,69,74} Furthermore, a pooled analysis of 2 studies suggests an increased risk of subsequent urticaria in children with AD (adjusted hazard ratio [aHR] of 1.76 [95% CI: 1.42-2.18])^{81,84}; Kitsioulis et al also found higher odds of

subsequent AD in children with chronic urticaria, suggesting the relationship may be bidirectional.¹⁸⁵

Attention deficit hyperactivity disorder and autism spectrum disorders

Attention deficit hyperactivity disorder. The pooled prevalence of attention deficit and hyperactivity disorder (ADHD) in children with AD ($n = 158,832$) is 8.2% (95% CI: 6.4-10.0),^{63,64,68,82,208-210,213-215,218,223} but prevalence rates varied widely across studies ranging from 1.2% to 23.7%; this may be secondary to various measures used to assess outcomes across studies (Supplementary Table XXIII, available via Mendeley at <https://data.mendeley.com/datasets/zjfknbhdd/1>). The pooled analysis of 9 studies examining the association between ADHD and AD demonstrated children with AD, compared to those without AD, have higher odds of ADHD (aOR: 1.43 [95% CI: 1.26-1.63]).^{68,69,187,189,208-211,213} Studies examining the occurrence of ADHD in early onset AD (under 4 years of age) and AD in general were mixed—some suggest an association with early onset AD and AD in general^{217,219-222} while others do not,^{81,89,216,218} and some suggest a greater association with more severe AD cases,¹⁹¹ while others do not.⁸⁹

Autism spectrum disorder. The association between AD in children and autism spectrum

Table IV. Recommendations for primary AD prevention interventions

Statement	Strength	Certainty of evidence	Evidence
Skin care interventions			
Evidence suggests regular use of moisturizing skin care before the age of 2 years in children at risk for atopic dermatitis may reduce the risk of developing atopic dermatitis.	Conditional	Low	10-23
<i>Remark:</i> The evidence does not support a protective benefit with the use of moisturizing skincare in the general population.			
Environmental interventions (water softening, allergen avoidance)			
There is insufficient evidence to recommend water softening or dust mite avoidance interventions before the age of 2 years in children at risk of developing atopic dermatitis.	NA	Very low	24-26
Dietary interventions			
Evidence suggests no benefit to early food introduction for the prevention AD.	Conditional	Very low	20,27
Evidence suggests no benefit of the consumption of human milk for the prevention of AD.	Conditional	Very low	28
Evidence suggests no benefit from probiotic supplementation for the prevention of AD.	Conditional	Low	29-37
Evidence suggests no benefit from vitamin D supplementation for the prevention of AD.	Conditional	Low	38
There is insufficient evidence to recommend prebiotic supplementation for the prevention of AD.	NA	Very low	39-42
There is insufficient evidence to recommend synbiotic supplementation for the prevention of AD.	NA	Low	43
There is insufficient evidence to recommend the consumption of goat milk for the prevention of AD.	NA	Very low	44,45
There is insufficient evidence to recommend fatty acid supplementation for the prevention of AD.	NA	Very low	25,46-48
There is insufficient evidence to recommend an enriched formula for the prevention of AD.	NA	Low	49
There is insufficient evidence to recommend partially hydrolyzed whey formula for the prevention of AD.	NA	Very low	50-58
There is insufficient evidence to recommend the short-term early consumption of hydrolyzed formula.	NA	Very low	53
There is insufficient evidence to recommend soy formula for the prevention of AD.	NA	Low	51,54

disorder (ASD) is uncertain (Supplementary Table XXIV, available via Mendeley at <https://data.mendeley.com/datasets/zjfknbhdd/1>). This was due to low certainty of evidence and conflicting results across studies, as well as a small magnitude of association. In a pooled analysis of 4 studies, children with AD, compared to those without AD, had higher odds of ASD (aOR: 2.12 [95%CI: 1.35-3.33]).^{187,189,209,210} Conversely, a pooled analysis of 2 studies found ASD in children was not associated with AD (aOR: 1.27 [95%CI: 0.90-1.79]).^{207,226} Prevalence rates of ASD in children with AD varied widely across studies, and rates were both lower and greater than expected rates.^{63,82,189,210,225,226,228} Additionally, Wan et al did not find severity of AD to be associated with increased risk of subsequent ASD diagnosis.⁸⁹

