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ORIGINAL RESEARCH

Download Clinical Guidelines

Atopic dermatitis in adults: An Australian management consensus

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ABSTRACT

Background/Objectives: Atopic dermatitis (AD) has significant negative impact on health-related quality of life, mood, sleep, work productivity and everyday activities. Research into the use of new drugs in the management of AD continues to develop, and international updates and recommendations have been published. However, questions remain in the Australian setting. This consensus aims to provide evidence-based insights and practical advice on the management of adult AD in Australia.

Methods: A panel (five dermatologists and one clinical immunologist) met to review the literature, critically examine clinical questions of relevance to Australian healthcare practitioners and develop a series of recommendation statements. A consensus panel, comprising the initial panel plus nine additional members, used a 2-round Delphi voting process to determine a set of final guidance statements. Consensus: ≥75% agreement in the range 7–9.

Results: Round 1 voting comprised 66 guidance statements. Of these, consensus was reached on 26, which were retained, and five were removed. The remainder (35) were modified and one new guidance statement was added for inclusion in round 2 voting. After round 2, consensus was reached on 35, which were retained, and one was removed (considered redundant). The 61 guidance statements upon which consensus was reached were then used to support a series of core consensus recommendations and a management flow chart.

Conclusions: Expert consensus recommendations providing practical guidance of clinical relevance to specialists and primary care physicians in Australia have been developed. Dissemination of this guidance and evaluation of its impact on patient outcomes remain to be undertaken.

Key words: algorithm, atopic dermatitis, recommendations, severity, treatment.

INTRODUCTION

Atopic dermatitis (AD) is a chronic, relapsing, inflammatory, pruritic skin condition, affecting both children and adults, that negatively impacts on quality of life (QoL).[1] Its aetiology involves a complex interaction of a dysfunctional skin barrier, immune dysregulation, individual genetics and environmental factors. There is now focused research interest on the interplay of the epidermis and immune system in patients with AD;[2] multiple molecular targets are being explored with agents in development that target specific components of the immune system[2] and inflammation-related itch.[2] This has prompted several international updates, and consensus 'best practice' recommendations have been published.[3–5] The aim of this consensus is to provide evidence-based insights and practical advice on the management of adult AD in Australia.

MATERIALS AND METHODS

A core panel, comprising five dermatologists and one clinical immunologist, met to discuss current practices, identify key clinical questions in the management of AD in Australia (Table S1) and to agree on programme objectives and methodology. A systematic literature review was then conducted with the assistance of a medical writer (Table S2). Two of the core panel members examined the literature and developed a summary report comprising background information and draft guidance statements to answer the previously identified clinical questions. Where appropriate data existed, the quality of evidence supporting each draft guidance statement was rated using the National Health and Medical Research Council Evidence Hierarchy and Assessment Matrix.

The six core panel members reviewed, revised and refined the draft guidance statements. They also developed a draft AD management flow chart, based on a combination of clinical acumen, existing published algorithms and the draft guidance statements. After this, a multidisciplinary consensus panel (the Panel) of 15 participants was formed, comprising three additional dermatologists, two additional clinical immunologists, two general practitioners, a dermatology nurse and a pharmacist to ensure a panel representative in terms of both clinical expertise, geography and practice type. The Panel reviewed and voted on the draft guidance statements and the management flow chart, using a modified Delphi process. The consensus process included two rounds of remote voting, during which members voted anonymously using a 9-point scale (1 strongly disagree; 9 strongly agree). For each statement and for the management flow chart, consensus was defined as achievement of ≥75% agreement in the range 7–9.

After round 1 voting (12-26 April 2018), the medical writer collated all responses and prepared an anonymised summary report independently of the Panel. The report was provided to the panel, and a second round of voting was undertaken. Statements voted on in round 2 (3-14 May 2018) were fewer and comprised re-phrased items for which there was either no consensus or for which wording clarification was suggested in round 1 voting. A further anonymised summary report was prepared after round 2 voting. At the completion of both voting rounds, a strength score (the median score) and a level of consensus (proportion of voters with a score of 7-9) were assigned to each guidance statement. During manuscript preparation, word count restriction necessitated that the guidance statements be divided into those deemed of core relevance to clinical practice and those that provided additional context.

RESULTS

Literature searching identified 3377 references, of which 104 were relevant to the current consensus project. Initially, 66 draft guidance statements were developed, and, at the completion of the round 1 voting, 36 draft guidance statements were refined and voted on again in round 2.

