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A systematic review of guidelines for the management of atopic dermatitis in children

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ABSTRACT

Atopic dermatitis (AD) is a chronic disease that is increasing in prevalence, particularly in children and people with skin of colour. Current management involves topical treatments, phototherapy and immunosuppressants, as well as newer therapies like dupilumab. Health professionals should also be aware of the specific management considerations for AD in people with skin of colour. This systematic review was conducted to examine global guidelines for the management of AD in children, compare management recommendations, examine specific recommendations for children with skin of colour, and assess the quality of the guidelines.

The databases Medline, Embase, CINAHL, Scopus, Guidelines International Network, and Emcare Nursing and Allied Health were searched to identify guidelines or articles relating to the management of AD in children from 1990 to 2023. A grey literature search was also undertaken. The recommendations from the guidelines were extracted and compared, and the quality of the guidelines was assessed using the Appraisal Guidelines for Research and Evaluation (AGREE) II tool.

A total of 1644 articles were identified from the initial search. Title and abstract screening, full text screening, and reference checking yielded 28 guidelines for the final appraisal and data extraction. The main variations in management recommendations were the timing of emollients, bleach baths, bath additives, oral antihistamines, and the age cut-offs for topical calcineurin inhibitors. Many guidelines were not updated to reflect newer therapies like dupilumab and topical phosphodiesterase-4 (PDE4) inhibitors. There were minimal recommendations regarding management of skin of colour. Only 12/28 guidelines met the satisfactory cut-off score for the AGREE II appraisal, largely due to a lack of well-documented methodology.

This review showed that the recommendations for AD management in skin of colour were consistently lacking. Despite generally consistent management strategies over the last 5 years, less than half of the guidelines met high-quality criteria, emphasising the importance of using tools like AGREE II in future guideline development.

Keywords: Atopic dermatitis, Eczema, Guidelines

http://doi.org/10.1016/j.waojou.2024.100989

INTRODUCTION

Atopic dermatitis (AD) is a chronic, inflammatory disease of the skin that commonly presents during childhood. There has been an overall increase in prevalence of this condition, and it is estimated to affect 20% of children and 10% of adults worldwide. 1-3 AD arises from a combination of genetic factors, skin barrier defects, and dysregulated immune response.4 It is commonly the first step in the "atopic march", with higher risks of developing other atopic diseases like food allergies, allergic rhinitis, and asthma. Although not life threatening, AD poses significant health risks includina secondary bacterial or viral infections and potentially more severe food allergic reactions, and it greatly impacts quality of life through decreased sleep, productivity, behavioural issues, low selfesteem, anxiety, depression, and stress caregivers.5

The mainstay of management for AD has not changed significantly over the last 20 years, with key aspects involving emollient use, bathing, topical steroids, topical calcineurin inhibitors, wet dressings, phototherapy, and immunosuppressants. In the last 5 years, however, biologics such as dupilumab have changed the landscape of AD management, decreasing the need for systemic immunosuppressants and with a minimal sideeffect profile. These management options are reflected in the different guidelines, as well as other aspects of management like environmental modification, psychological support, and educational interventions. Managing AD in children with skin of colour has become increasingly important with AD becoming more common in these patients. Skin of colour refers to the increased melanin and darker pigmentation found in many different ethnic groups such as Asian, African, Middle Eastern, Latin, and First Nations Peoples. 7-9

As guidelines underpin evidence-based medicinal practice, it is important to ensure that these documents correspond with the best management recommendations and abide by a transparent, robust development processes. ¹⁰ A commonly used tool to appraise guideline quality is the Appraisal Guidelines for Research and Evaluation (AGREE II) standardised guideline appraisal tool. This tool has been shown to successfully identify high quality guidelines using a twenty-three-item questionnaire

that reviewers use to rate aspects of the guidelines on a scale of 1-7 (7 being the highest).¹¹

This systematic review examined the existing guidelines regarding the management of AD in the paediatric population globally. The term guideline refers to all documents that contain recommendations for clinical practice or health policy as outlined by the World Health Organization (WHO), and includes evidence-based guidelines, expert recommendations, protocols, and consensus statements.¹²

The 3 main goals of the analysis were: 1) to compare management strategies in the guidelines for AD in children, 2) to determine whether specific reference is made to managing AD in children with skin of colour, and 3) to assess the quality of the guidelines using the AGREE II standardised guideline appraisal tool. ¹³

METHODS

Search strategy

Systematic search methods were used to identify relevant guidelines. The initial search was performed on the databases Medline, Embase, CINAHL. Scopus. Guidelines International Network, and Emcare Nursing and Allied Health. Guideline documents addressing the management of AD in children (birth to 18 years) were included. The search was limited to articles published from 1990 to 2023, referenced children (from birth-18 years of age), and were in English. The following search terms were used: (child OR infant OR toddler OR paediatric OR minor OR baby OR teenager OR adolescent OR "young person" OR "young people") AND (eczema OR "atopic dermatitis" OR "atopic eczema") AND (quideline OR strategy OR policy OR statement OR protocol OR recommendation OR consensus OR "clinical practice") AND ("health professionals" OR "general practitioner" OR nurse OR paediatrician OR doctor OR "medical practitioner"). A grey literature search was also undertaken. This yielded a total of 1644 articles for title and abstract screening once duplicates were removed.

Article screening

Two independent reviewers screened the articles. The first stage involved title and abstract

screening, resulting in 189 included articles. After full text screening, 114 were selected with reasons for exclusion listed in Fig. 1. The second stage involved extracting details about any guideline documents mentioned in the full texts (either from the text itself or the reference list). This resulted in 176 potential guideline documents. After another full text screen, the reviewers decided to exclude any guidelines that were not specifically about AD (for example those that were about food allergies), and those

relating to only 1 aspect of management. To reflect nation-wide practices, guidelines owned by individuals were excluded. A total of 58 guidelines remained, however only 28 were included in the final appraisal and data extraction. Twenty outdated versions of guidelines were excluded, as updated versions were available, and 4 articles were excluded as they were not considered guidelines. Guidelines that had been published in several sections were combined for appraisal.

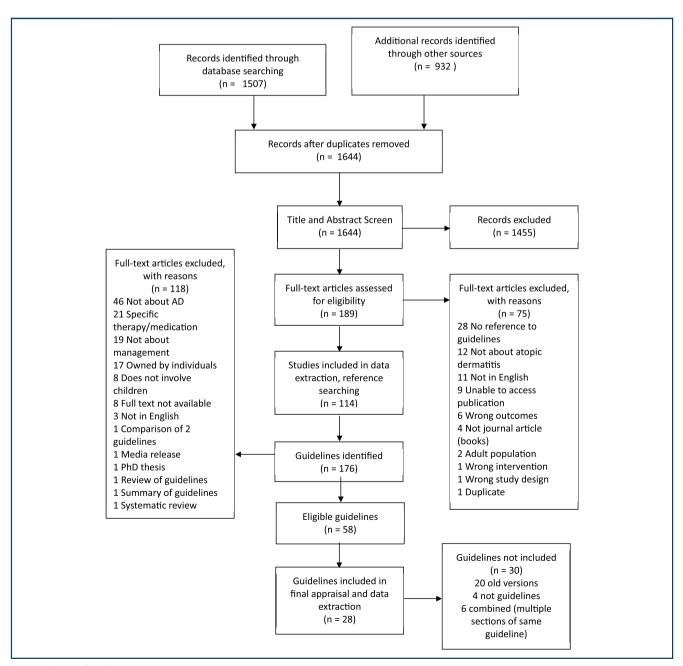


Fig. 1 PRISMA flowchart.

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Guideline comparison

Descriptive data including the title, organisation, year of development, region developed, and type of document was extracted. The recommendations from each guideline regarding specific aspects of management and whether the guidelines made a specific reference to managing skin of colour were summarized.

Quality appraisal

The guidelines identified were appraised using the AGREE II tool. 13 The tool outlines 23 criteria under 6 domains that can be used to assess guideline quality, which include: scope/purpose (objectives, question, population); stakeholder involvement (group membership, target population, target users); rigor of development (search methods, evidence criteria, evidence strengths and limitations, recommendations, benefits considerations. harms recommendations and evidence link, external review, updating procedures); presentation clarity (specific, unambiguous recommendations, management options, identifiable recommendations); applicability (application facilitators and barriers, implementation of advice/tools, resource implications, monitor/ audit criteria); and editorial independence (funding body, competing interests).

Guidelines were given a score from 1 to 7 by each reviewer (7 being the best) for the 23 criteria. A score of 1 was given either when the criteria was not met, or that section was missing from the guideline, ie, no funding statement provided. After scoring independently, the reviewers discussed any large differences (>4 points) to resolve major discrepancies or errors during scoring. Domain scores were then calculated using the formula:

high-quality evidence base and the process underpinning recommendations is clear. Therefore, the domain cut-off scores for a high-quality guideline were set to include at least 50% in the "Rigor of Development" domain and at least 2 other domains, which is consistent with previously published use of the AGREE II tool. 14

RESULTS

Overview of guidelines

Twenty-eight guideline documents were located 2005-2021.¹⁵⁻⁴⁸ Of these. guidelines, 15-19,22,23,25,26,28,29,31,32,35-39,41,44,47,48 7 were consensus documents, 20,21,24,34,40,42,43,46 2 were position papers, 27,45 1 was a clinical report, and 1 was an expert statement. 33 Five documents were for children only, and the remaining 23 were for adults and children. In terms of geographical location, 11 developed in Asia, 8 in Europe, 4 in North America, 2 in South America, 2 in Africa, and 1 joint in Europe and the United States. A list of these guidelines can be seen in Table 1. Recommendations from the guidelines published from 2018 to 2023 are summarized below and in Tables 2 and 3.

