

# Management of Atopic Dermatitis in Adults in Saudi Arabia: Consensus Recommendations from the Dermatological Expert Group

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**Background:** Atopic dermatitis (AD) is a long-term, pruritic, recurrent, systemic, inflammatory skin disorder. In the Middle East region, the burden of AD is understudied, and there is a dearth of AD guideline documents for practitioners.

**Methods:** An expert panel meeting, encompassing 12 dermatologists from the Kingdom of Saudi Arabia (KSA), was congregated to develop evidence- and experience-based consensus recommendations for AD management, especially in adults in KSA. They completed a questionnaire with seven clinical statements, and a consensus was defined when the responses of  $\geq 75\%$  of participants coincided.

**Results:** The expert recommendations were as follows: American Association of Dermatology guidelines are to be followed for defining AD; Eczema Area and Severity Index or SCORing atopic dermatitis index may be used to quantify the disease severity; Dermatology Life Quality Index may be used to determine the impact of AD on patients' quality of life; Atopic Dermatitis Control Tool may be used to assess long-term disease control in AD patients; and the European guidelines are to be followed for the management of AD. In AD patients who are inadequately controlled with topical or systemic therapies, the preferred systemic agent for use either alone or in combination with topical treatments is dupilumab, cyclosporine, methotrexate, phototherapy, or other available systemic treatments that may include mycophenolate mofetil or oral corticosteroids.

**Conclusion:** These expert recommendations assist physicians by providing a reference framework for optimal care of adult AD patients.

**Keywords:** atopic dermatitis, Dermatology Life Quality Index, Eczema Area and Severity Index, SCORing atopic dermatitis

## Introduction

Atopic dermatitis (AD), well-known as atopic eczema, is a long-term, pruritic, recurrent, systemic, inflammatory cutaneous disorder commonly linked with other atopic systemic diseases such as asthma, allergic rhinitis, and food allergy.<sup>1,2</sup> Globally, 95% of cases with AD are detected before 5 years of age.<sup>1</sup> Early diagnosis and timely treatment are pivotal in preventing AD complications and improving the quality of life (QoL).<sup>1</sup> AD is most prevalent among children, affecting approximately 15–20% of children and 2–10% of young adults.<sup>1,3</sup> The prevalence of AD has been observed to be increasing among developing countries, including Africa and the Middle East region.<sup>4,5</sup> However, owing to underdiagnosis and the unavailability of sufficient AD

literature specific to these regions, there is a dearth of information, necessitating a better understanding of the increasing burden of AD.<sup>5</sup> According to the symptom-based questionnaire of the International Study of Asthma and Allergies in Childhood, the depicted prevalence of eczema in young adults (age: 13–14 years) from Syria, Iran, Kuwait, and Oman is 3.9%,<sup>6</sup> 10.1%,<sup>7</sup> 11.3%,<sup>8</sup> and 14.4%,<sup>9</sup> respectively.<sup>10</sup> A pioneering study in Saudi Arabia conducted between April 2008 and March 2009 among 854 Taif citizens (age-group: 3–65 years) reported the highest prevalence of AD, which was 45.4% in 2010.<sup>10,11</sup> Therefore, a clear-cut increase in AD prevalence in the Kingdom of Saudi Arabia (KSA) suggests an utmost need for early diagnosis and effective patient management.

The AD pathogenesis is multifaceted, encompassing genetic, immunologic, and environmental risk factors.<sup>12</sup> Structural and functional abnormalities in the epidermal region and inflammatory conditions in the cutaneous region, which are due to improper immune responses mounted against antigens invaded in the skin, are the two major pathophysiological characteristics of the disease.<sup>13</sup> In addition, increased numbers of Th2 cells are identified in AD lesions and are the reasons for inflammation in a local region.<sup>14,15</sup> The key pathophysiologic peculiarities of AD lesions are enhanced epidermal thickness with nerve fibers sprouting, increased immunostimulatory chemokine expression, and marked infiltration. This infiltration is characterized specifically by Th2 cells, dendritic cells in the epidermal region, as well as varying amounts of Th22 and Th17 cells among multiple AD subtypes, including acute and chronic AD.<sup>13</sup>

