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SAIGE III: The Role of Environmental Factors in the Development and Severity of Atopic Dermatitis in Young Children

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ABSTRACT

Background: Atopic dermatitis (AD) often manifests in infancy or early childhood, with significant impacts on quality of life and potential persistence into adulthood. Environmental factors are key contributors to pruritus, barrier dysfunction, and inflammation associated with AD.

Methods: A panel of 7 pediatric dermatology experts employed a modified Delphi process, including a face-to-face meeting and online follow-up, to evaluate current evidence and formulate consensus recommendations for managing pediatric AD.

Results: The panel identified environmental factors that affect skin barrier function and contribute to the development and severity of pediatric AD. Consensus recommendations emphasize minimizing environmental exposures and highlight strategies to reduce skin barrier disruption. Early and continuous use of gentle, non-alkaline cleansers and ceramide-containing moisturizers, initiated from birth, may help mitigate AD risk and severity, particularly in high-risk children.

Conclusions: Recognizing and addressing environmental factors is an important component of pediatric AD management. Addressing modifiable environmental factors and initiating early barrier-supportive skincare, including ceramide-containing moisturizers, represents a practical approach to reducing disease severity and flare development. These findings highlight the importance of clinician education to improve awareness of environmental risk factors and effective mitigation strategies.

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INTRODUCTION

Atopic dermatitis (AD) is a chronic inflammatory skin condition that typically begins in infancy, peaks in early childhood, and persists into adulthood.[1,2] Clinical features of pediatric AD include a relapsing course with eczematous lesions, xerosis, intense pruritus, and a genetic predisposition to atopy.[1] AD affects up to 20% of the pediatric population, and prevalence rates are expected to continue increasing, with published prevalence rates likely an underestimation.[1,3] Pediatric AD significantly impacts affected children and caregivers and has been associated with an increased risk of attention deficit hyperactivity disorder (ADHD).[1,4] The early disease onset and significant patient burden highlight the importance of early prevention and management strategies.

AD pathophysiology involves a complex interplay of factors that affect skin barrier function, including *Staphylococcus aureus*, immunological, genetic, and environmental (SAIGE) factors. Variability in the clinical presentation of pediatric AD reflects the complex SAIGE mechanisms underlying the disease.[1] In addition to their role in disease development, environmental exposures may exacerbate AD by interacting with other pathogenic pathways.[1]

The SAIGE factors project seeks to mitigate AD by understanding and addressing (when possible) the SAIGE risk factors. This manuscript focuses on environmental factors that contribute to skin barrier dysfunction and AD development, including (1) climate (UV radiation, latitude, humidity) (2) air pollutants (tobacco smoke exposure, urban living, indoor, outdoor) (3) allergic sensitization (skin dysbiosis, antibiotic use) (4) water (increased hardness) (5) skincare (gentle cleansers and moisturizers).

MATERIALS AND METHODS

The SAIGE I publication[1] reviewed these factors and the role skincare plays in mitigating pediatric AD, and the SAIGE II publication reviewed the role of *S. aureus* in the development of AD. The current manuscript focuses on environmental factors affecting the development of pediatric AD and on the potential role of ceramide-containing skincare in influencing the impact of these factors.

Literature Review

This project used a modified Delphi process comprising face-to-face expert panel discussions and online follow-up. AA and HA conducted a systematic literature review of English-language publications before the panel meeting, using PubMed and Google Scholar as secondary sources. The searches addressed SAIGE factors in pediatric AD, focusing on environmental factors influencing AD development. Searches were limited to the following categories: climate (UV radiation, latitude, humidity), air pollutants (tobacco smoke exposure, urban living, indoor, outdoor), allergic sensitization (skin dysbiosis, antibiotic use), water (increased hardness), and skincare (gentle cleansers and moisturizers).

The searches encompassed clinical studies, algorithms, consensus papers, guidelines, meta-analyses, review papers, and systematic reviews from 2010 to 20th January 2025. The literature search was based on 2 key questions:

1. What is known about AD development in neonates, infants, and children influenced by SAIGE factors, focusing on environmental-driven exacerbation of AD compromising skin barrier function?
2. What is the role of skin care and ceramide-containing skincare from birth in addressing SAIGE factors, focusing on environmental factors attenuating pediatric AD and promoting a healthy skin barrier?

TABLE 1.