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Conflict of Interest: SS, PF, CB, KG, DR and BF received an honorarium from Sanofi Genzyme Australia Pty Ltd for their involvement in an initial working group to determine the parameters of this research project. The authors were responsible for all content, interpretation of the data and the decision to publish the results; they received no honoraria related to the development of this manuscript. The authors confirm independence from the sponsor. Sanofi Genzyme Australia Pty Ltd markets dupilumab (Dupixent®). The sponsor was given the opportunity to review the manuscript prior to submission, but has not influenced the content of the article. SS, KG, DR, AH, PF and EM have received honoraria from Sanofi Genzyme (Australia) for advisory board participation. CB, DR, KG and PF have received research support and funding from Sanofi Genzyme (Australia). AH has received speaker fees from Sanofi Genzyme (Australia). MS has received sponsorship from Sanofi Genzyme (Australia) to attend a conference. All other authors declare that they have no conflict of interest. SS has received honoraria from Pfizer (Australia) for advisory board participation and has been a Principal Investigator for clinical trials with AbbVie. PF and KG have received honoraria from AbbVie, Leo Pharma, Lilly, Novartis and Pfizer (Australia) for advisory board participation. PF has received research support and funding from AbbVie, Leo Pharma, Lilly, Novartis and Pfizer. DR has received research support and provided consultation services for AbbVie, Botanix, Leo Pharma, Lilly, Novartis and Pfizer. WW has received honoraria from AbbVie, Leo Pharma, Novartis, Lilly, Pfizer and Mayne Pharma for advisory board participation. BF, NL, MR, CS, JB, MS, HPS and WW report having no conflicts to declare.

A/Prof Saxon Smith accepts full responsibility for this work, had access to the data and controlled the decision to publish.

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Voting analysis

Members of the Panel were invited to vote on all guidance statements at each voting round, but were permitted to abstain from voting on statements outside their area of expertise. The majority voted on all statements at each voting round. In round 1, 5/15 (33%) respondents declined to vote on at least one statement; in total, 15 statements were not voted on by all members of the Panel, but there was no overlap on these statements (three respondents each declined to vote on a single statement, one respondent 2 statements and a third respondent 12 statements). In round 2, only one respondent declined to vote and did so for 8 statements.

After round 1 voting, the median strength of recommendation was ≥7 for all 66 statements, with the exception of one item in the treatment goals section relating to the timeframe of response to emollients and wet dressings, for which the median score was 5.5. The target level for consensus (≥75%) was met for 56/66 (84.8%) of the statements. Amongst these, 26 were retained, 4 were removed and 26 were modified (required wording clarification) and of the 10 statements for which consensus was not reached, 9 were modified and 1 was removed. Items voted on in round 2 were fewer and comprised re-phrased statements for which there was either no consensus (9 statements) or for which wording clarification was suggested (26 statements) in round 1 voting and one new statement. After round 2 voting, the median strength of recommendation was ≥7 and consensus was achieved for all 36 statements. One statement was removed as it was deemed to be redundant, and wording clarification was suggested for 7/36 (19.4%) statements.

Consensus recommendations

At the completion of the two voting rounds, consensus (≥75%) was achieved on 61 separate guidance statements (Table S3), which support the core consensus recommendations (Tables 1, 2 and 3) and management flow chart (Fig. 1).

DISCUSSION

While most adults with AD have a history of childhood disease, new onset in adulthood is common ranging from 18.5% (Germany)[6] to 54% [USA].[7] Prevalence of AD is rising,[8] but there is considerable countrywide variation in both prevalence and severity. The most widely accepted 1-year prevalence is 10.3%.[8] Gender differences have been reported, with a higher prevalence of adult AD amongst females (11.1% vs 9.1%, $P < 0.001$).[8] While a substantial (5-10%) increase in the prevalence of AD recently has been reported in Australia,[9] the true prevalence of AD in Australia is unknown.

Definition, diagnosis and severity of AD in adult patients

The Panel agreed that AD should be divided into two main categories, mild and moderate–severe, on the basis of treatment response. There was general agreement with the previously published definitions of mild and moderate–severe AD.[5] In addition, the Panel determined that further clarification of these definitions was required and agreed that '*responds adequately*' should be defined as '*significant periods of stable control of disease*'.

There was unanimous agreement on the definition of a flare (Table 1). However, defining flares based on intensity scoring is difficult because the level of tolerance to symptoms, particularly pruritus, can vary significantly between individuals. There was unanimous agreement that patients with AD are more likely to have disturbed sleep than healthy controls and that sleep disturbance worsens with AD severity.