General skin care measures

All 12 guidelines from 2018 to 2023 recommended liberal emollient use after bathing. 17,19,37-48 The type of emollient depends on patient preference; however 1 guideline recommended traditional emollients like coconut oil, 37 whereas 2 others found this increased xerosis. 38,39,42,43 Bathing was discussed in all guidelines, with some specifying lukewarm water for 5-10 min. 38-40,42-47 There were differing recommendations for bath additives, with 6/12 guidelines recommending bleach baths, 17,19,38-40,46,47 and 4/12

 $\frac{obtained\ domain\ score\ -\ minimum\ possible\ domain\ score}{maximum\ possible\ domain\ score\ -\ minimum\ possible\ domain\ score}\times 100\%$

A higher AGREE II score is likely to be achieved by having a well-documented, robust development process as this ensures guidelines have a recommending bath oils.³⁸⁻⁴¹ Furthermore, 10/12 guidelines recommended cleansing with soap free, neutral pH, hypoallergenic cleansers.³⁷⁻⁴⁸

Guideline	Organisation	Name of document	Type of document	Region	Year	Target
1	Allergy Society of South Africa	Childhood Atopic Eczema Consensus Document ²⁰	Consensus document	South Africa	2005	Children
2	European Academy of Allergology and Clinical Immunology/American Academy of Allergy, Asthma and Immunology/PRACTALL	Diagnosis and treatment of atopic dermatitis in children and adults: European Academy of Allergology and Clinical Immunology/American Academy of Allergy, Asthma and Immunology/PRACTALL Consensus Report ²¹	Consensus document	Europe/ United States	2006	Children and adults
3	Dermatological, Paediatric (SAPA) and Allergy (ALLSA) Societies of South Africa	Guidelines on the management of atopic dermatitis in South Africa ¹⁵	Guideline	South Africa	2008	Children and adults
4	Primary Care Dermatology Society/ Scottish Intercollegiate Guidelines network	Management of Atopic Eczema in Primary Care: A national clinical guideline ¹⁸	Guideline	Scotland	2011	Children and adults
5	American Academy of Allergy, Asthma and Immunology, American College of Allergy, Asthma & Immunology (ACAAI); and the Joint Council of Allergy, Asthma and Immunology	Atopic dermatitis: a practice parameter update 2012 ²⁴	Consensus document	United States	2012	Children and adults
6	Hong Kong College of Paediatricians	Clinical guidelines on management of atopic dermatitis in children ²²	Guideline	Hong Kong	2012	Children

(continued)

Guideline	Organisation	Name of document	Type of document	Region	Year	Target
8	Asia-Pacific Consensus Group for Atopic Dermatitis	Consensus guidelines for the management of atopic dermatitis - an Asia-Pacific perspective ²³	Guideline	Asia- Pacific	2013	Children and adults
7	National Institute for Health and Care Excellence (NICE)	Atopic eczema in under 12s ¹⁶	Guideline	UK	2013	Children
9	American Academy of Paediatrics	Clinical report on atopic dermatitis - skin-directed management ³⁰	Clinical report	United States	2014	Children
10	American Academy of Dermatology	Guidelines of care for the management of atopic dermatitis: Section 1. Diagnosis and Assessment of Atopic Dermatitis ²⁶ Guidelines of care for the management of atopic dermatitis: Section 2: Management and Treatment of Atopic Dermatitis with Topical Therapies ²⁵ Guidelines of care for the management of atopic dermatitis: section 3. Management and treatment with phototherapy and systemic agents ²⁸ Guidelines of care for the management of atopic dermatitis: Section 4. Prevention of disease flares and use of adjunctive therapies and approaches ²⁹	Guideline	United States	2014	Children and adults

11	Latin American Society of Allergy, Asthma and Immunology	Atopic dermatitis guideline. Position paper from the Latin American Society of Allergy, Asthma and Immunology ²⁷	Position paper	Latin America	2014	Children and adults
12	Polish society of allergology, and the allergology section, Polish society of dermatology	Atopic dermatitis: current treatment guidelines. Statement of the experts of the dermatological section, Polish society of allergology, and the allergology section, Polish society of dermatology ³³	Expert statement	Poland	2015	Children and adults
13	Korean Atopic Dermatitis Association	Consensus guidelines for the treatment of atopic dermatitis in Korea (Part I): general management and topical treatment ³² Consensus guidelines for the treatment of atopic dermatitis in Korea (Part II): Systemic Treatment ³¹	Guideline	Korea	2015	Children and adults
14	Italian Society of Paediatric Allergology and Immunology (SIAIP) and the Italian Society of Paediatric Dermatology (SIDerP)	Consensus Conference on Clinical Management of paediatric Atopic Dermatitis ³⁴	Consensus document	Italy	2016	Children
15	German Dermatological Society	S2k guideline on diagnosis and treatment of atopic dermatitis— Short version ³⁶	Guideline	Germany	2016	Children and adults
16	Dermatological Society of Singapore	Guidelines for the management of atopic dermatitis in Singapore ³⁵	Guideline	Singapore	2016	Children and adults

Guideline	Organisation	Name of document	Type of document	Region	Year	Target
17	Asian Academy of Dermatology and Venereology Expert Panel on Atopic Dermatitis	A clinician's reference guide for the management of atopic dermatitis in Asians ³⁷	Guideline	Asia	2018	Children and adults
18	European Dermatology Forum (EDF), European Academy of Dermatology and Venereology (EADV), European Academy of Allergy and Clinical Immunology (EAACI), European Task Force on Atopic Dermatitis (ETFAD), European Federation of Allergy and Airways Diseases Patients' Associations (EFA), European Society for Dermatology and Psychiatry (ESDaP), European Society of Pediatric Dermatology (ESPD), Global Allergy and Asthma European Network (GA2LEN), and European Union of Medical Specialists (UEMS)	Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis) in adults and children: part I ³⁹ Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis) in adults and children: part II ³⁸	Guideline	Europe	2018	Children and adults
19	Ministry of Health Malaysia	Management of Atopic Eczema ¹⁷	Guideline	Malaysia	2018	Children and adults
20	Turkish Society of Dermatology	Turkish Guideline for Atopic Dermatitis 2018 ¹⁹	Guideline	Turkey	2018	Children and adults
21	European Task Force on Atopic Dermatitis/ European Academy of Dermatology and Venereology	Position paper of the diagnosis and treatment of atopic dermatitis in adults and children ⁴⁵	Position paper	Europe	2018	Children and adults

23	Brazilian Society of Dermatology	Consensus on the therapeutic management of atopic dermatitis - Brazilian Society of Dermatology ⁴⁰	Consensus document	Brazil	2019	Children and adults
22	Canadian Dermatology Association	Approach to the Assessment and Management of Pediatric Patients With Atopic Dermatitis: A Consensus Document. Section 3 ⁴² Approach to the Assessment and Management of Pediatric Patients With Atopic Dermatitis: A Consensus Document. Section 4 ⁴³	Consensus document	Canada	2019	Children
24	Indian Dermatology Expert Board Members	Guidelines on Management of Atopic Dermatitis in India: An Evidence -based Review and an Expert Consensus	Guideline	India	2019	Children and adults
25	Italian Society of Medical, Surgical and Aesthetic Dermatology and Venereology (SIDEMAST), Italian Society of Dermatologists and Venereologists Hospital- based and Public Health (ADOI), and Italian Society of Allergological Occupational and Environmental Dermatology (SIDAPA)	Italian guidelines for therapy of atopic dermatitis—Adapted from consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis) ⁴¹	Guideline	Italy	2019	Children and adults

(continued)

Guideline	Organisation	Name of document	Type of document	Region	Year	Target
26	Taiwanese dermatological association	Taiwanese Dermatological Association consensus for the management of atopic dermatitis: A 2020 update ⁴⁶	Consensus document	Taiwan	2020	Children and adults
27	Chinese Society of Dermatology Immunology	Guidelines for the diagnosis and treatment of atopic dermatitis in China ⁴⁷	Guideline	China	2020	Children and adults
28	Japanese Dermatological Association	English Version of Clinical practice guidelines for the Management of Atopic Dermatitis 2021 ⁴⁸	Guideline	Japan	2021	Children and adults

Table 1. (Continued) Overview of guideline documents

Topical therapy

Topical steroids were indicated in acute flares. with the minimum dose possible in all guidelines. 17,19,37-48 With regards to dosage, 4/12 recommended the unit, 17,37,42-44 3/12 used grams, 19,40,45 and 5/12 used the site and size of the lesions. 38,39,41,46-48 One guideline recommended using topical therapies prior to emollients 42,43 while another recommended 15 minutes after emollients.45 Twice weekly proactive use for remission was recommended in 9/12 guidelines, 19,38-41,44-48 2 of which specified a duration of 20 weeks. 38,39,41 Topical calcineurin inhibitors were indicated in all guidelines for second line use in acute flares, or first line for sensitive areas like the face, anogenital region, and skin folds; however only 3/12 recommended the use in under 2 years of age. 38,39,44,45 Proactive use was also supported in 10/12 guidelines. 17,19,38,39,41-48 Wet wrap therapy (wet dressings) was recommended in 10/ 12 guidelines, mostly for short-term use in severe refractory cases. 17,19,37-40,42-45,47,48 Topical Phosphodiesterase-4 (PDE4) inhibitors were recommended in 4/12 guidelines for children 2 years and over. 38,39,42-44,47 The Turkish guidelines also recommended topical coal tar preparations in children. 19

Systemic therapy

All quidelines supported the use of narrow band Ultraviolet B (UVB) for chronic AD. 17,19,37-48 UVA1 was recommended for acute flares in 10/12 auidelines. 17,19,37-41,44,45,47,48 One quideline discussed the use of psoralen plus ultraviolet-A radiation (PUVA) for lichenification in stable disease.³⁷ quidelines, oral prednisone recommended in acute flares for short term use. Cyclosporine was the first-line long term therapy, followed by methotrexate or azathioprine. 17,19,37-48 Furthermore, 8/12 guidelines also recommended mycophenolate mofetil as a third-line option for off label use in children. 17,19,37-39,41-43,45,46 If using systemic therapies in children under 2 years, specialist input was advised guidelines.40,45 Systemic immunosuppressants were not approved for paediatric patients in the guidelines.48 Dupilumab recommended for use in children 12 years and older in 4/12 guidelines. 38,39,42,43,45,46 While 1/12

guidelines did not specify a minimum age for use. The remaining 6/12 guidelines only supported dupilumab use in adults. Tr, 19, 37, 40, 41, 44, 46 Other biologics recommended for trial in severe cases include mepolizumab 38,39 and baricitinib.

Managing infections

For staphylococcus aureus bacterial infections, all guidelines recommended a short course of systemic or topical antibiotics depending on the lesions. Systemic antivirals were advised for eczema herpeticum. For head and neck AD with known Malassezia colonisation, topical or systemic antifungals can be used. 17,19,37-48 Short term topical antiseptics were recommended for bacterial infections in 5/12 guidelines, 19,38-41,45 of which also recommended long term use in chronic treatment resistant AD. 38,39

Pruritis control

There was differing recommendations regarding antihistamine use for pruritis control. While 11/12 guidelines supported the short-term use of sedating antihistamines, 17,19,37-41,44-48 3/ 12 guidelines advised non-sedating antihistamines could be used in a subset of patients with allergic rhinitis, urticaria, bronchial asthma or dermographism.45-47 Other therapies included melatonin in the Taiwanese quideline⁴⁶ and mirtazapine, pregabalin, paroxetine or naltrexone in the Chinese guidelines.47

Dietary measures

The Chinese guideline recommended trialling diagnostic elimination diets for 4-6 weeks.⁴⁷ Others did not support the use of elimination diets or supplements like probiotics or vitamin D unless there were clinically proven allergies.

Allergy testing

One guideline advised routine allergy testing for cow's milk, egg, wheat, soy, and peanut allergies in children under 3 with moderate-severe AD. This guideline also recommended routinely avoiding contact allergens like nickel, preservatives, and rubber. No other guidelines recommended allergy testing unless there was high clinical suspicion. Allergen specific immunotherapy was recommended in 3/12

guidelines for severe AD cases with allergies to dust mite, birch, or grass pollen and a history of exacerbation with exposure. Patch testing was recommended for atypical skin lesions or triggers in 2/12 guidelines.