AD is associated with debilitating signs and symptoms and is accompanied by other disease conditions such as food allergy, allergic rhinitis, allergic conjunctivitis, asthma, and viral, bacterial, and fungal skin infections.<sup>2</sup> The clinical manifestations of AD include dryness (xerosis); diffuse erythematous patches; excoriated, oozing papulovesicular, and lichenified plaques with chronic lesions; pruritus; and pain.<sup>2</sup> Severe AD adversely affects a patient's QoL, as symptoms include frequent sleep disruptions, discomfort, pain, sadness, anxiety, and impairments in everyday activities, such as self-care and mobility.<sup>2</sup> Therefore, all aspects of the disease, including clinical manifestations and QoL of AD patients, should be addressed to control and manage AD.

There are two prevailing criteria for AD diagnosis: Hanifin and Rajka diagnostic criteria and a version modified by the American Association of Dermatology (AAD).<sup>16,17</sup> Hanifin and Rajka diagnostic criteria include 4 major and 23 minor criteria. Major criteria include family or personal history of atopy, pruritus, chronic relapsing dermatitis, and skin lesion distribution, while minor criteria include early age at onset, xerosis, folds in the anterior neck region, intolerance to food, intolerance to wool, white dermographism, itch when sweating, foot and/or hand dermatitis, a course influenced by emotional factors, a tendency toward cutaneous infection, cheilitis, eczema in the nipple region, pityriasis alba, orbital darkening, subcapsular cataracts in the anterior region, immediate skin test reactivity, recurrent conjunctivitis, ichthyosis and/or keratosis pilaris, increased serum immunoglobulin E (IgE), Dennie–Morgan infraorbital fold, and keratoconus.<sup>16</sup> AD is diagnosed if Hanifin and Rajka criteria, that is, three of both major and minor criteria, are met.<sup>16</sup> According to AAD guidelines, the following features have to be taken into consideration for AD diagnosis: (a) essential features, which must be surely reported (pruritus and eczema); (b) important features, which are seen in most cases (early-onset, xerosis, and atopy); and (c) associated features, which may just help to suggest AD diagnosis (atypical vascular responses, keratosis pilaris, ocular changes, periauricular lesions/perioral changes, and lichenification).<sup>17</sup> Also, there are several clinical parameters to determine AD severity and assess the outcomes of the treatment. The healthcare professionals depend on these clinical measures and are of two types: subjective and objective tools.<sup>18</sup> The physician's assessment of AD severity is categorized under objective tool and include the Eczema Area and Severity Index (EASI), SCORing atopic dermatitis (SCORAD), Investigator's Global Assessment and Physician's Global Assessment (IGA/PGA), body surface area (BSA), Atopic Dermatitis Severity Index (ADSI), and Six Area, Six Sign Atopic Dermatitis (SASSAD), whereas patient-reported symptoms and QoL outcomes are categorized under subjective tool and include Dermatology Life Quality Index (DLQI), Patient-Oriented Eczema Measure (POEM), and Pruritus Numerical Rating Scale (NRS) score.<sup>18</sup>

The current AD management guidelines recommended that the therapeutic armamentarium for treating AD consisted primarily of nonpharmacologic interventions, such as bathing practices, and moisturizers, topical pharmacotherapies, anti-inflammatory agents, and systemic therapies.<sup>19</sup> According to the AAD and the Joint Task Force (JTF) guidelines, phototherapy is the recommended systemic therapy for patients with AD who are refractory to topical regimens.<sup>19</sup> The next choice of recommendation for patients with severe AD and poor QoL, who were unresponsive to topical therapies and phototherapy, would be immunosuppressants.<sup>19</sup> According to the European Academy of

Dermatology and Venereology (EADV) guidelines, the severity of disease symptoms decides the management of AD.<sup>20</sup> The initial therapy, specifically skin moisturizers, and topical corticosteroids (TCS) remain the gold standard of treatment; however, in specific locations, topical calcineurin inhibitors (TCIs), such as tacrolimus and pimecrolimus, are preferred choices of management. In severe refractory AD, systemic immunosuppressive agents remain the mainstay of therapy.<sup>20</sup>

In the Middle East region, there is a dearth of published data, specifically regional guidelines, on accurate diagnostic and management approaches of AD. Guidelines or consensus recommendations on contemporary regional clinical practices for the diagnosis and treatment of AD are warranted. In particular, optimal quality of treatment does not reach patients in the KSA region due to a lack of regionally specific diagnostic tools as well as a lack of knowledge on the disease and therapeutic development. Hence, a region-specific guideline is a prerequisite for every region due to varying differences in socioeconomic conditions, wide-ranging differences in skin types, varying weather patterns, and differing access to the existing treatment approaches.<sup>21</sup> In this review, an expert panel from Saudi Arabia gathered to explore AD severity assessment and treatment recommendations for addressing the unmet therapeutic needs of this region with the consideration of ethnic factors that are often encountered in the KSA setting.