Mental health and substance use

Substance use. While it is important for all providers to look for signs of substance use in their pediatric patients, AD in children is probably not associated with drinking alcohol, cigarette smoking, or illicit drug use based on available data (Supplementary Tables XXV-XXVII, available via Mendeley at <https://data.mendeley.com/datasets/zjfknbhdd/1>).^{68,198-201,203-205} Nonetheless, age is an important consideration as adolescents with AD may be more likely to engage in substance use than younger children.

Mental health. Although AD in children is probably associated with anxiety, the association between pediatric AD and depression is uncertain (Supplementary Tables XXVIII and XXIX, available via Mendeley at <https://data.mendeley.com/>

Table V. Pediatric AD comorbidities statements of association

Statement of association	Certainty of evidence	Evidence
Atopic and allergic conditions		
The association between AD in children and allergic conjunctivitis is uncertain.	Low	63-65
AD in children is associated with allergic rhinitis.	Moderate	63,64,66-92
AD in children is associated with eosinophilic esophagitis.	High	64,69,84,93-98
AD in children is associated with food allergies.	Moderate	64,69,77,79,81,82,87,91,99-119,120-139
<i>Remark:</i> The majority of studies used strict definitions of IgE-mediated food allergy (including symptoms plus evidence of allergic sensitization and/or oral food challenge).		
Greater AD severity in children may be associated with increasing food allergy prevalence	Low	79,116,119,126,135
AD in children is associated with asthma	Moderate	64,66-69,72,74,75,77,79,81-84,86-91,116,118,124,131,135,140-173
Greater AD severity in children may be associated with increasing asthma prevalence	Moderate	67,89,135
Immune-mediated conditions		
AD in children may be associated with alopecia areata.	Low	69,75,81,174-180
AD in children is associated with urticaria	Moderate	65,67,69,74,75,79,81,84,181-186
Mental health and substance use		
AD in children is probably associated with anxiety	Moderate	63,64,67-69,81,82,89,187-192
The association between AD in children and depression is uncertain	Very low	63,67,68,75,81,89,187,189-193
AD in children is probably <i>not</i> associated with suicide	Moderate	63,89,194-197
AD in children is probably <i>not</i> associated with drinking alcohol	Moderate	198-202
AD in children is probably <i>not</i> associated with cigarette smoking	Moderate	198-200,203-205
AD in children is probably <i>not</i> associated with illicit drug use	Moderate	68,198
ADHD and autism spectrum disorders		
AD in children is associated with ADHD	Moderate	63,64,68,69,81,82,89,187,189,191,206-224
The association between AD in children and autism spectrum disorder is uncertain	Low	63,81,82,89,187,189,209,210,219,220,225-228
Cardiovascular diseases		
AD in children may be associated with hypertension	Low	68,69,75,229,230
<i>Remark:</i> The evidence suggests a small magnitude of association between AD and hypertension in children.		
The association between AD in children and ischemic heart disease is uncertain.	Low	68,75
AD in children is probably <i>not</i> associated with peripheral vascular disease.	Moderate	68
AD in children is probably <i>not</i> associated with cardiac arrhythmia.	Moderate	68,81
AD in children is probably <i>not</i> associated with congestive heart failure.	Moderate	68
Metabolic disorders		
AD in children is probably associated with obesity	Moderate	68,69,75,143,229,231-241
AD in children may be associated with metabolic syndrome	Moderate	69,241

Continued

Table V. Cont'd

Statement of association	Certainty of evidence	Evidence
AD in children may <i>not</i> be associated with dyslipidemia	Low	68,69,75,229,235
AD in children is probably <i>not</i> associated with diabetes	Moderate	68,69,75,229,236
Bone health		
The association between AD in children and fractures is uncertain	Low	69,81,242,243
AD in children may <i>not</i> be associated with osteoporosis	Low	68
Skin infection		
AD in children is associated with bacterial, viral, and fungal skin infections	Moderate	65,67,69,151,230,244-253