Systematic Literature Review Search Terms
Search Terms
Pediatric/childhood AD AND epidermal barrier dysfunction OR UV radiation OR latitude OR humidity OR tobacco smoke exposure OR urban living OR air pollution indoor/outdoor OR water pH OR diet OR in utero stress (maternal anxiety, depression, medication, substance abuse, smoking).
Pediatric/childhood AD AND Prevention OR attenuation OR treatment OR maintenance AND prescription OR adjunctive OR skincare OR moisturizer OR emollient OR ceramide

Search terms are provided in Table 1. Abstracts and then full articles were evaluated for inclusion and categorized by publication type (Figure 1). Each clinical publication that included skincare was graded by consensus of the reviewers, and any discrepancies were resolved through discussion. The reviewers (AA, HA) assigned a level of evidence to each treatment (A, B, C, and 1-4) using the established criteria. Publications in a language other than English, and those not addressing pediatric patients, topical treatments, or environmental factors that exacerbate AD, were excluded.

Role of the Panel

An expert panel of 7 pediatric dermatologists with extensive experience treating pediatric patients convened on February 7, 2025, in Miami, Florida. They reviewed and discussed the literature to identify the role of environmental factors influencing AD development.

During the meeting, advisors divided into 3 groups. The systematic literature search results informed 18 draft statements, and coupled with the panel's opinion and experience, advisors agreed (consensus ≥80% of the panel) on 6 statements supporting healthcare providers who treat pediatric patients with AD. The voting (consensus ≥80% of the panel) results were: statements 1 to 3 and 5: N=7 [100%]; and statements 4 and 6: N=6/7 [88%].

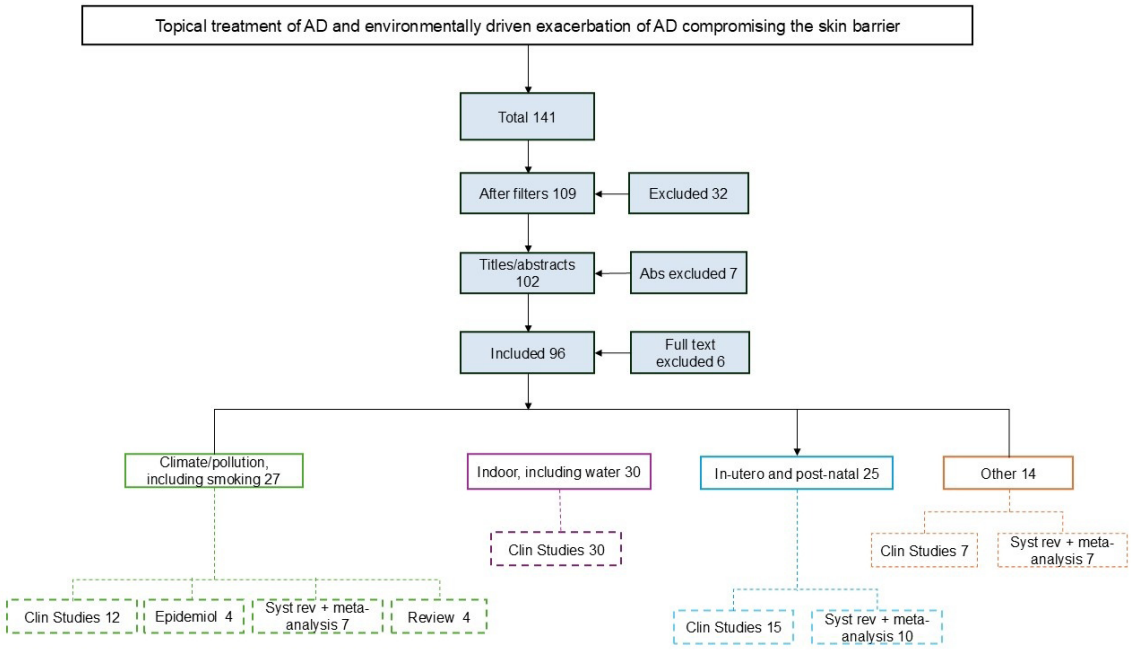
RESULTS

The consensus statements were developed from draft statements fine-tuned in a workshop and serve as the basis for the manuscript on the environmental factors that contribute to pediatric AD and the role of skincare in mitigating them.