## Materials and Methods

The expert panel comprising 12 renowned dermatologists from Saudi Arabia, with expertise in the management of AD, was convened on October 9, 2020, aiming to develop consensus recommendations to aid dermatologists and general practitioners with the diagnosis and treatment of AD in adults in Saudi Arabia. In addition to the EADV guidelines, the AAD and JTF guidelines for the management of AD were taken into consideration for generating consensus recommendations. Recent peer-reviewed articles using the Cochrane library, PubMed database, and clinical experiences were also considered for the development of recommendations.

Relevant guidance statements addressing AD definition, disease severity assessment tools, and systemic treatment were prioritized and consolidated to be voted on by the expert panel. The panel members were asked to rate agreement/disagreement based on a survey questionnaire with seven clinical statements in the context of AD practice and research (for detailed questions, refer to [Table 1](#)).

The consensus process included one round of voting, and the consensus was defined as the achievement of  $\geq 75\%$  agreement for each statement. When consensus was not reached, clarification of a guidance statement was requested, and the potential amendments or deletions of these statements by the panel members were recommended. Overall, the final consensus was reached based on published international guidelines<sup>19,20</sup> and expert guidance on AD; relevant articles that were published up to October 2020; and regional treatment practices. A total of seven survey questions covering three clinical domains were presented for the sake of amendments to the expert panel for a single round of voting. No modification of statements was discussed among participants. The consensus was reached on seven statements by the panel of experts. The complete list of guidance statements and voting results are included. The guidance statements that achieved consensus were used to develop practice recommendations. The flowchart representation of the meeting plan and development of consensus statements is presented in [Figure 1](#).

## Results

### Survey Results

The responses of the expert panel to the survey questionnaire are shown in [Table 1](#).

### Approved AAD Guideline Definition of AD Consensus Statement I

AD is a chronic, pruritic, inflammatory skin disease that occurs most frequently in children but can also affect adults. It follows a relapsing course. AD is often associated with elevated serum IgE levels and a personal or family history of type I allergies, allergic rhinitis, and asthma. Atopic eczema is synonymous with AD.<sup>17,19</sup>

**Table 1** Overview of Responses Given by KSA Dermatologists for the Development of Consensus

Survey Questions	Percentage of Expert Response (No. of Experts, N = 12)	Expert Panel Response
Which definition of AD is approved locally?	75% (9/12)	Approval of the AAD definition to guide the clinical practice at the regional level.
Do you routinely use objective clinical tools in evaluating AD severity in routine clinical practice? If yes, which tool do you mostly use: EASI, SCORAD, or IGA/PGA?	92% (11/12)	Either EASI or SCORAD is recommended to be used as per the treating physician's preference.
Do you routinely use subjective patient-reported assessment tools in evaluating AD severity in clinical settings? If yes, which tool do you mostly use: DLQI, POEM, or Pruritus NRS score? If no, which tool do you recommend as a single tool to be used nationally: DLQI, POEM, or Pruritus NRS score?	75% (9/12)	DLQI is the preferred tool to assess the impact of AD on patients' quality of life.
To define controlled vs uncontrolled AD, which signs and symptoms matter to you most: pruritus, QoL, eczema bother, sleep pattern, recurrent flares, or others?	92% (11/12)	ADCT may be considered an efficient measure to assess AD long-term control.
Do you recommend ADCT to be used to define control in AD patient management follow-up?	92% (11/12)	ADCT could be considered to define control in AD patient management follow-up.
Which guidelines do you prefer to follow for AD management: American guidelines, European guidelines, or others?	100% (12/12)	In the absence of national or institutional guidelines, reference could be made to the European guidelines in the management of AD.
In your current practice, what is your preferred systemic therapy after topical treatment or in combination with topical treatment for AD management: cyclosporine-A, methotrexate, dupilumab, or others?	100% (12/12)	In AD patients who are not adequately controlled with topical therapy or systemic therapies, the preferred systemic agent for use either alone or in combination with topical treatments is dupilumab*, cyclosporine, methotrexate, phototherapy, or other available systemic treatments <sup>#</sup> .