[datasets/zjfknbhdd/1](https://data.mendeley.com/datasets/zjfknbhdd/1)). In the pooled analysis of 4 studies, children with AD, compared to those without, have increased odds of anxiety [aOR: 1.33 (95% CI 1.14, 1.57)],^{68,69,188,189} and a study by Yaghmaie et al found increasing odds of anxiety with increasing AD severity as reported by caregivers [mild AD aOR: 1.44 (95% CI: 1.01-2.05), moderate AD aOR 2.18 (95% CI: 1.47-3.23), severe AD aOR: 2.81 (95% CI: 1.28-6.17)].¹⁸⁹ Alternatively, the pooled analysis of 2 studies suggests no association between AD and a diagnosis of depression [aOR: 1.45 (95% CI: 0.77-2.73)].^{68,189} However, Yaghmaie et al suggested the frequency of depression in children with AD increased with increasing AD severity as reported by caregivers (mild AD: 5.4%, moderate AD: 7.2%, severe AD: 14.1%), and increasing self-reported AD severity may be associated with increased odds of depression.¹⁸⁹

Atopic dermatitis in children is probably not associated with suicide, though the data are limited and mixed. Some studies suggest suicide and suicidal ideation/attempts are not associated with AD,⁸⁹ while the pooled analysis of 2 studies suggests children with AD, compared to those without AD, have higher adjusted odds of suicidal ideation [aOR: 1.15 (95% CI: 1.02-1.30)] (Supplementary Table XXX, available via Mendeley at <https://data.mendeley.com/datasets/zjfknbhdd/1>).^{196,197} As with substance abuse above, age is an important consideration as adolescent patients may be more likely to present with anxiety, depression and suicidal ideation than their younger counterparts.

Metabolic disorders

Obesity. AD in children is probably associated with obesity with the pooled analysis of 9 studies demonstrating children with AD had higher adjusted odds of obesity than did controls without AD [aOR:

1.35 (95% CI: 1.15-1.58)] (Supplementary Table XXI, available via Mendeley at <https://data.mendeley.com/datasets/zjfknbhdd/1>).^{68,69,143,229,231,233,235,237,241} The pooled unadjusted analysis of 5 studies also suggests higher odds of obesity in children with AD.^{75,232,237-239} One study suggests the odds of obesity are higher in children with moderate-to-severe AD compared to children with mild AD [aOR: 2.59 (95% CI: 1.64-4.10)].²³⁷

Dyslipidemia. Atopic dermatitis in children may not be associated with dyslipidemia based on available evidence (Supplementary Table XXXII, available via Mendeley at <https://data.mendeley.com/datasets/zjfknbhdd/1>). A study of 30,354 patients reports the prevalence of hyperlipidemia in children with AD is 0.71%.⁷⁵ Two studies suggest dyslipidemia is not associated with AD in children: 1 study found hypercholesterolemia is not associated with AD, while 2 other studies suggested increased odds of hyperlipidemia in children with AD.^{68,69,75,235}

Diabetes and metabolic syndrome. There are few studies examining the association between AD in children and diabetes. The available data are limited and mixed, suggesting AD in children is probably not associated with diabetes (Supplementary Table XXXIII, available via Mendeley at <https://data.mendeley.com/datasets/zjfknbhdd/1>). Included studies varied in assessment and definition of diabetes and most do not distinguish between type 1 and type 2 diabetes. A retrospective analysis of 86,969 pediatric patients with AD and 116,564 matched controls, demonstrated the odds of metabolic syndrome may be increased in children with AD [aOR: 1.61 (95% CI: 1.28-2.01)] (Supplementary Table XXXIV, available via Mendeley at <https://data.mendeley.com/datasets/zjfknbhdd/1>). An additional body of literature suggests an inverse association between AD and type I diabetes.²⁵⁴⁻²⁵⁷