Statement 1: *The worldwide prevalence of AD has dramatically increased over the last 50 years and likely reflects a complex interplay between genetic and immunologic predisposing factors and environmental triggers that damage the skin barrier.*

While the increasing prevalence of AD likely stems from a complex interplay between various factors, the increasing incidence in industrialized countries suggests that environmental triggers are key drivers of this trend.[5] Recent studies have found

FIGURE 1. Results of the literature searches on topical treatment of atopic dermatitis and environmental factors exacerbating atopic dermatitis.



Excluded: Publication language other than English, not including pediatric patients, topical treatment, or environmental factors exacerbating AD.

an association between urbanization and pediatric AD, as well as evidence that climate and climate change influence the concentration of air pollutants.[5,6,7] Factors like ultraviolet (UV) exposure also play a role, as regions with a higher UV index report lower rates of pediatric AD.[8,9]

The significant impact of environmental factors is linked to the compromised skin barrier characteristic of AD – including decreased lipid content – such as ceramides. Barrier dysfunction increases permeability to environmental allergens and irritants, and elicits greater epidermal inflammatory responses in patients with AD. Common environmental factors that contribute to AD exacerbation include air pollutants, environmental irritants, seasonal changes, temperature variation, and microbial exposures.[10]

Given the role of skin barrier dysfunction, early interventions aimed at supporting the skin barrier may promote skin health. Applied from birth onward, gentle cleansers and lipid-containing moisturizers may help maintain the skin barrier, thereby mitigating the onset and severity of AD in predisposed infants.[11–13]

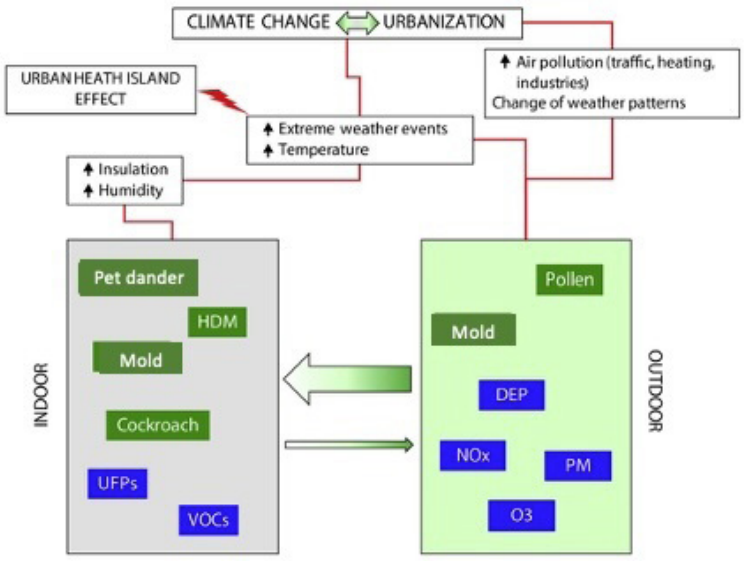
Statement 2: *Potentially modifiable environmental factors that may impact the skin barrier and exacerbate AD flares include the changing climate, urbanization, air pollutants, allergic sensitization, hard water, and poor skincare.*

Environmental variables play a significant role in the development and severity of AD (Figure 2).[5] Macro-environmental exposures associated with urbanization, air pollution, and climate change have been linked to increased risk of AD. Traffic-related air pollution, especially particulate matter <2.5 µm (PM 2.5) and nitrogen dioxide (NO_2), has been associated with increased incidence and frequency of AD.[5] In children, the odds of developing AD rise with proximity to a high-traffic road, supporting the link between urbanization and AD prevalence.[5] In addition, exposure to specific air pollutants, including NO_2, SO_2, and SO_3, has been associated with higher odds of pediatric AD (Table 2).[6]

Climate and climate change further impact AD by affecting the sources, emissions, and concentrations of aeroallergens and air pollutants, and potentially increasing the number of patients with AD.[7] Climate also influences the prevalence of pediatric AD independently of pollution. Lower AD prevalence was found in areas with higher relative humidity, higher UV index, higher mean temperatures, lower precipitation, and less indoor heating.[5]

Beyond these macro-environmental factors, everyday environmental exposures also impact AD risk and severity. While fragrances are highly prevalent in today's world, they have been shown to increase inflammatory responses in individuals with AD.[10] Females have been shown to be more

FIGURE 2. Connection between various environmental factors and atopic dermatitis development.