Other management strategies

All guidelines recommended patient and family education, with strategies like nurse-led education programs, videos, multidisciplinary school programs, workshops, community support groups and written action plans. 17,19,37-48 Complementary therapy including acupuncture, homeopathy, aromatherapy were not recommended over traditional therapy; however, 2/12 guidelines supported trialling thermal spring water 38,39,41 and 1/12 trialling unsaturated fatty acid supplements. 41 Chinese herbal medicine was recommended in combination with traditional measures in 2/12 guidelines. 47,48

Environmental measures like avoiding irritants such as wool, dust mites, and occupational triggers were discussed in 3/12 guidelines. 40,45,46 In addition, 3/12 guidelines emphasised the importance of routine vaccinations. 17,38,39,41 Psychological support, behavioural therapies, and relaxation techniques were recommended when clinically relevant in 5/12 guidelines. 38,39,41,44-46

Recommendations for skin of colour

Six auidelines commented on skin of colour to varying degrees. The Asian Academy of Dermatology and Venerology guidelines discussed the phenotypical differences between Asian and Caucasian skin in AD.³⁷ The Asia-Pacific Consensus Group for Atopic Dermatitis included studies based on the Asia-Pacific population in the evidence base, ensuring more targeted recommendations.²³ The NICE guidelines mentioned the different ways AD can present in Asian, Black Caribbean, and Black African children, as well as the difficulty of assessing severity in darker skin tones; however, they do not suggest any other severity scoring systems. They also mentioned cultural sensitivity when discussing skin care practices. 16 The Latin American guidelines described environmental factors contributing to AD in the region like helminth infections and the tropical climate; however, they do not refer specifically to skin of colour. ²⁷ The Chinese guidelines mentioned a diagnostic criteria that was specifically made for paediatric Asian skin which can help with severity assessment and management. The Taiwanese guideline specified that patients and caregivers should be educated surrounding the risk of hyper or hypopigmentation for AD on pigmented skin. These recommendations have been summarized in Box 1.

AGREE II

Domain scores for each guideline are shown in Table 4. Only 12/28 met the satisfactory cut-off criteria for a high-quality guideline. ^{16-18,24-29,31,32,36,38,39,41-43,48} On average, the guidelines scored higher in Domain 1 (scope and purpose) and Domain 4 (clarity of presentation), with average scores of over 70%. Domain 5

Box 1. Summary of recommendations for skin of colour extracted from guidelines

- There are phenotypical differences between Asian and Caucasian skin in AD, such as a unique cytokine profiles (Asian Academy of Dermatology and Venerology)³⁷
- AD can present differently in Asian, Black Caribbean and Black African children (Asian Academy of Dermatology and Venerology and NICE)^{16,37}
- 3. There can be difficulty assessing the severity of atopic dermatitis in darker skin tones (NICE)¹⁶
- 4. Cultural sensitivity is important when discussing skin care practices (NICE)¹⁶
- Specific diagnostic criteria can be used for paediatric Asian skin, which can help with severity assessment and management (Chinese Society of Dermatology Immunology)^{47,49}
- Patients and caregivers should be educated surrounding the risk of hyper or hypopigmentation for atopic dermatitis on pigmented skin (Taiwanese Dermatological Association)⁴⁶

Author, Title, Year	Emollients	Bathing and cleansing	TCS	Topical calcineurin inhibitors	Wet wraps	Phototherapy	Immunosuppressants
Asian Academy of Dermatology and Venereology Expert Panel on Atopic Dermatitis, A clinician's reference guide for the management of atopic dermatitis in Asians ³⁷ 2018	Moisturisers directly after bathing on damp skin, 2-3 times daily Support the use of traditional emollients like coconut oil, olive oil	Limited use of hypoallergenic, fragrance free, physiological pH soap free cleansers	Indicated in flares, FTU recommended. Start with mild potency twice/day after bathing	Indicated when recalcitrant to steroids, prolonged uninterrupted steroid use, steroid atrophy or sensitive areas including face, anogenital, skin folds, paediatric, Use twice/day after bathing	Recommended Can use 'double pyjama method'	Narrow band UVB for maintenance therapy in chronic disease UVA1 as an adjunct for flares PUVA for lichenification, active and stable disease	Recommended when refractory to conventional therapy, severe disease with large body surface area, generalised exfoliative dermatitis Requires dermatologist referral. All require monitoring bloods Oral prednisone: minimum duration and dose for acute flares or bridging therapy, 0.5-1mg/m2/day Cyclosporine first line. Methotrexate recommended for children. Azathioprine in older children and teenagers, second line, recommend checking TMPT. Mycophenolate mofetil third line
EDF, EADV, EAACI, ETFAD, EFA, ESDaP, ESPD, GA2LEN, and UEMS Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis) in adults and children: part 139 + 1138 2018	Moisturisers directly after bathing on damp skin, 2–3 times daily Do not recommend pure oils like coconut oil	Limited use of hypoallergenic, fragrance free, physiological pH soap free cleansers Bathing at 27-30°, 5- 10 min. Can add bleach or bath oils (in last 2 min)	Reactive use in flares, proactive use 2x weekly can be used as maintenance for 20 weeks Avoid super potent steroids in children	Use after topical steroids in acute flares and proactively. First line for sensitive areas. Pimecrolimus in mild AD, tacrolimus in moderat-severe. Can use off label in under 2 years	Wet wrap therapy for 14 days for severe/ refractory cases	Narrow band UVB for maintenance therapy in chronic disease UVA1 as an adjunct for flares	Oral prednisone: 1 week short term, acute flares 0.2-0.5mg/m2/day Cyclosporine first line, azathioprine (check TPMT), methotrexate, mycophenolate mofetil can be used off label for children/adolescents Systemic immunotherapy should not be used in combination with UV
Ministry of Health Malaysia Management of Atopic	Emollients based on patient preference	No specific recommendations Bleach baths recommended, avoid long term use	Use with emollients, FTU for amount, use in flares and proactively	Age 2 and above, use in flares and proactively	Wet wrap therapy for 14 days for non- infected mod- severe AD	Narrow band UVB for maintenance therapy in chronic	Oral prednisone: short course Cyclosporine first line, azathioprine (check TPMT), methotrexate,

Author, Title, Year	Emollients	Bathing and cleansing	тсѕ	Topical calcineurin inhibitors	Wet wraps	Phototherapy	Immunosuppressants
Eczema ¹⁷ 2018						disease UVA1 as an adjunct for flares	mycophenolate mofetil recommended for severe AD
Turkish Society of Dermatology Turkish Guideline for Atopic Dermatitis 2018 ¹⁹ 2018	Moisturisers directly after bathing on damp skin, 1-3 times daily Do not apply topical medications concurrently with emollient	No specific recommendations Bleach baths recommended twice weekly	Reactive use in flares, proactive use 2x weekly can be used as maintenance Base amount on age, site, size of lesions	Use after topical steroids in acute flares and proactively or for sensitive areas	Use in treatment resistant AD	Narrow band UVB for maintenance therapy in chronic disease UVA1 as an adjunct for flares in age 12+ years	Oral prednisone: short course First line - cyclosporine, second line - azathioprine (check TPMT), third line - methotrexate, mycophenolate mofetil recommended for severe unresponsive AD, IFN gamma recommended as last line Monitoring recommended for all
European Task Force on Atopic Dermatitis/ European Academy of Dermatology and Venereology Position paper of the diagnosis and treatment of atopic dermatitis in adults and children ⁴⁵ 2018	Moisturisers directly after bathing on damp skin, at least 30 g/day. Base type on patient preference, however glycerol better tolerated than urea in <5 years	Limited use of hypoallergenic, fragrance free, physiological pH soap free cleansers Bathing at 27-30°, 2- 7 times/week. Can use emollient bath additives based on patient choice	Apply topical therapies 15 min after bathing Reactive use in flares, proactive use 2x weekly can be used as maintenance. Avoid super potent steroids in children. 15 g/month in infants, 30 g/month in children, 60-90 g in adolescents	Use after topical steroids in acute flares and proactively. First line for sensitive areas. Pimecrolimus in mild AD, tacrolimus in moderatesevere. Can use off label in under 2 years	Wet wrap therapy for 14 days for flares or acute oozing/ erosive lesions	Not enough evidence for use in prepubertal age group, otherwise narrow band UVB for chronic, UVA1 for acute flares	Systemic therapy in under <2 years requires specialist input Oral prednisone: short course or bridging therapy First line - cyclosporine, second line - azathioprine (check TPMT, methotrexate, third line - mycophenolate mofetil
Brazilian Society of Dermatology Consensus on the therapeutic management of atopic dermatitis - Brazilian Society of Dermatology ⁴⁰ 2019	Moisturisers directly after bathing on damp skin, 2 times daily. Choice based on patient preference	Cleansing with physiological pH soap free cleansers, up to 5 min Bathing for up to 5 min Bleach baths recommended	Reactive use in flares, proactive use 2x weekly can be used as maintenance. 15 g/month in infants, 30 g/month in children, 60-90 g in adolescents	Second line agent	Wet wraps used if hospitalised	Narrow band UVB for chronic, UVA1 for acute flares. Avoid in eczema herpeticum	Systemic therapy in under <2 years requires specialist input Oral prednisone: short course Cyclosporine and methotrexate most widely used, few dermatologists have experience with mycophenolate mofetil or azathioprine

Canadian Dermatology Association Approach to a Assessment a Management Pediatric Patients With Atopic Dermatitis: A Consensus Document. Section 3 ⁴² + Section 4, ⁴³ 2019	nd preference of Not enough evidence for bleach baths Olive oil should be avoided, exacerbates xerosis	Bathing once daily with lukewarm water Limited use of hypoallergenic, fragrance free, physiological pH soap free cleansers Lack of evidence for bleach baths Bath additives not recommended	Use topical therapies prior to moisturiser Recommend FTU for TCS	Use in flares 0.03% tacrolimus and 1% pimecrolimus for >2y. 0.1% tacrolimus for mod-severe in >16 years Proactive use recommended	Short term use, no standard protocols for duration, frequency, potency	Narrowband UVB in mod- severe AD UVA1 not discussed	Oral prednisone: short course First line - cyclosporine, second line - azathioprine (check TPMT, methotrexate, third line - mycophenolate mofetil
Indian Dermatology Expert Board Members Guidelines or Management Atopic Dermatitis in India: An Evidence -based Revie and an Exper Consensus 44 2019	of No clear evidence on frequency, technique, bath additives	Limited use of hypoallergenic, fragrance free, physiological pH soap free cleansers Bathing at 27-30 deg, 5-10 min once daily	Reactive use in flares, proactive use 2x weekly can be used as maintenance. Recommend using FTU	Use in flares 0.03% tacrolimus and 1% pimecrolimus for >2years. 0.1% tacrolimus for mod-severe in >16 years Pimecrolimus preferred in <2 years	Use in >6 months old, for severe/ resistant AD	Narrowband UVB in mod- severe AD UVA1 in acute flares	Oral prednisone: short course First line - cyclosporine, second line - azathioprine, methotrexate (over 8 years old) Mycophenolate mofetil only recommended for adults
SIDEMAST, ADOI, SIDAP, -Adapted fro consensus- based European guidelines fo treatment of atopic eczem (atopic dermatitis) ⁴¹ 2019	m frequently	Bath oils and soap substitutes recommended	Reactive use in flares, proactive use 2x weekly can be used as maintenance for up to 20 weeks	Use in flares 0.03% tacrolimus and 1% pimecrolimus for >2 years. 0.1% tacrolimus for mod-severe in >16 years Recommend sun protection	Not discussed	Narrowband UVB in mod- severe AD for >10 years UVA1 in acute flares for >11 years	Oral prednisone: short course First line - cyclosporine, second line - azathioprine, methotrexate, mycophenolate mofetil can be used off label for children
Taiwanese dermatologic association Taiwanese Dermatologic Association consensus fo the management atopic dermatitis: A 2020 update 2020	damp skin, 2 times daily	Limited use of hypoallergenic, fragrance free, physiological pH soap free cleansers Bathing for 5-10 min daily Lack of evidence for bath additives Bleach baths or hypochlorous acid for maintenance in mod-severe	Reactive use in flares, proactive use 2x weekly can be used as maintenance	Use after topical steroids in acute flares and proactively or for sensitive areas	Not common practice, low quality evidence	Narrowband UVB best option for children	Oral prednisone: short course First line - cyclosporine, second line - azathioprine, methotrexate, mycophenolate mofetil can be used off label for children