While mild AD is often well managed in the primary care setting, the Panel agreed on criteria that should prompt referral. Specific timeframes for referral were excluded from the definition because the time taken to achieve therapeutic response varies between individuals and because of national variations in specialist access. Of note, standard therapy was explicitly not defined because it was agreed that therapy choices would (and should) be individualised according to patient disease status and severity.

Diagnosis of AD in adults is often achieved via a process of exclusion. The validated diagnostic criteria suggested by Hanifin & Rakja[10] were reviewed alongside systematic reviews and international AD guidelines (III C level evidence), and a diagnostic framework was agreed. There was majority consensus that there are no specific biomarkers that can be recommended for diagnosis and/or assessment of eczema severity, but this is an area of active research.[11] Food elimination diets and allergy tests are of limited benefit unless there is a personal history of IgE-mediated food allergy.[12]

In a systematic review of 135 studies that had assessed AD disease severity, 62 disease severity measures and 28 QoL scales were identified.[13] The Panel agreed that monitoring of immunoglobulin E level is not recommended for the routine assessment of disease severity and/or response to treatment. Similarly, the Panel determined that the routine use of the disease severity scales and scoring systems commonly used in clinical trials are too time-consuming for use in everyday clinical practice. However, adopting a simple scoring system for routine use in the specialist setting might be appropriate, and collecting serial data would more clinically meaningful than a single static score.

Although there is limited information about how AD severity is actually rated by patients and physicians, there is a reported discrepancy between how physicians and patients rate the severity of AD: patients tend to focus more on skin-related QoL outcomes while clinicians focus more on sleep disturbance.[14] The Panel unanimously agreed that effective communication between patients and physicians should be encouraged to ensure the management of atopic dermatitis is directed towards the needs of the patient and that patient-reported measures of disease severity are likely to be a useful adjunct to objective clinician assessment. The Panel further agreed that moderate–severe AD

Table 1 Definitions, diagnosis and severity of atopic dermatitis (AD)

Consensus recommendations	Strength	Consensus
Definition of mild AD: Mild AD refers to any patient whose condition responds adequately to optimised outpatient emollient use, avoidance of irritants and disease triggers, and standard topical anti-inflammatory therapies	9	93%
Definition of moderate-to-severe AD: Moderate-to-severe AD refers to any patient whose condition does not respond adequately to optimised outpatient emollient use, avoidance of irritants and disease triggers, and standard topical anti-inflammatory therapies	8	87%
Definition of a flare: A flare is an 'acute, clinically substantial worsening of signs and symptoms of AD requiring therapeutic intervention with increased quantities of anti-inflammatory therapy, or escalation to more potent immunosuppressive treatment, or hospitalisation'	9	100%
Criteria for specialist referral: Referral to a dermatologist/immunologist is advisable if a person's dermatitis is not responsive to standard treatment, if it causes significant distress and is interfering with sleep, school or work, if an allergy is suspected and/or if there are recurrent bacterial or viral infections	9	100%
Diagnosis of AD: Patients with presumed atopic dermatitis should have their diagnosis based on documentation of pruritus, typical morphology and distribution, chronic (or chronic relapsing) course and consideration of other diagnostic features, including: •Family history (bronchial asthma, allergic rhinitis and/or conjunctivitis, atopic dermatitis, IgE-mediated food type allergy) •Personal history (bronchial asthma, allergic rhinitis and/or conjunctivitis, IgE-mediated food allergy) •Follicular papules •Elevated serum IgE levels	8	87%
Severity of AD		
Choice of scales: Currently available scales for eliciting information on itch, sleep, impact on daily activity and persistence of disease should be used mainly when practical	8	93%
Suitable scales for measuring AD severity: For the purposes of quantifying severity, there should be a minimum of two patient-related measurements plus a direct measurement of sleep impact	8	93%
Measurement of disease impact: Validated QoL scales may be used to help document the impact of AD on the patient. Such tools include the dermatology life quality index (DLQI) and Skindex-16	8	100%
Measurement of sleep impact: Sleep impact can be measured using the 5-D pruritus scale (item 4) or the Patient-Oriented Eczema Measure (POEM) scale (item 2)	8	93%
Quantification of moderate–severe AD: Scores on the following scales are deemed to be representative of moderate-to-severe disease: •Dermatology life quality index (DLQI) ≥ 10 •Patient/physician global assessment (PGA) ≥ 3 •Body surface area (BSA) ≥ 10% •Pruritus ≥ 4	8	100%

could also be defined based on the extent and severity of lesions and/or significant impact on QoL and that when determining disease severity, other qualifying situations that could be taken into account include lesion location (hands, face, genitals, scalp), frequency of flares and frequent hospital admissions due to flares.