Cardiovascular disease

AD in children may be associated with hypertension (small magnitude), though the evidence is limited (Supplementary Table XXXV, available via Mendeley at <https://data.mendeley.com/datasets/zjfknbhdd/1>). This association may be multifactorial and influenced by lifestyle factors (eg, obesity, diet, physical activity). In the pooled analysis of 3 studies, children with AD, compared to those without AD, had higher adjusted odds of hypertension (aOR: 1.20 [95% CI: 1.03-1.39]),^{68,69,229} but an unadjusted analysis reported no association.⁷⁵ The association between AD in children and ischemic heart disease is uncertain—an adjusted analysis reported no association between AD and ischemic heart disease,⁶⁸ but an unadjusted analysis reported higher odds of ischemic heart disease in children with AD.⁷⁵ Additionally, our analysis showed no association between AD and peripheral vascular disease, cardiac arrhythmia, and congestive heart failure.

Fractures and osteoporosis

One study found no association between pathologic fracture and AD,⁶⁹ while another suggested AD is associated with a small increase in the risk of any bone fracture [adjusted risk ratio (RR): 1.08 (95% CI: 1.05-1.10) (Supplementary Tables XXXVI and XXXVII, available via Mendeley at <https://data.mendeley.com/datasets/zjfknbhdd/1>).²⁴² Similarly, a pooled estimate from 2 studies suggests a small increase in the subsequent risk of fracture in children with AD compared to those without AD; furthermore, the risk of fracture increased with increasing AD severity [mild AD: aHR 1.12 (95% CI 1.11-1.14) versus moderate-to-severe: aHR: 1.23 (95% CI: 1.20-1.26)].^{81,243} Only 1 study met inclusion criteria regarding osteoporosis, with wide confidence intervals precluding conclusions about an association with AD [aOR: 2.15 (95% CI: 0.78-5.92)].

Skin infections

It is well known that AD predisposes to skin infections (Supplementary Tables XXXVIII-XLI, available via Mendeley at <https://data.mendeley.com/datasets/zjfknbhdd/1>). Ren and Silverberg reported higher odds of skin infections in children with AD compared to those without AD [aOR: 2.23 (95% CI: 2.16-2.31) $P < .0001$] and Narla and Silverberg, using multivariable models to control for age, race, sex and insurance status, reported AD was associated with cutaneous infections.^{244,245} This association between pediatric AD and skin infection includes: (1) bacterial infections (bacterial impetigo,^{65,69,249} bacterial cellulitis,⁶⁹ and *Staphylococcus aureus* skin infection²⁴⁸), (2) viral

infections (molluscum contagiosum infections,^{65,69,249} warts,^{65,69,151,249} coxsackie viral infection,⁶⁹ and herpes simplex infection²⁴⁹), and (3) fungal infections.^{65,69,249}

Gaps in research

While genetic factors may predispose a child to AD, early exposures and environmental factors likely contribute to pathogenesis. More studies on AD prevention will be useful—the ability to reduce the incidence of AD would be very impactful; we know that the disease is difficult to manage for patients and their caregivers and can affect their ability to perform well in school and adapt socially.

Larger studies examining associations, particularly as they relate to the severity of AD and more data about the association of AD with mental disorders, autism, and ADHD could help providers target these patients earlier and make appropriate referrals. Additionally, these guidelines do not make recommendations for screening or management of comorbidities in children with AD. Rather, the evidence for the association between pediatric AD and comorbid conditions, including allergic conditions, alopecia areata (AA), ADHD, cardiovascular disease, and fractures among others, was evaluated with the aim of improving awareness and understanding among dermatologists and other clinicians.

CONCLUSIONS

These guidelines provide evidence-based recommendations for the primary prevention of AD in favor of regular use of moisturizer and to date insufficient evidence or no benefit to environmental or dietary interventions. There are also associations between pediatric AD and other atopic and allergic conditions, immune-mediated conditions such as urticaria, anxiety, ADHD, skin infection, and some metabolic disorders.

Declaration of generative AI and AI-assisted technologies in the writing process

Not used in the preparation of this manuscript.