HDM, house dust mite; NOx, nitrogen oxides: UFPs, ultrafine particles; VOCs, volatile organic compounds; PM, particulate matter; DEPs, diesel exhaust particles; O3, ozone.
Reproduced with permission from Cecchi, Lorenzo, et al. External exposome and allergic respiratory and skin diseases. *J Allergy Clin Immunol.* 2018;141(3):846-857.

TABLE 2.

AD Air Pollution Meta-Analysis a Systematic Reviews	
Subject	**Reference**
Air pollution and global healthcare use for AD: A systematic review.	Fadadu RP et al. *J Eur Acad Dermatol Venereol.* 2023 Oct;37(10):1958-1970.
Child asthma tied to specific urban air pollutants.	Larkin HD. *JAMA.* 2023;329(5):363. doi:10.1001/jama.2022.24493
Maternal tobacco exposure during pregnancy and atopic dermatitis in offspring: A systematic review and meta-analysis.	Chao L et al. *J Eur Acad Dermatol Venereol.* 2024 Oct;38(10):1947-1953.
Smoke exposure and childhood atopic eczema and food allergy: A systematic review and meta-analysis.	Lau HX et al. *Pediatr Allergy Immunol.* 2023 Aug;34(8):e14010.
The prenatal and postnatal effects of air pollution on asthma in children with AD.	Chen H et al. *Pediatr Pulmonol.* 2022 Nov;57(11):2724-2734.
The relationship between outdoor air pollutants and AD of adults: A systematic review and meta-analysis.	Chen H et al. Asian Pacific *J Allergy Immunol.* 40 (2021): 295–307
AD is an environmental disease.	Luschkova D et al. *Allergol Select 5.* (2021): 244–250.
the role of photoprotection in optimizing the treatment of ad.	Piquero-Casals J et al. *Dermatol Ther (Heidelb).* 2021 Apr;11(2):315-325.
Association of atopic dermatitis with smoking: A systematic review and meta-analysis.	Kantor R et al. *J Am Acad Dermatol.* 2016 Dec;75(6):1119-1125.e1.
Is there a rural/urban gradient in the prevalence of eczema? A systematic review.	Schram ME et al. *Br J Dermatol.* 2010;162:964–973.

AD, Atopic dermatitis (AD).

susceptible to AD reactions towards fragrances than males, and younger populations also tend to have higher rates of fragrance-triggered AD compared with older populations.[10] Similarly, harsh detergents, increasingly present in everyday products, can be irritating to individuals with AD. Repeated exposure may further irritate the skin barrier and promote microbial imbalance, increasing vulnerability to allergic sensitization.

Water quality represents another modifiable factor. Higher AD prevalence has been reported in areas with hard water, particularly among infants and school-aged children. In these settings, minimizing exposure to hard water (eg, via shower/faucet filters) may be beneficial.[14] In addition, poor skincare can exacerbate barrier dysfunction and contribute to ongoing inflammation and sensitization. Individuals with AD benefit from appropriate skincare that supports barrier repair and improves AD symptoms.[2]

TABLE 3.

Indoor Pollution Clinical Studies	
Subject	**Reference**
Effects of residential environment and lifestyle on atopic eczema among preschool children in Shenzhen, China.	Liu Y et al. *Front Public Health* 10 (2022).
Household environmental microbiota influences early-life eczema development.	Ta LDH et al. *Environ Microbiol* 23 (2021): 7710–7722.
Sources of indoor particulate matter (PM) and outdoor air pollution in China in relation to asthma, wheeze, rhinitis and eczema among pre-school children: Synergistic effects between antibiotics use and PM10 and second-hand smoke.	Norbäck D, et al. *Environ Internat* 125 (2019): 252–260.
Microbiota and organophosphates.	Roman P et al. N*euroToxicol* 75 (2019): 200–208
Effects of household environmental exposure and ventilation in association with adverse birth outcomes: A prospective cohort study in rural China.	Pan D et al. *Sci Total Environ* 822 (2018): 153519.
Impact of home humidifier on children & eczema.	Wang L et al. *Chinese Sci Bulletin* 61 (2016): 1721–1727.
Household environment, lifestyle behaviors, and dietary habits in relation to childhood atopic eczema in Shanghai, China.	Cai J et al. *Int Arch Occup Environ Health* 90 (2016): 141–159.
Indoor Air Pollution Aggravates Symptoms of Atopic Dermatitis in Children.	Kim AH et al. *Plos One* 10 (2015): e0119501.
Effects of home environment and lifestyles on prevalence of atopic eczema among children in Wuhan area of China.	*Zhang M et al.* Chinese Science Bulletin 58 (2013): 4217–4222.
Symptoms of atopic dermatitis are influenced by outdoor air pollution.	Kim J et al. *J Allergy Clin Immunol* 132 (2013): 495–498.
Exposure to gene-environment interactions before 1 year of age may favor the development of atopic dermatitis.	Lee J-Y et al. Int Arch Allergy Immunol. 2012;157:363–371.
Surveillance of home environment in children with atopic dermatitis: a questionnaire survey.	Lee JH et al. *Asia Pac Allergy.* 2012;2:59–66.
Association between indoor renovation activities and eczema in early childhood.	Herbarth O et al. *Int J Hygiene Environ Health* 209 (2006): *241–247.*
Association between ventilation rates in 390 Swedish homes and allergic symptoms in children.	Bornehag CG et al. *Indoor Air.* 2005;15:275–280.