The final, and unanimous, position of the Panel was that for the purposes of quantifying severity, there should be a minimum of two patient-related measurements plus a direct measurement of sleep impact. It was determined that the dermatology life quality index (DLQI) is suitable for use in the specialist setting, but not for use in the primary care setting, leading to the recommendation that for general practitioners, it may be sufficient to adopt an open-ended approach in which the patient is asked about the impact of itch on sleep (e.g. in the last week, month, 3 months [depending on timing between consults]) and how frequently they woke up due to pruritus. To aid with quantification, if DLQI and pruritus scores are not undertaken, either a visual analogue scale or numerical rating scale was deemed suitable for evaluating overall severity, pruritus or sleep disturbance, in daily clinical practice. In such instances, patients should indicate their average and maximum pruritus within the past 4 weeks on a scale from 0 (no pruritus) to 10 (maximum pruritus).

Impact of comorbidities and QoL

Risk of major comorbidities is significantly increased in adult patients with AD compared with controls.[15] Elucidating the comorbidities of AD, such as depression, anxiety and suicidal ideation, is therefore important for disease management and improving overall clinical outcomes.[15]

Atopic dermatitis has a significant impact on mood and sleep, health-related QoL, work productivity and everyday activities, similar to psoriasis.[16] Australian data show that 36% of patients spent over 10 min per day applying treatments, 28% indicated that their skin disease influenced the clothes they wore, 21% felt embarrassed by their skin and 15% reported problems with treatments.[17] However, there appeared to be a relationship between increased morbidity and increased severity. In clinical trials, despite 48.2% of patients using systemic therapies in the past year, many reported problems with itch frequency (85% of patients), duration (41.5% reported itching ≥18 h/day) and severity (6.5 of 10 on numeric rating scale), and 55%

Table 2 Treatment goals and treatment choices

Consensus recommendations	Strength	Consensus
Treatment goals		
Overall treatment goal: The goal of treatment is to reach and maintain a state in which symptoms are absent or mild without daily activities being disturbed by AD, treatment impacts minimally on quality of life, and there are no/minimal drug-related toxicities	9	100%
Definition of treatment failure: Treatment failure, despite appropriate dose and duration of and adherence to a therapeutic agent, may be defined by one or more of the following: •Inadequate clinical improvement, •Failure to achieve stable long-term disease control, •Presence of ongoing impairment (e.g. pruritus, pain, loss of sleep and poor quality of life) while on treatment, •Unacceptable adverse events or poor tolerability experienced with the treatment	8	100%
Quantification of treatment success:† If DLQI ≤ 5 and/or PGA‡ has improved by at least 2 points from a baseline of ≥ 3, then treatment success has been achieved and appropriate maintenance therapy can be commenced	8	87%
Quantification of treatment failure: If DLQI ≥ 6 and PGA has either not improved or improved by less than 2 points, then treatment success has NOT been achieved and a change or modification to the treatment regimen is recommended	8	93%
Treatment choices		
Considerations to escalate therapy: It is important to ascertain whether failure of topical treatment is due to the severity of the disease (lack of efficacy of topical therapy), incorrect usage (dose/application), intolerance or lack of adherence to the treatment when making the decision to begin systemic therapy	9	100%
Definition of intolerance to topical treatment: Patient's opinion of worsening of lesions after 1-2 weeks of therapy with a new topical treatment or any difficulty to apply the drug (pain, burning or any uncomfortable sensation, which may develop sooner	8	100%
Definition of resistance to topical treatment: Physician's opinion of a situation with unchanged or aggravated clinical score after at least 4 weeks of appropriately dosed and performed treatment, in the absence of an acute adverse reaction	8	100%
Choice of phototherapy: Phototherapy (narrowband ultraviolet B [NB-UVB] or ultraviolet A1 [UVA1]) should be considered before the use of other systemic therapy if accessible and practical	8	93%
Compliance considerations: Phototherapy is usually safe and well tolerated, but adverse events due to sensitive skin in AD patients may impact compliance	8	100%
Use of systemic corticosteroids: Systemic corticosteroids are effective, but associated with short-term and long-term adverse events; use should be limited to bridging, rescue of flares, anticipation of a major life event or in patients with severe AD	9	93%
Use of systemic antimicrobial agents: Systemic antimicrobials should be reserved for short-term use only in the majority of patients with infected AD, excluding those with hyper-IgE and immunosuppression	8	93%
Use of other systemic therapies: Considering currently available data and the safety profiles of systemic therapies that are approved by the Australian Therapeutic Goods Administration (TGA) to treat AD, it is recommended that dupilumab could be considered as a first-line systemic treatment option in adults with moderate-to-severe AD who are uncontrolled with topical therapies	8	86%

†This is not intended to be a definitive measure of clinically meaningful improvement, rather a gauge as to whether the optimal goal for a patient's condition has been reached.