Conflicts of interest

Drs Alikhan, Bercovitch, Davis, Frazer-Green, and Darr, LCSW, have no relationships to disclose. Cohen serves on the board of directors for Timber and Evomune receiving stock options and/or fees; as a consultant for Asana Biosciences, Ferndale Laboratories, Inc, Novartis, Facilitation of International Dermatology Education, Dermavant Sciences, Leo Pharma, Inc, UCB, and Cosmetic Ingredient Review receiving honoraria and/or stock options. Drucker receives research grants paid to his institution from the National Eczema Association, Eczema Society of Canada, Canadian Dermatology Foundation,

Canadian Institutes for Health Research, US National Institutes of Health, and Physician Services Incorporated Foundation. Eichenfield serves on the board of directors for Forte Biosciences and Verrica Pharmaceuticals, Inc, receiving honoraria and/or stock options; as an investigator for AbbVie, Arcutis, Dermavant, Galderma Laboratories, Pfizer and Bausch, receiving research grants, fees and/or honoraria; as a consultant for AbbVie, Almirall, Arcutis, Asana, Dermavant, Eli Lilly, Galderma, Ichnos/Glenmark, Incyte, Janssen, Leo Pharma, Novartis, Ortho Dermatologics, Otsuka, Pfizer, Regeneron, and Sanofi Genzyme, honoraria; as an independent contractor for Elsevier, Inc receiving royalties. Paller serves as a consultant for Abeona, Arcutis, BioCryst, Boehringer-Ingelheim, Castle Creek, Chiesi, Dermavant, Johnson & Johnson Innovative Medicine, Krystal, LEO, Lilly, L'Oreal, MoonLake Immunotherapeutics, Peltheos, Quoin, Regeneron, and Sanofi receiving honoraria; on a data safety monitoring board for AbbVie, Abeona, Biocryst, Daiichi Sankyo, and Galderma receiving compensation; and as an investigator for AbbVie, Biomendics, Dermavant, Eli Lilly, Incyte, Johnson & Johnson Innovative Medicine, Regeneron, and UCB receiving no compensation. Schwarzenberger is the founder of Pretel, Inc and serves as a data safety monitoring board member for Pfizer, Inc receiving fees. Sidbury serves as an advisory board member for Pfizer, Inc receiving honoraria; as a principal investigator for Regeneron receiving grants and research funding; as an investigator for Brickell Biotech, Inc, and Galderma USA receiving grants and research funding; as a consultant for Galderma Global and Microes receiving fees or no compensation. Silverberg serves as an advisory board member for BioMX, Boehringer-Ingelheim, RAPT Therapeutics, Celgene, Ortho Dermatologics, TARGET Pharma, AFYX Therapeutics, Corrona, Inc, Dermira, Pfizer, Inc, Leo Pharma, Inc, and Menlo Therapeutics receiving honoraria and/or fees; as an investigator for DS Pharma, TARGET Pharma, Kiniksa Pharmaceuticals, Ltd, Menlo Therapeutics, GlaxoSmithKline, AbbVie, Leo Pharma, Inc, and Regeneron receiving research funding, honoraria, or no compensation; as a consultant for AOBiome, Bluefin Biomedicine, Bodewell, BiomX, Inc, Galderma Research & Development, LLC, Arena Pharmaceuticals, Dermavant Sciences, Incyte Corporation, DS Biopharma, Sun Pharmaceutical Industries, Ltd, AnaptysBio, Asana Biosciences, LLC, Pfizer, Inc, Glenmark Generics, Inc, Sanofi, Kiniksa Pharmaceuticals, Ltd, GlaxoSmithKlein, Eli Lilly and Company, AbbVie, Regeneron, and Medimmune receiving honoraria or fees; as a speaker for the Fall Clinical Dermatology Conference, Maui Derm, and Regeneron receiving honoraria or fees. Singh as an advisory board member for Incyte receiving honoraria. Peggy Wu, MD, MPH is an author for UpToDate, Inc receiving honoraria.

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