Overall, monitoring pollutant levels, avoiding known irritants when possible, and adopting gentle skincare practices are practical strategies to mitigate environmental factors that influence the risk and severity of AD.[5]

Statement 3: *Some composite wood materials, flexible plastics, and new paint have all been associated with increased skin barrier damage and vulnerability to AD, representing a new class of underrecognized indoor risk factors for AD.*

Indoor exposure to housing materials commonly used during home renovation is an underrecognized but potentially modifiable risk factor for AD (Table 3). Composite wood products, flexible plastics, adhesives, and freshly applied paint are major sources of volatile organic compounds (VOCs), which can aggravate AD.[15] Indoor VOCs are especially high in newly built houses due to multiple new materials emitting VOC particles.[15]

In a study of over 20,000 mother and newborn pairs, renovation/painting in the house during pregnancy was significantly associated with early infantile AD.[15] Similarly, a study involving over 2,500 children identified a correlation between indoor renovation activities (painting, furniture installation, floor covering), and the development of AD from the antenatal period through infancy and early childhood.[16]

These exposures are particularly relevant during the "nesting process" when families undertake renovations to prepare for a newborn. Advisors speculated that exposure to these risk factors, especially when amplified by limited ventilation (ie, closed doors and windows), can increase the risk of AD in vulnerable individuals. This interpretation is supported by the literature, as moving into a newly built house before 1 year of age has been independently associated with a risk for AD, and indoor renovations within the previous five years have been associated with a higher severity of AD.[17,18]

To mitigate these risk factors, individuals should prioritize proper ventilation and reducing exposure. When possible, low-VOC or VOC-free materials (eg, silica-based wallpaper and plant-based flooring material) should be used in living and sleeping areas.[15] Regular ventilation, via exhaust fans or air filtration systems, may further reduce exposure. For infants and children with AD or increased susceptibility of AD, limiting time spent in freshly renovated rooms and maintaining optimal skin barrier care during periods of increased exposure may help mitigate AD symptoms.

Statement 4: *Evidence supports starting skincare early in life, as ongoing daily use of non-alkaline cleansers and moisturizers can promote a healthy skin barrier and reduce AD flares.*

International guidelines recommend daily moisturization as an integral part of AD management to treat skin barrier dysfunction and hydrate the skin.[2,19,20] Daily moisturizer use from birth to enhance skin barrier function may significantly delay the onset of AD in high-risk infants, and may delay or prevent AD flares when used continuously.[11–13]

Although a systematic review and meta-analysis by Zhong et al found no significant reduction in AD development in infants given prophylactic emollients during the first 6 weeks of infancy (RR 0.84, 95% CI, 0.64, 1.10) compared with the control group, prophylactic moisturizers improved skin condition (RR 0.75, 95% CI 0.62–1.11) in infants at high-risk for AD development (n=8 studies). Overall, the prophylactic application of emollients initiated in early infancy may delay AD, especially in high-risk populations and when used continuously.[11]

Nevertheless, conclusive evidence for the prophylactic use of moisturizers to prevent AD is lacking, and results across prevention trials vary.[21] For example, a large-scale RCT found no evidence that daily emollient use during the first year of life prevents AD in high-risk children.[21] While further research is needed, early and consistent skincare is a low-risk strategy that may benefit barrier function.