Author, Title, Year	Emollients	Bathing and cleansing	TCS	Topical calcineurin inhibitors	Wet wraps	Phototherapy	Immunosuppressants
Chinese Society of Dermatology Immunology Guidelines for the diagnosis and treatment of atopic dermatitis in China ⁴⁷ 2020	Moisturisers directly after bathing on damp skin, 2 times daily	Limited use of hypoallergenic, fragrance free, physiological pH soap free cleansers Bathing at 27-30°, 5- 10 min once daily Bleach baths for high risk of infection, once every few days	Reactive use in flares, proactive use 2x weekly can be used as maintenance	Use second line in acute flares and proactively or for sensitive areas	Recommended for relapse	Narrowband UVB in mod- severe AD UVA1 in acute flares for >12 years	Oral prednisone: short course or bridging First line - cyclosporine, second line - azathioprine, methotrexate
Japanese Dermatological Association English Version of Clinical practice guidelines for the Management of Atopic Dermatitis 2021	Moisturisers directly after bathing on damp skin, 2 times daily Bleach baths not recommended	Limited use of hypoallergenic, fragrance free, physiological pH soap free cleansers	Reactive use in flares, proactive use 2x weekly can be used as maintenance for 2+ weeks	Second line, not to use under occlusion, tacrolimus can be prophylactic Only age 2+ years	Use for severe flares	Narrowband UVB in mod- severe AD UVA1 in acute flares for >12 years	Oral prednisone: short course Cyclosporin not approved for children in Japan
Asian Academy of Dermatology and Venereology Expert Panel on Atopic Dermatitis, A clinician's reference guide for the management of atopic dermatitis in Asians ³⁷ 2018	Moisturisers directly after bathing on damp skin, 2–3 times daily Support the use of traditional emollients like coconut oil, olive oil	Limited use of hypoallergenic, fragrance free, physiological pH soap free cleansers	Indicated in flares, FTU recommended. Start with mild potency twice/day after bathing	Indicated when recalcitrant to steroids, prolonged uninterrupted steroid use, steroid atrophy or sensitive areas including face, anogenital, skin folds, paediatric, Use twice/day after bathing	Recommended, can use 'double pyjama method'	Narrow band UVB for maintenance therapy in chronic disease UVA1 as an adjunct for flares PUVA for lichenification, active and stable disease	Recommended when refractory to conventional therapy, severe disease with large body surface area, generalised exfoliative dermatitis Requires dermatologist referral. All require monitoring bloods Oral prednisone: minimum duration and dose for acute flares or bridging therapy, 0.5-1mg/m2/day Cyclosporine first line. Methotrexate recommended for children. Azathioprine in older children and teenagers, second line, recommend checking TMPT. Mycophenolate mofetil third line

EDF, EADV, EAACI, ETFAD, EFA, ESDaP, ESPD, GA2LEN, and UEMS Consensusbased European guidelines for treatment of atopic eczema (atopic dermatitis) in adults and children: part 1 ³⁹ + 11 ³⁸ 2018	Moisturisers directly after bathing on damp skin, 2-3 times daily Do not recommend pure oils like coconut oil	Limited use of hypoallergenic, fragrance free, physiological pH soap free cleansers Bathing at 27-30°, 5- 10 min. Can add bleach or bath oils (in last 2 min)	Reactive use in flares, proactive use 2x weekly can be used as maintenance for 20 weeks Avoid super potent steroids in children	Use after topical steroids in acute flares and proactively. First line for sensitive areas. Pimecrolimus in mild AD, tacrolimus in mod-severe. Can use off label in under 2 years	Wet wrap therapy for 14 days for severe/ refractory cases	Narrow band UVB for maintenance therapy in chronic disease UVA1 as an adjunct for flares	Oral prednisone: 1 week short term, acute flares 0.2-0.5mg/m2/day Cyclosporine first line, azathioprine (check TPMT), methotrexate, mycophenolate mofetil can be used off label for children/adolescents Systemic immunotherapy should not be used in combination with UV
Ministry of Health Malaysia Management of Atopic Eczema ¹⁷ 2018	Emollients based on patient preference	No specific recommendations Bleach baths recommended, avoid long term use	Use with emollients, FTU for amount, use in flares and proactively	Age 2 and above, use in flares and proactively	Wet wrap therapy for 14 days for non- infected mod- severe AD	Narrow band UVB for maintenance therapy in chronic disease UVA1 as an adjunct for flares	Oral prednisone: short course Cyclosporine first line, azathioprine (check TPMT), methotrexate, mycophenolate mofetil recommended for severe AD
Turkish Society of Dermatology Turkish Guideline for Atopic Dermatitis 2018 ¹⁹ 2018	Moisturisers directly after bathing on damp skin, 1-3 times daily Do not apply topical medications concurrently with emollient	No specific recommendations Bleach baths recommended twice weekly	Reactive use in flares, proactive use 2x weekly can be used as maintenance Base amount on age, site, size of lesions	Use after topical steroids in acute flares and proactively or for sensitive areas	Use in treatment resistant AD	Narrow band UVB for maintenance therapy in chronic disease UVA1 as an adjunct for flares in age 12+ years	Oral prednisone: short course First line - cyclosporine, second line - azathioprine (check TPMT), third line - methotrexate, mycophenolate mofetil recommended for severe unresponsive AD, IFN gamma recommended as last line Monitoring recommended for all
European Task Force on Atopic Dermatitis/ European Academy of Dermatology and Venereology	Moisturisers directly after bathing on damp skin, at least 30 g/day. Base type on patient preference, however glycerol better	Limited use of hypoallergenic, fragrance free, physiological pH soap free cleansers Bathing at 27-30°, 2- 7 times/week. Can use emollient bath	Apply topical therapies 15 min after bathing Reactive use in flares, proactive use 2x weekly can be used as maintenance. Avoid	Use after topical steroids in acute flares and proactively. First line for sensitive areas. Pimecrolimus in mild AD,	Wet wrap therapy for 14 days for flares or acute oozing/ erosive lesions	Not enough evidence for use in prepubertal age group, otherwise narrow band UVB for	Systemic therapy in under <2 years requires specialist input Oral prednisone: short course or bridging therapy First line - cyclosporine, second line -

Author, Title, Year	Emollients	Bathing and cleansing	TCS	Topical calcineurin inhibitors	Wet wraps	Phototherapy	Immunosuppressants
Position paper of the diagnosis and treatment of atopic dermatitis in adults and children ⁴⁵ 2018	tolerated than urea in <5 years	additives based on patient choice	super potent steroids in children. 15 g/month in infants, 30 g/month in children, 60-90 g in adolescents	tacrolimus in moderate- severe. Can use off label in under 2 years		chronic, UVA1 for acute flares	azathioprine (check TPMT, methotrexate, third line - mycophenolate mofetil
Brazilian Society of Dermatology Consensus on the therapeutic management of atopic dermatitis - Brazilian Society of Dermatology ⁴⁰ 2019	Moisturisers directly after bathing on damp skin, 2 times daily. Choice based on patient preference	Cleansing with physiological pH soap free cleansers, up to 5 min Bathing for up to 5 min Bleach baths recommended	Reactive use in flares, proactive use 2x weekly can be used as maintenance. 15 g/month in infants, 30 g/month in children, 60-90 g in adolescents	Second line agent	Wet wraps used if hospitalised	Narrow band UVB for chronic, UVA1 for acute flares. Avoid in eczema herpeticum	Systemic therapy in under <2 years requires specialist input Oral prednisone: short course Cyclosporine and methotrexate most widely used, few dermatologists have experience with mycophenolate mofetil or azathioprine
Canadian Dermatology Association Approach to the Assessment and Management of Pediatric Patients With Atopic Dermatitis: A Consensus Document. Section 3 ⁴² + Section 4, ⁴³ 2019	Moisturisers daily immediately after bathing. Choice based on patient preference Not enough evidence for bleach baths Olive oil should be avoided, exacerbates xerosis	Bathing once daily with lukewarm water Limited use of hypoallergenic, fragrance free, physiological pH soap free cleansers Lack of evidence for bleach baths Bath additives not recommended	Use topical therapies prior to moisturiser Recommend FTU for TCS	Use in flares 0.03% tacrolimus and 1% pimecrolimus for >2 years. 0.1% tacrolimus for mod-severe in >16 years Proactive use recommended	Short term use, no standard protocols for duration, frequency, potency	Narrowband UVB in mod- severe AD UVA1 not discussed	Oral prednisone: short course First line - cyclosporine, second line - azathioprine (check TPMT, methotrexate, third line - mycophenolate mofetil
Indian Dermatology Expert Board Members Guidelines on Management of Atopic Dermatitis in India: An Evidence -based Review and an Expert Consensus ⁴⁴ 2019	Moisturisers recommended 2 or more times daily, choice based on patient preference. No clear evidence on frequency, technique, bath additives	Limited use of hypoallergenic, fragrance free, physiological pH soap free cleansers Bathing at 27-30 deg, 5-10 min once daily	Reactive use in flares, proactive use 2x weekly can be used as maintenance. Recommend using FTU	Use in flares 0.03% tacrolimus and 1% pimecrolimus for >2 years. 0.1% tacrolimus for mod-severe in >16 years Pimecrolimus preferred in < 2y	Use in >6 months old, for severe/ resistant AD	Narrowband UVB in mod- severe AD UVA1 in acute flares	Oral prednisone: short course First line - cyclosporine, second line - azathioprine, methotrexate (over 8 years old) Mycophenolate mofetil only recommended for adults