‡PGA = physician's global assessment: How is the patient's atopic dermatitis today? [0] Clear, [1] Almost clear, [2] Mild, [3] Moderate, [4] Severe.

reported AD-related sleep disturbances on 5 days or more each week.[18] Hospital Anxiety and Depression Scale scores suggesting clinically relevant anxiety or depression were reported by 21.8% of patients.

The overall impact of AD on the patient's QoL was a core focus of Panel discussions with resultant recommendations regarding how to elicit and utilise QoL information in clinical practice.

Treatment goals

The Panel reached a unanimous decision on the overall goal of AD treatment. However, they also established that there are no formally published criteria for defining treatment failure, leading them to adopt the definition proposed by Boguniewicz *et al.*[3]

Specific quantifications for treatment success and failure were evaluated, resulting in recommendations. Success was defined as a DLQI ≤ 5, and/or physician global assessment (PGA, 5-point measure) has improved by at least 2 points from a baseline of ≥3. Failure was defined as a DLQI ≥ 6, and PGA has either not improved or improved by less than 2 points. Although these numerical cut-off targets offer some level of guidance, it remains important to take a pragmatic view and consider the individual patient holistically. For example, serial measurements, and related change scores, may provide more information about overall response than does a single static score.[5] Within the confines of these definitions, commencement of maintenance therapy refers to continuing on the current therapy or tapering doses of current therapies depending on the individual patient's treatment regimen.

Table 3 Patient perspectives: comorbidities, quality of life and education

Consensus recommendations:	Strength	Consensus
Impact of comorbidities and quality of life		
The impact of AD on QoL should be assessed when determining treatment options	9	100%
Physicians should be aware of, and assess for, conditions associated with AD	9	100%
The presence of comorbidities has an increased, and overall negative, impact on QoL in patients with AD	9	100%
In patients with AD, the presence of comorbidities compounds the effects of usual care and impacts on treatment choices	9	93%
Understanding the patient's perspective is relevant when considering management options	9	100%
Patient education and trigger avoidance		
Educational intervention: Both Internet-based and face-to-face approaches probably improve self-management and outcomes for patients, but the optimum means of delivering support in a cost-effective way has yet to be determined	8	79%
Trigger avoidance: Available clinical trials provide some limited support of a benefit of dust mite avoidance measures in dust mite allergic individuals. There is not sufficient high-quality evidence to make recommendations for environmental trigger avoidance measures in patients with AD	8	100%

Noting that timeframes to response times will likely differ according to disease severity, disease location and patient factors, the Panel considered the optimal duration of a trial of different therapeutic options before an inadequate response could be considered a treatment failure (Table 4).

Treatment choices

General measures

All general skin measures (soap-free wash, moisturiser, short, lukewarm showers, bath oils) should be maintained as a constant background therapy in all patients. Moisturisers are a cornerstone of therapy and should be included in the daily management plan.[19] Clinicians should optimise general measures and topical therapy before considering systemic medications for AD, unless the impact on QoL is substantial at the initial consultation.

Susceptibility to *Staphylococcus spp.* colonisation is recognised in AD, where it is associated with increased frequency and severity of flare.[20] Topical anti-staphylococcal agents are increasingly used as ancillary therapy for the management of AD, either clinically to manage existing infection or prophylactically in individuals who are at risk of colonisation or infection.[21] While available studies suggest some benefit to the use of such agents in AD management, good-quality clinical data supporting their use are limited, particularly with regard to long-term outcomes. Available data support the daily use of emollients and topical corticosteroids as a strategy to reduce colonisation.[21] Regulatory authorities in Europe and the United States have removed triclosan from personal care soap products. Given the ongoing regulatory debate, consensus on the use of antimicrobial agents as ancillary therapy in the management of AD was not formally collected. Current best practices include the use of systemic antibiotics and initiation of antiseptics (particularly dilute bleach baths).[22]