Skincare can be introduced within the first weeks of life, using non-alkaline cleansers and applying moisturizer immediately after bathing.[2] Healthcare providers can maximize compliance and outcomes by educating patients on the benefits of liberally applying the moisturizer twice daily to support the skin barrier and to help reduce the incidence of flares.[20]

Statement 5: *Cleansers used in children with AD should be free of potential irritants such as fragrance, alcohol, essential oils, botanicals, and harsh detergents.*

US guidelines recommend limited use of nonsoap cleansers that are neutral to low pH, hypoallergenic, and fragrance-free.[2] While normal skin pH ranges from 4 to 5.5, most soaps are alkaline, leading to skin damage, irritation, and dry skin. Therefore, nonsoap-based surfactants and synthetic detergents (syndets) that are gentle, non-alkaline, and free of potential irritants (eg, fragrance, alcohol, essential oils, botanicals, and harsh detergents) are recommended for better tolerance in children with AD.[2]

Statement 6: *Moisturizers containing skin lipids such as ceramides may offer additional benefits to children with AD by helping to maintain the skin barrier and reducing AD flare-ups.*

Moisturizers are a cornerstone of AD therapy. They increase skin hydration and can lessen AD symptoms, including pruritus, erythema, fissuring, and lichenification.[2] Moisturizers can reduce AD inflammation and severity, as well as lower the amount of prescription anti-inflammatory treatments required for disease control.[2]

However, not all moisturizers are equally effective; both the active ingredients and the vehicle influence clinical outcomes. While head-to-head studies are limited, the ongoing, daily use of moisturizers containing lipids, such as ceramides, has been shown to reduce the rate of AD flares and the need for topical steroid treatment.[22,23]

In a randomized controlled trial (RCT) of infants (n=100) at high risk for AD development based on family history, the intervention group received once-daily full-body application of an emollient containing ceramides and amino acids, while the control arm used an emollient of their choice for dry skin, applied irregularly.[23] In the intervention and control groups, AD was diagnosed in 13.2% vs 25.0% at month 12 (P=0.204) and 19.4% vs 31.0% at year 2 (P=0.296), respectively. Although the observed trend was in favor of the intervention, results were not statistically significant, likely due to lack of power from under-enrolment. Nevertheless, the observed trends suggest a protective effect of the ceramide-containing study emollient therapy compared to control.[23]

US guidelines recommend including moisturizers in AD management plans.[2] For children with AD, recommended moisturizers should be gentle, non-alkaline, free of additives, fragrances, perfumes, and other potentially sensitizing agents, and formulated with barrier-supporting lipids such as ceramides, to support the skin barrier.[2,12]

DISCUSSION

Environmental factors play a key role in the development and severity of AD in children. Potentially and partly modifiable environmental factors that can damage the skin barrier and exacerbate AD flares include climate, air pollutants, allergic sensitization, hard water, and poor skincare. Indoor environmental exposures to composite wood materials, flexible plastics, and new paint have also been associated with increased skin barrier damage and vulnerability to AD. Many of these exposures are potentially modifiable, presenting opportunities for risk mitigation, particularly early in life when the skin barrier is still developing.

Evidence supports early initiation of skincare, with some studies reporting benefits of consistent daily use of non-alkaline cleansers and moisturizers to promote a healthy skin barrier. Applied from birth onwards, gentle cleansers and moisturizers

containing barrier lipids may help maintain the protective skin barrier, possibly delaying AD occurrence and severity in predisposed infants.

Limitations

AD is a complex disease influenced by genetic, microbial, and environmental factors. This manuscript focuses on environmental contributors to AD and is not intended to provide a comprehensive review of all pathogenic mechanisms. The literature review was limited to studies published between 2010 and 20th January 2025 and therefore does not capture research published beyond this period. The systematic search was also restricted to English-language publications; relevant evidence published in other languages was not included.

CONCLUSION

The current understanding of AD has broadened to include the complex interplay between SAIGE factors. While the environment has long been recognized as a contributor to AD, it now represents a heightened risk due to increasing urbanization and climate change. Clinicians have an opportunity to mitigate the impact of these environmental factors in vulnerable neonates and young children by using appropriate cleansers and moisturizers. While more evidence is needed, early and consistent use of non-irritating, barrier-supportive skincare may help promote a healthy skin barrier and reduce AD flares in high-risk children.

DISCLOSURES

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