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SIDEMAST, ADOI, SIDAPA -Adapted from consensus- based European guidelines for treatment of atopic eczema (atopic dermatitis) ⁴¹ 2019	Moisturisers recommended frequently	Bath oils and soap substitutes recommended	Reactive use in flares, proactive use 2x weekly can be used as maintenance for up to 20 weeks	Use in flares 0.03% tacrolimus and 1% pimecrolimus for >2 years. 0.1% tacrolimus for mod-severe in >16 years Recommend sun protection	Not discussed	Narrowband UVB in mod- severe AD for >10 years UVA1 in acute flares for >11 years	Oral prednisone: short course First line - cyclosporine, second line - azathioprine, methotrexate, mycophenolate mofetil can be used off label for children
Taiwanese dermatological association Taiwanese Dermatological Association consensus for the management of atopic dermatitis: A 2020 update 46 2020	Moisturisers directly after bathing on damp skin, 2 times daily	Limited use of hypoallergenic, fragrance free, physiological pH soap free cleansers Bathing for 5-10 min daily Lack of evidence for bath additives Bleach baths or hypochlorous acid for maintenance in mod-severe	Reactive use in flares, proactive use 2x weekly can be used as maintenance	Use after topical steroids in acute flares and proactively or for sensitive areas	Not common practice, low quality evidence	Narrowband UVB best option for children	Oral prednisone: short course First line - cyclosporine, second line - azathioprine, methotrexate, mycophenolate mofetil can be used off label for children
Chinese Society of Dermatology Immunology Guidelines for the diagnosis and treatment of atopic dermatitis in China ⁴⁷ 2020	Moisturisers directly after bathing on damp skin, 2 times daily	Limited use of hypoallergenic, fragrance free, physiological pH soap free cleansers Bathing at 27-30°, 5- 10 min once daily Bleach baths for high risk of infection, once every few days	Reactive use in flares, proactive use 2x weekly can be used as maintenance	Use second line in acute flares and proactively or for sensitive areas	Recommended for relapse	Narrowband UVB in mod- severe AD UVA1 in acute flares for >12 years	Oral prednisone: short course or bridging First line - cyclosporine, second line - azathioprine, methotrexate
Japanese Dermatological Association English Version of Clinical practice guidelines for the Management of Atopic Dermatitis 2021	Moisturisers directly after bathing on damp skin, 2 times daily Bleach baths not recommended	Limited use of hypoallergenic, fragrance free, physiological pH soap free cleansers	Reactive use in flares, proactive use 2x weekly can be used as maintenance for 2+ weeks	Second line, not to use under occlusion, tacrolimus can be prophylactic Only age 2+ years	Use for severe flares	Narrowband UVB in mod- severe AD UVA1 in acute flares for >12 years	Oral prednisone: short course Cyclosporin not approved for children in Japan

Table 2. (Continued) Mainstay management recommendations from guidelines 2018–2023. Abbreviations: AD - Atopic dermatitis; EDF - European Dermatology Forum; EADV - European Academy of Dermatology and Venereology; EAACI - European Academy of Allergy and Clinical Immunology; ETFAD - European Task Force on Atopic Dermatitis; EFA - European Federation of Allergy and Airways Disease; ESDaP - European Society for Dermatology and Psychiatry; ESPD - European Society of Pediatric Dermatology; GA2LEN - Global Allergy and Asthma European Network; UEMS - European Union of Medical Specialists; SIDEMAST - Italian Society of Medical, Surgical and Aesthetic Dermatology and Venereology; ADOI - Italian Society of Dermatologists Hospital-based and Public Health; SIDPAP - Italian Society of Allergological Occupational and Environmental Dermatology; FTU - finger tip unit; PUVA - Psoralens ultraviolet A; TMPT - Thiopurine methyl transferase; UV - ultraviolet; UVA - ultraviolet A; USV - ultraviolet B; TCS - topical corticosteroids; IFN - interferon

Author, Title, Year	Biologics	Education	Dietary and allergy testing	Complementary therapy and Chinese Herbal Medicine	Pruritis control	Infection control	Other
Asian Academy of Dermatology and Venereology Expert Panel on Atopic Dermatitis, A clinician's reference guide for the management of atopic dermatitis in Asians ³⁷ 2018	Dupilumab for adults only	Eczema action plan, nurse led education programs, instructional videos	Elimination diets not recommended unless proven allergy by food challenge Not enough evidence for nutrient supplements e.g. probiotics, prebiotics, vitamin D tablets	Limited evidence, not recommended	Keep nails short, wear light clothing, avoid synthetic fabrics Sedating antihistamines can be used for sleep in short term	Staph aureus infections - systemic antibiotics Eczema herpeticum-systemic antivirals Topical antibiotics - focal infections	Avoid clinically relevant environmental triggers however exposure to pets is recommended New therapies mentioned however need further research: Naltrexone, antioxidant moisturisers, topical PDE4 inhibitors
EDF, EADV, EAACI, ETFAD, EFA, ESDaP, ESPD, GA2LEN, and UEMS Consensusbased European guidelines for treatment of atopic eczema (atopic dermatitis) in adults and children: part I ³⁹ + II ³⁸ 2018	Dupilumab for moderate to severe when topical or systemic therapies not sufficient Do not recommend rituximab, omalizumab, ustekinumab Mepolizumab can be trialled in severe cases	Nurse led education programs, multidisciplinary school programs	Elimination diets not recommended unless proven allergy by food challenge Early introduction of solids Probiotics, unsaturated fatty acids not recommended Allergen specific immunotherapy for severe AD with allergies to dust mite, birch and grass pollen with history of clinical exacerbation or patch test	Thermal spring water may be considered for mild-moderate AD	Sedating antihistamines can be used for sleep in short term Do not recommend routine antihistamines, topical cannabinoid receptor agonists, mu receptor antagonists, anaesthetics	Staph aureus infections - systemic antibiotics Eczema herpeticum-systemic antivirals H + N AD with Malassezia colonisation: topical or systemic antifungals Topical antiseptics e.g. diluted sodium hypochlorite for bacterial infection, chronic treatment resistant AD	Avoid clinically relevant environmental triggers, patch test when necessary. Avoid pets. Avoid hot humid climates Vaccinations recommended as per national plan Sun protection Psychosomatic counselling, behavioural therapy techniques, relaxation techniques Hospitalisation for severe cases Not recommending tofacitinib, mast cell stabilisers, leukotriene antagonists, IVIG PDE4 inhibitors in select cases
Ministry of Health Malaysia Management of Atopic Eczema ¹⁷ 2018	Dupilumab: Adults No omalizumab, infliximab	Workshops, written action plans	Elimination diets or supplements not recommended Consider food allergy diagnoses. Allergen specific immunotherapy not recommended	Not recommended over conventional therapy	Sedating antihistamines can be used for sleep in short term	Systemic antibiotics for staph aureus	Avoid clinically relevant environmental triggers Routine vaccinations PDE4 and JAK inhibitors under study No IVIG, leukotriene antagonists, interferon gamma

Turkish Society of Dermatology Turkish Guideline for Atopic Dermatitis 2018 ¹⁹ 2018	Dupilumab - adults Ustekinumab and Omalizumab - lack of evidence	Support programs, linking with community support groups	Elimination diets or probiotics not recommended Fatty acid supplementation could be considered, replace vitamin D only if deficient	Do not recommend Chinese herbal medicine	Sedating antihistamines can be used for sleep in short term	Staph aureus infections - systemic antibiotics Eczema herpeticum-systemic antivirals H + N AD with Malassezia colonisation: topical or systemic antifungals Lack evidence for antiseptic baths Topical antiseptics for bacterial infection, not long term	Avoid clinically relevant environmental triggers Topical coal tar recommended in children Further research required for PDE4 inhibitors, polidocanol, tannins Do not recommend zinc, topical NSAIDs Consider psychiatric input
European Task Force on Atopic Dermatitis/ European Academy of Dermatology and Venereology Position paper of the diagnosis and treatment of atopic dermatitis in adults and children ⁴⁵ 2018	Dupilumab - moderate to severe, age 12+ years	Therapeutic parent and child education - interdisciplinary programs e.g., eczema school, written action plans Multimodal education programs e.g., relaxation and habit-reversal techniques	Elimination diets or supplements not recommended Allergy workup including serum IgE, skin prick tests, patch testing depending on individual history for moderate-severe eczema Mild eczema - test for allergies based on clinical suspicion Patch testing for refractory with atypical skin lesions or triggers Allergen specific immunotherapy for select patients with dust mite birch or grass pollen sensitisation + severe AD and clinical exacerbation or patch test positive	Not recommended	Antihistamines: H1RA could be used for treatment as 3rd line Sedating antihistamines can be used for sleep in short term	Staph aureus infections - systemic antibiotics Eczema herpeticum-systemic antivirals H + N AD with Malassezia colonisation: topical or systemic antifungals Topical antiseptics for bacterial infection, not long term Can consider high quality silver garments in patients with high risk of infection	Further research required for JAK inhibitors, topical tar, PDE4 inhibitors Alitretinoin in hand eczema Aim to minimise treatment cost, follow up frequently, send reminders Special attention to adolescents including counselling about body image, relationships, psychotherapy, avoiding careers with high risk of complications e.g., chefs, bakers, painters
Brazilian Society of Dermatology Consensus on the therapeutic management of atopic	Dupilumab - requires ongoing studies	Recommended, no details	Elimination diets not recommended, however consider investigating allergies in severe, treatment-resistant AD and history of flares following	Not mentioned	Sedating antihistamines can be used for sleep in short term	Staph aureus infections - systemic antibiotics Eczema herpeticum-	Further research required for PDE4 inhibitors

Author, Title, Year	Biologics	Education	Dietary and allergy testing	Complementary therapy and Chinese Herbal Medicine	Pruritis control	Infection control	Other
dermatitis - Brazilian Society of Dermatology ⁴⁰ 2019			ingestion of specific foods Patch testing for refractory with atypical skin lesions Routine skin prick tests or RAST tests not recommended			systemic antivirals H + N AD with Malassezia colonisation: topical or systemic antifungals Topical antiseptics for bacterial infection, not long term	
Canadian Dermatology Association Approach to the Assessment and Management of Pediatric Patients With Atopic Dermatitis: A Consensus Document. Section 3 ⁴² + Section 4, ⁴³ 2019	Dupilumab - mod-severe in 12+ years	Eczema action plan, pictograms for counselling and education	Elimination diets or supplementation not recommended Routine allergy testing not recommended	Not recommended	Sedating antihistamines not recommended in paediatric patients	Not discussed	Avoid clinically relevant environmental triggers Further research into JAK inhibitors, other biologics PDE4 inhibitors first line - 2% crisaborole in mild-moderate AD ≥2years
Indian Dermatology Expert Board Members Guidelines on Management of Atopic Dermatitis in India: An Evidence -based Review and an Expert Consensus 44 2019	Dupilumab - adults only Aprelimast 3rd line	Recommend education at each consult	Elimination diets or supplementation not recommended unless vitamin D deficiency	Not discussed	Antihistamines recommended in patients with concurrent allergic rhinitis and bronchial asthma Sedating antihistamines can be used for sleep in short term for >2years	Short course topical/oral antibiotics for overt infection. Not for long term use.	Avoid clinically relevant environmental triggers, tight clothing, occupational triggers PDE4 inhibitors can be used off label Psychosomatic and psychological interventions Alitretinoin for hand eczema
SIDEMAST, ADOI, SIDAPA -Adapted from consensus- based European guidelines for	Dupilumab - adults only Neolizumab for second line - adults	Internet based education programs	Elimination diets or supplementation not recommended Allergen specific immunotherapy for select patients with dust mite birch or grass pollen	Thermal spring water and unsaturated fatty acids may be considered	Sedating antihistamines can be used for sleep in short term	Staph aureus infections - systemic antibiotics Eczema herpeticum- systemic	Avoid clinically relevant environmental triggers, including smoking, occupational triggers Routine vaccinations