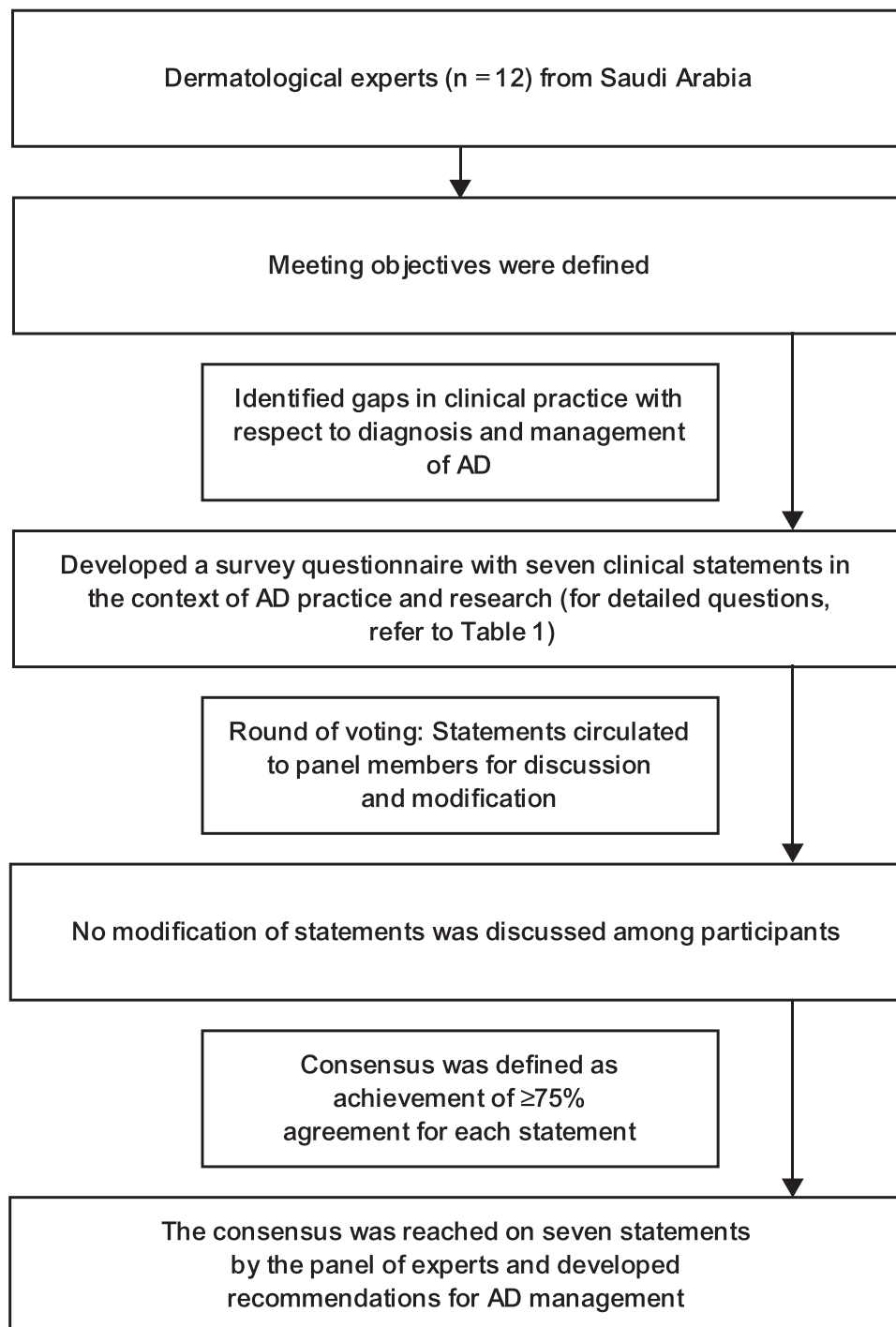
**Notes:** \*Dupilumab is the only approved biologic treatment by the Saudi Food and Drug Authority (SFDA) Health Authority in Saudi Arabia for managing moderate-to-severe AD patients following topical treatment. Of note, the meeting was held before the approval of a newer agent (baricitinib). <sup>#</sup>Other available systemic treatments may include mycophenolate mofetil or oral corticosteroids. Other approved systemic biologics or small molecules were not approved in Saudi Arabia till the date of the consensus meeting held on October 8, 2020.