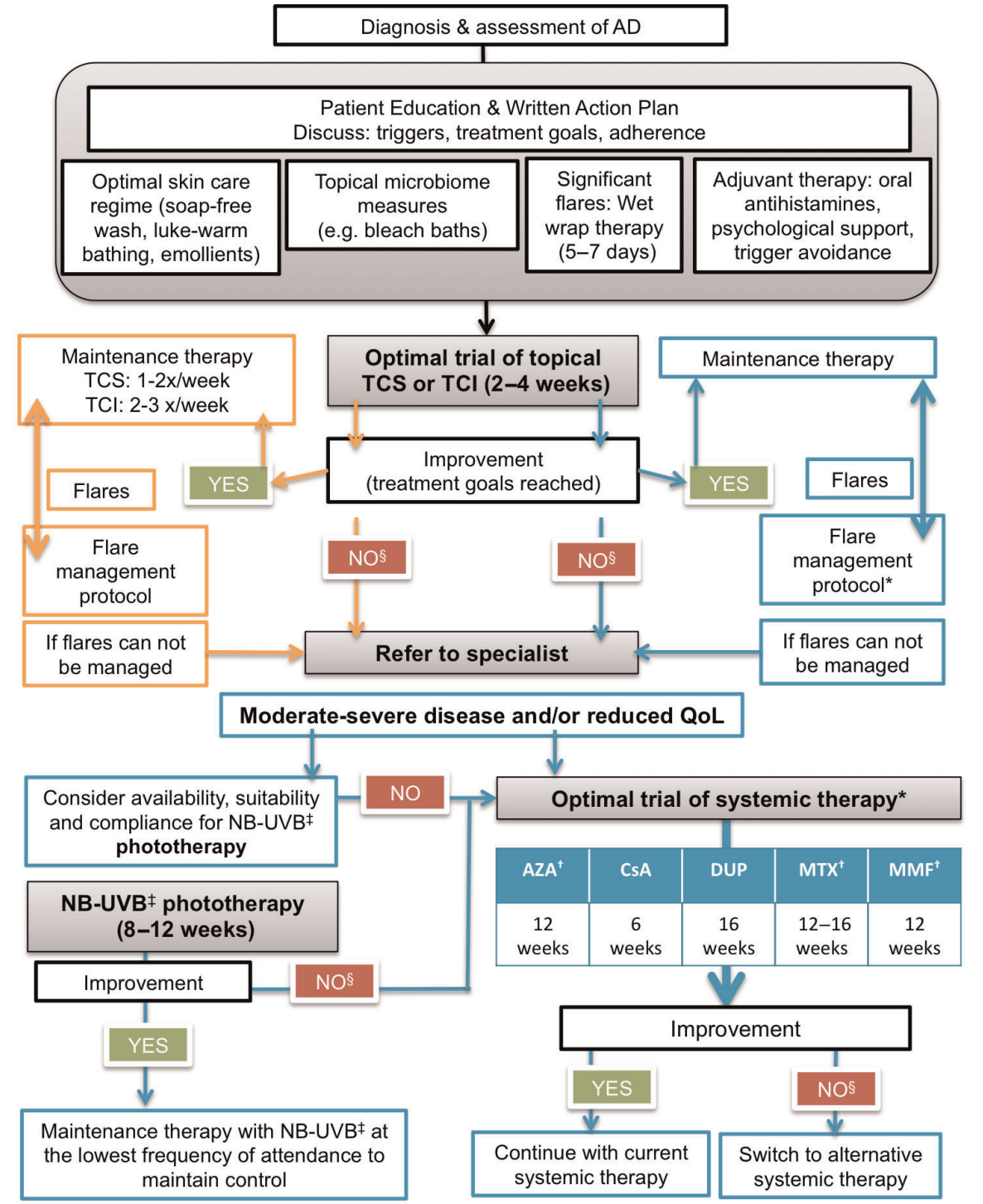
While much research has been undertaken to better define environmental risk factors in AD, the Panel agreed that, with the exception of dust mite avoidance measures in dust mite allergic individuals,[23] there is not sufficient high-quality evidence to make recommendations for environmental trigger avoidance measures (such as food elimination diets) in patients with AD.

Topical therapies

When considering the use of topical corticosteroids (TCS), the Panel adopted the same position as Boguniewicz *et al.*[3]: '*Given the range of potency and dosage forms of corticosteroids, the recommended regimen for topical treatment use is up to 4 weeks at a time for active treatment and 2-3 times weekly application at sites prone to recurrence for preventative treatment. In selected patients and specific body sites, treatment for longer than 4 weeks may be necessary*'. Judicious use of TCS is warranted; continuous application for long periods of time should be avoided to limit cutaneous side effects (e.g. skin atrophy, folliculitis).