treatment of atopic eczema (atopic dermatitis) ⁴¹ 2019			sensitisation + severe AD and clinical exacerbation or patch test positive			antivirals H + N AD with Malassezia colonisation: topical or systemic antifungals Topical antiseptics for bacterial infection, not long term	recommended aside from intracutaneous smallpox vaccination with attenuated live vaccine - may lead to life- threatening eczema vaccinatum Further research required for aprelimast and JAK inhibitors Leukotrienes, IVIG not recommended Psychological support - behavioural therapy, relaxation techniques, counselling
Taiwanese dermatological association Taiwanese Dermatological Association consensus for the management of atopic dermatitis: A 2020 update 46 2020	Dupilumab - >12years	Recommended, no preference for specific tool	Not discussed	Not recommended	Recommended in initial acute control in those with urticaria, dermographism, allergic rhinitis and bronchial asthma Sedating antihistamines can be used for sleep in short term for >2years	Staph aureus infections - systemic antibiotics Eczema herpeticum-systemic antivirals H + N AD with Malassezia colonisation: topical or systemic antifungals Antiseptics not recommended	Patients and caregivers should be informed that in patients with more pigmented skin, AD may temporarily cause the skin to lighten or darken Melatonin for sleep disturbance Assess mental health comorbidities through psychologists and multidisciplinary teams
Chinese Society of Dermatology Immunology Guidelines for the diagnosis and treatment of atopic dermatitis in China ⁴⁷ 2020	Dupilumab - adults JAK inhibitors - adults	Recommended, no specific recommendations	For mod-severe AD in <3y, routinely test for cow's milk, eggs, wheat, soy, peanut allergies In >5y, test based on history findings. Consider fish allergies in childhood, pollen/apples/celery/carrot in older kids Recommend diagnostic elimination diets for 4-6 weeks Avoid contact allergens like nickel, neomycin, fragrance, formaldehyde, preservatives, lanolin, rubber Recommend dust mite immunotherapy with severe AD and allergy to dust mite	Chinese herbal medicine based on clinical symptoms and signs	Non-sedating second generation antihistamines adjuvant for pruritis with concurrent urticaria, allergic rhinitis Sedating antihistamines can be used for sleep in short term Last line: mirtazapine, pregabalin, paroxetine, naltrexone	Staph aureus infections - systemic antibiotics Eczema herpeticum-systemic antivirals H + N AD with Malassezia colonisation: topical or systemic antifungals Antiseptics not recommended	Avoid clinically relevant environmental triggers PDE4 inhibitors recommended in >2years Sodium thiosulfate, glycyrrhizin injections - need more evidence Hospitalisation for severe AD

Author, Title, Year	Biologics	Education	Dietary and allergy testing	Complementary therapy and Chinese Herbal Medicine	Pruritis control	Infection control	Other
Japanese Dermatological Association English Version of Clinical practice guidelines for the Management of Atopic Dermatitis 2021	Dupilumab - mod-severe AD Baricitinib - orally in mod-severe AD Delgocitinib ointment is recommended for patients with AD aged ≥2 years	Recommended at each consult, community support groups, nurse led programs	Elimination diets and supplementation not recommended	Chinese herbal medicines may be used in combination with traditional therapy in refractory cases	Sedating antihistamines can be used for sleep in short term	Topical antibiotics for localised infections in short term, systemic for up to 1 week	Avoid clinically relevant environmental triggers Including dust mites
Asian Academy of Dermatology and Venereology Expert Panel on Atopic Dermatitis, A clinician's reference guide for the management of atopic dermatitis in Asians ³⁷ 2018	Dupilumab adults only	Eczema action plan, nurse led education programs, instructional videos	Elimination diets not recommended unless proven allergy by food challenge Not enough evidence for nutrient supplements e.g. probiotics, prebiotics, vitamin D tablets	Limited evidence, not recommended	Keep nails short, wear light clothing, avoid synthetic fabrics Sedating antihistamines can be used for sleep in short term	Staph aureus infections - systemic antibiotics Eczema herpeticum-systemic antivirals Topical antibiotics - focal infections	Avoid clinically relevant environmental triggers however exposure to pets is recommended New therapies mentioned however need further research: Naltrexone, antioxidant moisturisers, topical PDE4 inhibitors
EDF, EADV, EAACI, ETFAD, EFA, ESDaP, ESPD, GA2LEN, and UEMS Consensusbased European guidelines for treatment of atopic eczema (atopic dermatitis) in adults and children: part I ³⁹ + II ³⁸ 2018	Dupilumab for moderate to severe when topical or systemic therapies not sufficient Do not recommend rituximab, omalizumab, ustekinumab Mepolizumab can be trialled in severe cases	recommended unless proven allergy by food challenge Early introduction of solids Probiotics, unsaturated fatty acids not recommended Allergen specific immunotherapy for severe AD with allergies to dust mite, birch and grass pollen with history of clinical exacerbation or		Thermal spring water may be considered for mild-moderate AD	Sedating antihistamines can be used for sleep in short term Do not recommend routine antihistamines, topical cannabinoid receptor agonists, mu receptor antagonists, anaesthetics	Staph aureus infections - systemic antibiotics Eczema herpeticum-systemic antivirals H + N AD with Malassezia colonisation: topical or systemic antifungals Topical antiseptics e.g. diluted sodium hypochlorite for bacterial	Avoid clinically relevant environmental triggers, patch test when necessary. Avoid pets. Avoid hot humid climates Vaccinations recommended as per national plan Sun protection Psychosomatic counselling, behavioural therapy techniques, relaxation techniques Hospitalisation for severe cases Not recommending

						infection, chronic treatment resistant AD	tofacitinib, mast cell stabilisers, leukotriene antagonists, IVIG PDE4 inhibitors in select cases
Ministry of Health Malaysia Management of Atopic Eczema ¹⁷ 2018	Dupilumab: Adults No omalizumab, infliximab	Workshops, written action plans	Elimination diets or supplements not recommended Consider food allergy diagnoses. Allergen specific immunotherapy not recommended	Not recommended over conventional therapy	Sedating antihistamines can be used for sleep in short term	Systemic antibiotics for staph aureus	Avoid clinically relevant environmental triggers Routine vaccinations PDE4 and JAK inhibitors under study No IVIG, leukotriene antagonists, interferon gamma
Turkish Society of Dermatology Turkish Guideline for Atopic Dermatitis 2018 ¹⁹ 2018	Dupilumab - adults Ustekinumab and Omalizumab - lack of evidence	Support programs, linking with community support groups	Elimination diets or probiotics not recommended Fatty acid supplementation could be considered, replace vitamin D only if deficient	Do not recommend Chinese herbal medicine	Sedating antihistamines can be used for sleep in short term	Staph aureus infections - systemic antibiotics Eczema herpeticum-systemic antivirals H + N AD with Malassezia colonisation: topical or systemic antifungals Lack evidence for antiseptic baths Topical antiseptics for bacterial infection, not long term	Avoid clinically relevant environmental triggers Topical coal tar recommended in children Further research required for PDE4 inhibitors, polidocanol, tannins Do not recommend zinc, topical NSAIDs Consider psychiatric input
European Task Force on Atopic Dermatitis/ European Academy of Dermatology and Venereology Position paper of the diagnosis and treatment of atopic dermatitis in	Dupilumab - moderate to severe, age 12+	Therapeutic parent and child education - interdisciplinary programs e.g. eczema school, written action plans Multimodal education programs e.g. relaxation and habit-reversal techniques	Elimination diets or supplements not recommended Allergy workup including serum IgE, skin prick tests, patch testing depending on individual history for moderate-severe eczema Mild eczema - test for allergies based on clinical suspicion Patch testing for refractory with atypical skin lesions or	Not recommended	Antihistamines: H1RA could be used for treatment as 3rd line Sedating antihistamines can be used for sleep in short term	Staph aureus infections - systemic antibiotics Eczema herpeticum-systemic antivirals H + N AD with Malassezia colonisation: topical or systemic	Further research required for JAK inhibitors, topical tar, PDE4 inhibitors Alitretinoin in hand eczema Aim to minimise treatment cost, follow up frequently, send reminders Special attention to adolescents including counselling about

Author, Title, Year	Biologics	Education	Dietary and allergy testing	Complementary therapy and Chinese Herbal Medicine	Pruritis control	Infection control	Other
adults and children ⁴⁵ 2018			triggers Allergen specific immunotherapy for select patients with dust mite birch or grass pollen sensitisation + severe AD and clinical exacerbation or patch test positive			antifungals Topical antiseptics for bacterial infection, not long term Can consider high quality silver garments in patients with high risk of infection	body image, relationships, psychotherapy, avoiding careers with high risk of complications e.g. chefs, bakers, painters
Brazilian Society of Dermatology Consensus on the therapeutic management of atopic dermatitis - Brazilian Society of Dermatology ⁴⁰ 2019	Dupilumab - requires ongoing studies	Recommended, no details	Elimination diets not recommended, however consider investigating allergies in severe, treatment-resistant AD and history of flares following ingestion of specific foods Patch testing for refractory with atypical skin lesions Routine skin prick tests or RAST tests not recommended	Not mentioned	Sedating antihistamines can be used for sleep in short term	Staph aureus infections - systemic antibiotics Eczema herpeticum-systemic antivirals H + N AD with Malassezia colonisation: topical or systemic antifungals Topical antiseptics for bacterial infection, not long term	Further research required for PDE4 inhibitors
Canadian Dermatology Association Approach to the Assessment and Management of Pediatric Patients With Atopic Dermatitis: A Consensus Document. Section 3 ⁴² + Section 4, ⁴³ 2019	Dupilumab - mod-severe in 12+ years	Eczema action plan, pictograms for counselling and education	Elimination diets or supplementation not recommended Routine allergy testing not recommended	Not recommended	Sedating antihistamines not recommended in paediatric patients	Not discussed	Avoid clinically relevant environmental triggers Further research into JAK inhibitors, other biologics PDE4 inhibitors first line - 2% crisaborole in mild-moderate AD ≥2y