Consideration of when to escalate therapy resulted in the recommendation that it is important to ascertain whether failure of topical treatment is due to the severity of the disease (lack of efficacy of topical therapy), incorrect

Figure 1 Management flow chart for adult atopic dermatitis (AD) patients in Australia. Orange boxes and arrows depict patients with mild disease, and blue boxes and arrows depict patients with moderate–severe disease. Refer to main text and Table 1 for definitions of disease. * Short-term systemic corticosteroids should be limited to: bridging, rescue of acute flares, anticipation of a major life event or in patients with very severe disease. †Indication not approved for atopic dermatitis. ‡UVA1 where available. § Treatment failure, despite appropriate dose, duration and adherence = inadequate clinical improvement or failure to achieve stable long-term disease control or presence of ongoing impairment while on treatment or unacceptable adverse events or poor tolerability. The management flow chart is intended for use primarily in the specialist setting rather than in primary care. Algorithm originated from concepts presented in Lynde, 2017 (Canada),[4] Simpson, 2017 (International Eczema Council, IEC),[5] Saeki, 2017 (Japan),[1] Drucker, 2017 (IEC: Systemic corticosteroid guidance)[29] and Gooderham, 2017 (maintenance data topical corticosteroids [TCS] and topical calcineurin inhibitors [TCI]).[30]



Follow orange boxes for patients with mild disease and blue boxes for patients with moderate-severe disease

AZA= azathioprine, CsA = Ciclosporin A, DUP = dupilumab, MTX = methotrexate, MMF = mycophenolate mofetil
* Short-term systemic corticosteroids should be limited to: Bridging, rescue of acute flares, anticipation of a major life event or in patients with very severe disease. † Indication not approved for atopic dermatitis. ‡ UVA1 where available.
§ Treatment failure, despite appropriate dose, duration and adherence = inadequate clinical improvement OR failure to achieve stable long-term disease control OR presence of ongoing impairment while on treatment OR unacceptable adverse events OR poor tolerability.

usage (dose/application), or intolerance or lack of adherence to the treatment when making the decision to begin systemic therapy. Definitions of resistance and intolerance to topical treatment were largely similar to those suggested in the ETFAD/EADV Eczema Task Force position paper,[24] with additional leniency around the timeframes applied.

Phototherapy

Several established guidelines recommend phototherapy as second-line or adjuvant therapy in adults and appropriately aged children with moderate–severe AD.[5] Available options include narrowband ultraviolet B (NB-UVB; 311–313 nm), ultraviolet A1 (UVA-1; 340–400 nm) and UVA therapy plus 8-methoxypsoralen (PUVA).[25] Overall, the data support good efficacy (strength B, based on level II evidence); however, the beneficial effect varies depending on the modality used. NB-UVB is frequently chosen due to its efficacy, availability, good tolerability and good safety profile, but no significant differences in improvement of clinical scores have been observed in trials comparing it with UVA1 in patients with moderate-to-severe AD.[26] When utilising phototherapy, emphasis should be placed on selecting an appropriate treatment modality and setting (e.g. avoiding solariums).

For optimal benefit, a prolonged treatment course of UV is usually required which often results in poor compliance. Therefore, the Panel unanimously recommended a change or modification to the treatment regimen if the patient shows no observable response within 8–12 weeks, or if AD recurrently flares during phototherapy.

Lack of efficacy and other patient-centric factors limit compliance with phototherapy more often than do the occurrence of adverse events. However, the Panel agreed that due consideration should be given to discontinuation of phototherapy if some systemic treatments (e.g. ciclosporin or azathioprine) are initiated to avoid the synergistic risk of inducing skin malignancy. Adverse events related to the use of phototherapy in patients with psoriasis are well established (e.g. photodamage, xerosis, erythema, actinic keratosis and sunburn) and should therefore also be considered in patients with AD. Having considered the available data, consensus was reached that except for PUVA, the risk of carcinogenesis associated with phototherapy has not been established and is considered low.

Table 4 Optimal duration of trial to establish treatment response to different therapeutic approaches

Therapy	Optimal trial duration[†]	Strength	Consensus
Topical therapies:			
Wet dressings	Several (5–7) days	8	86%
Topical corticosteroids	2-4 weeks	8	100%
Topical calcineurin inhibitors	2-4 weeks	8	100%
Phototherapy[‡]	8-12 week	9	100%
Systemic therapies:			
Ciclosporin	6 weeks	8	93%
Azathioprine[§]	12 weeks	8	93%
Methotrexate[§]	12-16 weeks	8	93%
Mycophenolate mofetil[§]	12 weeks	8	93%
Dupilumab	16 weeks	8	93%

[†]Timeframes to response times may differ according to disease severity, disease location and patient factors.