Indian Dermatology Expert Board Members Guidelines on Management of Atopic Dermatitis in India: An Evidence -based Review and an Expert Consensus ⁴⁴ 2019	Dupilumab - adults only Aprelimast 3rd line	Recommend education at each consult	Elimination diets or supplementation not recommended unless vitamin D deficiency	Not discussed	Antihistamines recommended in patients with concurrent allergic rhinitis and bronchial asthma Sedating antihistamines can be used for sleep in short term for >2years	Short course topical/oral antibiotics for overt infection. Not for long term use.	Avoid clinically relevant environmental triggers, tight clothing, occupational triggers PDE4 inhibitors can be used off label Psychosomatic and psychological interventions Alitretinoin for hand eczema
SIDEMAST, ADOI, SIDAPA -Adapted from consensus- based European guidelines for treatment of atopic eczema (atopic dermatitis) ⁴¹ 2019	Dupilumab - adults only Neolizumab for second line - adults	Internet based education programs	Elimination diets or supplementation not recommended Allergen specific immunotherapy for select patients with dust mite birch or grass pollen sensitisation + severe AD and clinical exacerbation or patch test positive	Thermal spring water and unsaturated fatty acids may be considered	Sedating antihistamines can be used for sleep in short term	Staph aureus infections - systemic antibiotics Eczema herpeticum-systemic antivirals H + N AD with Malassezia colonisation: topical or systemic antifungals Topical antiseptics for bacterial infection, not long term	Avoid clinically relevant environmental triggers, including smoking, occupational triggers Routine vaccinations recommended aside from intracutaneous smallpox vaccination with attenuated live vaccine - may lead to life- threatening eczema vaccinatum Further research required for aprelimast and JAK inhibitors Leukotrienes, IVIG not recommended Psychological support - behavioural therapy, relaxation techniques, counselling
Taiwanese dermatological association Taiwanese Dermatological Association consensus for the management of atopic dermatitis: A	Dupilumab - >12years	Recommended, no preference for specific tool	Not discussed	Not recommended	Recommended in initial acute control in those with urticaria, dermographism, allergic rhinitis and bronchial asthma Sedating antihistamines can be used for	Staph aureus infections - systemic antibiotics Eczema herpeticum-systemic antivirals H + N AD with Malassezia colonisation: topical or	Patients and caregivers should be informed that in patients with more pigmented skin, AD may temporarily cause the skin to lighten or darken Melatonin for sleep disturbance Assess mental health comorbidities

Author, Title, Year	Biologics	Education	Dietary and allergy testing	Complementary therapy and Chinese Herbal Medicine	Pruritis control	Infection control	Other
2020 update ⁴⁶ 2020					sleep in short term for >2years	systemic antifungals Antiseptics not recommended	through psychologists and multidisciplinary teams
Chinese Society of Dermatology Immunology Guidelines for the diagnosis and treatment of atopic dermatitis in China ⁴⁷ 2020	Dupilumab - adults JAK inhibitors - adults	specific routinely test for cow's		Chinese herbal medicine based on clinical symptoms and signs	Non-sedating second generation antihistamines adjuvant for pruritis with concurrent urticaria, allergic rhinitis Sedating antihistamines can be used for sleep in short term Last line: mirtazapine, pregabalin, paroxetine, naltrexone	Staph aureus infections - systemic antibiotics Eczema herpeticum-systemic antivirals H + N AD with Malassezia colonisation: topical or systemic antifungals Antiseptics not recommended	Avoid clinically relevant environmental triggers PDE4 inhibitors recommended in >2 years Sodium thiosulfate, glycyrrhizin injections - need more evidence Hospitalisation for severe AD
Japanese Dermatological Association English Version of Clinical practice guidelines for the Management of Atopic Dermatitis 2021	Dupilumab - mod-severe AD Baricitinib - orally in mod-severe AD Delgocitinib ointment is recommended for patients with AD aged ≥2 years	Recommended at each consult, community support groups, nurse led programs	Elimination diets and supplementation not recommended	Chinese herbal medicines may be used in combination with traditional therapy in refractory cases	Sedating antihistamines can be used for sleep in short term	Topical antibiotics for localised infections in short term, systemic for up to 1 week	Avoid clinically relevant environmental triggers Including dust mites

Table 3. (Continued) Novel and complementary management recommendations from guidelines 2018-2023. Abbreviations: AD - Atopic dermatitis; EDF - European Dermatology Forum; EADV - European Academy of Dermatology and Venereology; EAACI - European Academy of Allergy and Clinical Immunology; ETFAD - European Task Force on Atopic Dermatitis; EFA - European Federation of Allergy and Airways Disease; ESDaP - European Society for Dermatology and Psychiatry; ESPD - European Society of Pediatric Dermatology; GA2LEN - Global Allergy and Asthma European Network; UEMS - European Union of Medical Specialists; SIDEMAST - Italian Society of Medical, Surgical and Aesthetic Dermatology and Venereology; ADOI - Italian Society of Dermatologists and Venereologists Hospital-based and Public Health; SIDAPA - Italian Society of Allergological Occupational and Environmental Dermatology

	Guideline Name	Domain 1: Total Score	Domain 2: Total Score	Domain 3: Total Score	Domain 4: Total Score	Domain 5: Total Score	Domain 6: Total Score	Overall quality	Cut-off met
1	Childhood Atopic Eczema Consensus Document - Allergy Society of South Africa ²⁰	30.56%	11.11%	15.63%	55.56%	0.00%	0.00%	33.33%	No
2	Diagnosis and treatment of atopic dermatitis in children and adults: European Academy of Allergology and Clinical Immunology/American Academy of Allergy, Asthma and Immunology/PRACTALL Consensus Report - European Academy of Allergology and Clinical Immunology/American Academy of Allergy, Asthma and Immunology/PRACTALL ²¹	44.44%	27.78%	18.75%	50.00%	8.33%	12.50%	41.67%	No
3	Guidelines on the management of atopic dermatitis in South Africa - Dermatological, Paediatric (SAPA) and Allergy (ALLSA) Societies of South Africa ¹⁵	75.00%	47.22%	35.42%	77.78%	16.67%	4.17%	41.67%	No
4	Eczema - atopic eczema - Scottish Guideline, Primary Care Dermatological Society ¹⁸	91.67%	69.44%	78.13%	86.11%	75.00%	58.33%	83.33%	Yes
5	Atopic dermatitis: a practice parameter update 2012 - American Academy of Allergy, Asthma and Immunology, American College of Allergy, Asthma & Immunology (ACAAI); and the Joint Council of Allergy, Asthma and Immunology ²⁴	63.89%	55.56%	48.96%	88.89%	22.92%	58.33%	67.67%	Yes
6	Clinical guidelines on management of atopic dermatitis in children - Hong Kong College of Paediatricians ²²	77.78%	25.00%	17.71%	61.11%	2.08%	0.00%	33.33%	No
7	Atopic eczema in children: Management of atopic eczema in children from birth up to the age of 12 years - NICE ¹⁶	100.00%	100.00%	97.92%	83.33%	93.75%	95.83%	100.00%	Yes
8	Consensus guidelines for the management of atopic dermatitis - an Asia-Pacific perspective - Asia-Pacific Consensus Group for Atopic Dermatitis ²³	77.78%	41.67%	14.58%	72.22%	16.67%	54.17%	41.67%	No

(continued)

	Guideline Name	Domain 1: Total Score	Domain 2: Total Score	Domain 3: Total Score	Domain 4: Total Score	Domain 5: Total Score	Domain 6: Total Score	Overall quality	Cut-off met
9	Clinical report on atopic dermatitis - skin-directed management - American Academy of Paediatrics ³⁰	77.78%	41.67%	21.88%	55.56%	6.25%	91.67%	50%	No
10	Guidelines of care for the management of atopic dermatitis: Section 1-4 - American Academy of Dermatology ^{25,26,28,29}	83.33%	38.89%	83.33%	94.44%	16.67%	91.67%	83.33%	Yes
11	Atopic dermatitis guideline. Position paper from the Latin American Society of Allergy, Asthma and Immunology ²⁷	75.00%	63.89%	69.79%	80.56%	20.83%	12.50%	58.33%	Yes
12	Atopic dermatitis: current treatment guidelines. Statement of the experts of the dermatological section - Polish society of allergology, and the allergology section, Polish society of dermatology ³³	30.56%	11.11%	14.58%	47.22%	0.00%	12.50%	25.00%	No
13	Consensus guidelines for the treatment of atopic dermatitis in Korea Part I,II - Korean Atopic Dermatitis Association ^{31,32}	72.22%	27.78%	64.58%	77.78%	12.50%	16.67%	66.67%	Yes
14	Consensus Conference on Clinical Management of pediatric Atopic Dermatitis - Italian Society of Pediatric Allergology and Immunology (SIAIP) and the Italian Society of Pediatric Dermatology (SIDerP) ³⁴	69.44%	27.78%	25.00%	77.78%	8.33%	8.33%	41.67%	No
15	S2k guideline on diagnosis and treatment of atopic dermatitis—Short version - German Society Dermatology ³⁶	91.67%	58.33%	65.63%	94.44%	16.67%	45.83%	83.33%	Yes
16	Guidelines for the management of atopic dermatitis in Singapore - Dermatological Society of Singapore	50.00%	19.44%	15.63%	61.11%	29.17%	0.00%	33.33%	No
17	A clinician's reference guide for the management of atopic dermatitis in Asians - Asian Academy of Dermatology and Venereology Expert Panel on Atopic Dermatitis ³⁷	77.78%	41.67%	39.58%	77.78%	33.33%	50.00%	50.00%	No

18	Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis) in adults and children: part I, II - European Dermatology Forum (EDF), EADV, European Academy of Allergy and Clinical Immunology (EAACI), ETFAD, European Federation of Allergy and Airways Diseases Patients' Associations (EFA), European Society for Dermatology and Psychiatry (ESDaP), European Society of Pediatric Dermatology (ESPD), Global Allergy and Asthma European Network (GA2LEN), and European Union of Medical Specialists (UEMS) ^{38,39}	91.67%	88.89%	83.33%	88.89%	37.50%	62.50%	91.67%	Yes
19	Management of Atopic Eczema - Ministry of Health Malaysia ¹⁷	94.44%	72.22%	89.58%	91.67%	91.67%	87.50%	91.67%	Yes
20	Turkish Guideline for Atopic Dermatitis 2018 - Turkish Society of Dermatology ¹⁹	25.00%	13.89%	16.67%	66.67%	8.33%	0.00%	25.00%	No
21	Position paper of the diagnosis and treatment of atopic dermatitis in adults and children - European Task Force on Atopic Dermatitis/ European Academy of Dermatology and Venereology ⁴⁵	52.78%	27.78%	32.29%	75.00%	16.67%	62.50%	58.33%	No
22	Approach to the Assessment and Management of Pediatric Patients With Atopic Dermatitis: A Consensus Document. Section III + IV Canadian Dermatological Association ^{42,43}	75.00%	52.78%	58.33%	75.00%	39.58%	66.67%	75%	Yes
23	Consensus on the therapeutic management of atopic dermatitis - Brazilian Society of Dermatology ⁴⁰	52.78%	25.00%	29.17%	69.44%	27.08%	58.33%	41.67%	No
24	Guidelines on Management of Atopic Dermatitis in India: An Evidence -based Review and an Expert Consensus - Indian Dermatology Expert Board Members	88.89%	41.67%	45.83%	83.33%	18.75%	8.33%	58.33%	No
25	Italian guidelines for therapy of atopic dermatitis—Adapted from consensus-based European	77.78%	47.22%	66.67%	61.11%	10.42%	16.67%	58.33%	Yes (continued)

	Guideline Name	Domain 1: Total Score	Domain 2: Total Score	Domain 3: Total Score	Domain 4: Total Score	Domain 5: Total Score	Domain 6: Total Score	Overall quality	Cut-off met
	guidelines for treatment of atopic eczema (atopic dermatitis) - SIDEMAST (Italian Society of Medical, Surgical and Aesthetic Dermatology and Venereology), ADOI (Italian Society of Dermatologists and Venereologists Hospital-based and Public Health), and SIDAPA (Italian Society of Allergological Occupational and Environmental Dermatology) ⁴¹								
26	Taiwanese Dermatological Association consensus for the management of atopic dermatitis: A 2020 update. ⁴⁶	77.78%	27.78%	40.63%	72.22%	4.17%	25.00%	50.00%	No
27	Guidelines for the diagnosis and treatment of atopic dermatitis in China - Chinese Society of Dermatology Immunology ⁴⁷	52.78%	36.11%	14.58%	50.00%	8.33%	8.33%	33.33%	No
28	Clinical practice guidelines for the Management of Atopic Dermatitis 2021 - Japanese Dermatological Association ⁴⁸	88.89%	47.22%	61.46%	75.00%	33.33%	95.83%	66.67%	Yes
	Average domain score	70.24%	42.46%	45.20%	73.21%	24.11%	39.43%	56.58%	

Table 4. (Continued) Domain scores for AGREE II appraisal

(applicability) had the lowest average score of 24%, with only 3/28 guidelines scoring over 50%. The score given for overall quality generally correlated with a satisfactory cut-off score, indicating a high value placed on rigour of development (Domain 3) by the reviewers. There were 2 guidelines that had an overall quality of over 50% that did not meet cut-off criteria as the score for rigour of development was below 50%. 44,45

DISCUSSION

This review identified, compared, and quality appraised 28 guidelines that included recommendations for the management of paediatric AD. While a similar review was conducted by Wang et al, ⁵⁰ this review differs as it considers guidelines developed between 2005 and 2021 and provides a more detailed comparison of management recommendations with specific reference to skin of colour.

Recommendations

There was little variation in management recommendations with regards to emollients, topical steroids, topical calcineurin inhibitors, phototherapy, managing infections, and immunosuppressants. Other similar management strategies included education and avoiding environmental triggers. Although early onset eczema is a risk factor for developing food allergies, ⁵¹ almost all guidelines were in line with recommendations to avoid elimination diets and allergy testing in patients unless clinically implicated. ^{17,19,37-48}

Some discrepancies were found regarding skin care measures. Three guidelines had differing information surrounding traditional emollients^{37-39,42,43} Emollients containing food protein are not usually recommended due to concerns related to the risk of allergic sensitisation. However, a review published in 2018 reported no adverse events when using coconut oil as an emollient for AD.⁵² There were differing recommendations as to whether emollients should be applied before or after topical therapies; however, a randomised controlled trial (RCT) that directly compared the 2 methods found no significant difference in severity and this was also reflected in the 2023 update for the

NICE guideline. 16,53 Use of bleach baths had degrees of evidence varvina recommended by 50% of the guidelines. In a systematic review from 2022, use of bleach baths was associated with a clinician-reported improvement in severity by 22% for patients with moderate-to-severe AD. There was low certainty evidence that bleach baths reduce staphylococcus aureus colonisation or patient-reported improvement in severity.⁵⁴ With regards to bath additives (recommended in 4/12 guidelines), a large RCT of 483 children examined their effectiveness, and found no significant change in severity compared to no additives for 12 months.⁵⁵ Further research beneficial support be to recommendations in future guidelines.

Overall, the guidelines lacked information about the age cut-offs for certain medications in AD management. Topical calcineurin inhibitors are only approved in children over 2 years of age, however, as stated in 3/12 guidelines, 0.1% tacrolimus is often used off-label in infants. There are a lack of studies in children under 2 years; however, 1 large 3-year clinical study from Finland found it was safe to use in moderate to severe AD. 56 In 2019, dupilumab was approved by the United States Food and Drug Administration (FDA) for use in children with moderate-severe AD 12 years and older. Multiple guidelines published after this time only recommended use in adults. 40,41,44,47 It was then extended for use in children 6 years and older in 2020, followed by 6 months in 2021. The most recent guideline from Japan in 2021, is the only guideline to recommend use in any age group.48 Future quidelines should be updated to reflect these changes.

Multiple guidelines recommended newer therapies such as topical PDE4 inhibitors. Crisaborole is approved by the Food and Drug Administration, Therapeutic Goods Administration, and European Union in mild-moderate AD for ages 2 and older. The 2021 NICE guideline did not recommend its use due to insufficient evidence from clinical trials. Oral antihistamines for pruritis are another point of contention. Although sedating antihistamines are widely used to help with sleep and pruritis, there remains low quality evidence for their use as an add-on therapy.

Skin of colour

Very few guidelines discussed eczema management in skin of colour in detail. Most guidelines were from Asia, 1 was from the United Kingdom and 1 from Latin America. As we live in a multicultural, alobalised world, it is important for all quidelines to generate an understanding of AD management in all skin types. Two guidelines mentioned phenotypical differences in skin of colour. These include differences Asian, European, and African peoples' filaggrin gene mutations, total epidermal water loss, and the expression of T helper (TH) 2, Th22, Th17, and Th1 pathways. The different ways AD can present were mentioned in 3 quidelines. Asian people are more likely to have psoriatiform lesions, and Black people may have distribution on the extensor surfaces, perifollicular papules, and a lichen planus appearance. Other known signs in skin of colour include Dennie-Morgan lines, diffuse xerosis, palmar hyperlinearity, prurigo nodularis and postinflammatory hypopigmentation. **7,9,59,60** The ability to recognise these features should be enforced in all guidelines.

Erythema often presents as violaceous in skin of colour, therefore scoring systems like the Scoring Atopic Dermatitis (SCORAD) index and the Eczema Area and Severity Index (EASI) which use redness as a marker of severity can be less accurate at identifying severe cases. 61-63 The pattern of lichenification in these scoring system also differs with skin of colour, where chronic lesions can appear follicular in darker skin rather than like deep furrows in Caucasian skin.⁶⁴ In addition these scores are often used to measure response to biological treatments, which again limits their use in skin of colour. The NICE guidelines did mention this, however did not provide alternatives to severity assessments. Some alternative scoring systems were mentioned in the Chinese guidelines. 47 Future guidelines should provide information on the different clinical presentations and markers of severity for skin of colour as described above. They should also incorporate specific information on the efficacy and side effects of these therapies for skin of colour. Some key differences in the literature include a risk of increased irritation from emollients due to higher rates of skin sensitivity, high-dose steroid induced hypopigmentation, and a lesser response to phototherapy or side effects of dyspigmentation and melasma. 7,9,59,60 There were no guidelines that discussed these management considerations in detail, therefore future guidelines should address this. The overall lack of information in the guidelines suggests that more research is needed with a diverse population to further characterise these differences.

AGREE II appraisal

Less than half of the guidelines met our criteria for a high-quality guideline based on the AGREE II assessment. Of the 19 guidelines in the Wang et al appraisal, 3 were recommended for use in practice (level A), 11 were recommended with revision (level B), and 5 were not recommended (level C). Our reviews, however, used different approaches to setting the standards for high quality guidelines. Our cut-off criteria required a score of >50% in Domain 3 (rigour of development) and 2 other domains. Wang et al. required scores of >60% across all domains for level A, and 30-60% for level B.⁵⁰ It is therefore difficult to compare our appraisal outcomes.

Most guidelines adequately outlined the intended audience and purpose of the document. Stakeholder involvement was generally well documented however lacked all relevant professional groups who would be involved in the care of AD such as allied health professionals and nurses. Moreover, researchers or methodology experts were rarely included, and only 3 guidelines included patients/community members in the development. As a chronic condition, a large component of management for AD includes patient education and family involvement, therefore involving the consumers in the guideline development process is essential to help create better outcomes for patients.

Guidelines that used systematic grading of evidence such as the Grading of Recommendations Assessment, Development and Evaluation (GRADE) tool scored higher, ^{15-18,25-29,31,32,37-39,44} as did those with summary tables of evidence under each recommendation. ^{15,18,25-29,31,32,37-39,41,48} The Malaysian, Scottish, and NICE guidelines scored highly and used the AGREE II tool in the development process. ¹⁶⁻¹⁸

Clarity of presentation was overall done well, however it was noted that some graphics did not correspond to the information in the guidelines, such as an image of a palm to describe a fingertip unit.³⁷ Most guidelines used clear headings and summary tables which assist the reader with identifying key points of information. This was consistent with the Wang et al appraisal, where clarity of presentation had the highest average scores.⁵⁰

Applicability had consistently low scoring across the guidelines. To achieve high scores in applicability according to AGREE II, guidelines had to describe facilitators and barriers to application, provide tools on how to put recommendations into practice, discuss resource implications and provide monitoring criteria. While many guidelines had some summary tables, they rarely documented barriers to application aside from mentioning factors like steroid phobia, without a clear plan to overcome this barrier. Furthermore, cost and resource implications were not discussed in detail beyond generic statements about AD having high costs to patients. These guidelines therefore received scores of 1-3 depending on their level of detail addressing this domain. Details of editorial independence were often lacking, and there was a range of scoring for this domain, with some guidelines having no funding or conflict of interest statements, giving a score of 1, and others having long lists of conflicts of interest without explaining how the conflicts of interest were addressed, which received a score of 2. Without these details, the transparency of the guidelines decreases. Applicability was similarly the lowest scoring domain in the Wang et al study. 50

Limitations

While systematic methods were used to search for the guidelines, a possible limitation would be missing guidelines due to the wide range of document types. The AGREE II tool itself is also subjective and can be interpreted differently by reviewers. The reviewers noted that the 7-point scale was challenging to use, especially the difference between scores of 3 and 4. One strategy that may help with minimising discrepancies could be for the reviewers to create their own checklist for each AGREE II domain for more consistent results. In addition, while the AGREE II tool can be useful in guideline development, it does not provide standardised cut off thresholds, resulting in differing outcomes of appraisals.

CONCLUSION

The results of this systematic review demonstrate the strengths and weaknesses of the existing AD guidelines and highlights areas for future guidelines to improve. Management strategies were generally consistent over the last 5 years. The quality of the guidelines varied with less than half of the guidelines meeting the criteria for a high-quality guideline, indicating that future guidelines would benefit from using a tool such as AGREE II in their development process. Recommendations regarding AD management in skin of colour were lacking across all guidelines. There is a strong need for future guidelines to consider these factors to better reflect the diverse population of patients with AD.

Abbreviations

AD: Atopic dermatitis; AGREE: Appraisal Guidelines for Research and Evaluation; PDE4: Phosphodiesterase-4; UVB: Ultraviolet B; PUVA: Psoralen plus ultraviolet-A radiation; RCT: Randomised controlled trial; TH: T helper; SCORAD: Scoring Atopic Dermatitis; EASI: Eczema Area and Severity Index; GRADE: Grading of Recommendations Assessment, Development and Evaluation

Availability of data and materials

Not applicable.

Author contributions

The lead author, SV and MN conducted the literature search, data extraction and the AGREE II appraisal. The lead author initially drafted the publication and all other authors have contributed substantially to the writing of this publication.

Ethics approval

Not applicable.

Consent for publication

All authors consent to this work being published.

Conflict of interests

Dr Deva reports no competing interests.
Dr Netting reports no competing interests.
Ms Weidinger reports no competing interests.
Dr Brand reports no competing interests.
A/Prof Loh reports no competing interests.
Dr Vale reports no competing interests.

Funding

The Perth Children's Hospital Foundation, Grant number 9774.

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