[‡]Narrowband ultraviolet B (NB-UVB) or ultraviolet A1 (UVA1).

[§]Not approved by the Australian Therapeutic Goods Administration (TGA) to treat atopic dermatitis.

Systemic therapies

Careful consideration is required before commencing systemic therapies to manage AD. The Panel agreed that all patients who fail to respond to optimised topical therapy should be evaluated for exacerbating factors (e.g. infection, psychiatric or behavioural issues) and for alternative diagnoses (e.g. allergic contact dermatitis). Additionally, there was agreement with the International Eczema Council recommendation that severity-based scoring systems alone cannot determine the need for systemic therapy and an holistic assessment is needed.[5] In considering what such an assessment should involve, it was determined that the decision to start systemic therapy depends on disease severity, impact on QoL, and the risks and benefits of systemic therapies for the individual patient. Noting that the application of topical therapies can be time-consuming, the Panel unanimously agreed that systemic therapy could also be justified in patients who require overly complex topical regimens that are unfeasible for their particular situation.

Choice of systemic therapy was reviewed in terms of the quality of data to support clinical efficacy and safety profiles. Approved systemic treatment options in patients with moderate–severe disease are limited, with many medications being used off-label. A review is currently underway with the aim of providing a comprehensive, comparative evaluation of systemic treatments in AD including ciclosporin, methotrexate, azathioprine, mycophenolate, corticosteroids, interferon-gamma, intravenous immunoglobulin, dupilumab and other novel systemic agents.[27] Recognising that current data are limited, and that new treatment options are becoming available, several recommendations were made regarding potential treatment pathways with regard to systemic therapies (Fig. 1); lack of comparative data precluded allocation as to which should be tried first.

Patient education

Given the discrepancy between clinician- and patient self-reported rating of adherence to medical instructions (80% vs 30%), education has emerged as a key component in the management of AD.[28] The Panel agreed that education was paramount and should be the first-line intervention of choice if topical therapy failure was related to lack of adherence and/or phobia regarding the use of TCS.

The literature defining specific factors contributing to poor treatment outcomes in adults with AD is limited, but

proposals include regimen complexity, frequency of follow-up and TCS phobia. Specific topics to be covered in patient education were not defined by the Panel. Optimal parameters for the delivery of patient education were equally hard to define. There was unanimous agreement that early and frequent follow-up of patients may facilitate treatment adherence and majority agreement that written action plans are useful education adjuncts to verbal instructions. The Pharmacist representative on the Panel noted concise directions written on the script can be reinforced at the time of dispensing and may further aid adherence. Structured educational programmes are of merit and can influence many aspects of patient care including coping behaviours and overall impact on QoL in adults with AD.[28] Other delivery mechanisms include both Internet and face-to-face education, but only marginal consensus was reached on the most cost-effective approach.

In conclusion, on the basis of this work, expert consensus recommendations have been developed that provide practical guidance on the management of AD, which are of clinical relevance to specialists and primary care physicians in Australia. Many of the clinical questions identified at the outset have been answered, although data gaps remain in some areas, particularly understanding the true prevalence of AD in Australia and best practices for patient education. Further work is required to disseminate this guidance and evaluate its impact on patient outcomes.

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AUTHORS' CONTRIBUTIONS

SS, PF, CB, DR, KG and BF conceived the concept of this work. SS and PF conceived the initial clinical questions upon which this consensus is based. CB, DR, KG and BF further refined the clinical questions prior to Delphi voting. All authors participated in the Delphi process and revised the manuscript critically for important intellectual content, and gave final approval of the version to be published. The authors acknowledge professional writing assistance provided by Hazel Palmer MSc, ISMPP CMPP™ (Scriptix Pty Ltd) in the preparation of this manuscript.

ETHICS APPROVAL

Not applicable.

INFORMED CONSENT

Not applicable.

ANIMAL RIGHTS

Not applicable.

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Supporting Information

Additional Supporting Information may be found online in Supporting Information:

Table S1. Clinical questions identified to be of most relevance to the management of adult atopic dermatitis (AD) in the Australian setting.
Table S2. Literature search strategy.
Table S3. Final guidance statements.