**Abbreviations:** ADCT, Atopic Dermatitis Control Tool; AD, atopic dermatitis; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; IGA/PGA, Investigator's Global Assessment and Physician's Global Assessment; KSA, Kingdom of Saudi Arabia; NRS, Numerical Rating Scale; POEM, Patient-Oriented Eczema Measure; QoL, Quality of life; SCORAD, SCORing Atopic Dermatitis index.

Pruritus and eczema with chronic or relapsing history are the characteristic features that have to be taken into consideration in AD diagnosis.

## Approach and the Preference for Objective Disease Severity Assessment Tools for AD

Based on the available literature from the study findings by Chopra et al and Gooderham et al and the 2014 AAD guidelines, the experts generated consensus recommendations.<sup>17,18,22</sup> Objective tools are the physician assessment tools used for assessing the severity of AD.<sup>18</sup> Currently, no gold standard clinical tools, laboratory tests, or biomarkers are available for evaluating the AD severity. Therefore, clinicians must depend on clinical assessments of disease parameters.<sup>22</sup> Various objective tools are summarized in Table 2.<sup>18,22</sup>



**Figure 1** Flowchart representation of the meeting plan and consensus development.

**Abbreviation:** AD, atopic dermatitis.

## Consensus Statement 2

Either EASI or SCORAD is recommended to be used as per the treating physician's preference.

## Approach and the Preference for Subjective Disease Severity Assessment Tools for AD

The study findings of Chopra et al, Gooderham et al, and Simpson et al were scrutinized by experts as a part of the literature analysis.<sup>18,22,23</sup> Three types of patient-reported outcome measures (PROMs) are currently available for

**Table 2** Comparison of Objective Clinical Tools of AD

Parameters	SCORAD	EASI	IGA/PGA
Abbreviation	SCORing atopic dermatitis.	Eczema Area and Severity Index (it is a modification of the well-established Psoriasis Area and Severity Index [PASI]).	Investigator's Global Assessment and Physician's Global Assessment.
Total number of signs assessed	Six (lichenification, excoriations, edema/papulation, xerosis, oozing/crusting, and erythema).	Four (lichenification, erythema, excoriation, and papulation/edema).	Most commonly three signs are assessed (erythema, papulation/edema, and oozing/weeping). Less often, lichenification, scaling, excoriation, and crusting are evaluated.
Point scale used for scoring	4-Point scale.	4-Point scale.	6-Point scale.
Assessment parameter	The extent and severity of the lesion as well as it incorporates a patient-reported component evaluating sleep deprivation and pruritus.	The extent in four defined body regions (legs and arms, neck and head, torso) and the intensity of four clinical signs.	The severity of clinical signs.
Measurement of the extent of lesions	Extent is measured via a calculation of body surface area, using the "rule of nines" or palmar method, and values range between 0% and 100%.	Lesion extent is measured from 0 (0% involvement) to 6 (90–100% involvement)—1%–9%, 10%–29%, 30%–49%, 50%–69%, 70%–89%, and 90%–100%.	–
Measurement of intensity/severity of lesions	Each sign is scored as: 0 = not present, 1 = barely perceptible, 2 = clearly perceptible, or 3 = very prominent. The maximum score is 103.	Each sign is scored as: 0 = not present, 1 = barely perceptible, 2 = clearly perceptible, or 3 = very prominent. The maximum score is 72.	Each sign is scored as: 0 = clear; 1 = almost clear; 2 = mild; 3 = moderate; 4 = severe; 5 = very severe.
Total score calculation	Extent is calculated by percent disease involvement (A), and symptom severity is measured from 0 to 3 (B) for each sign. Subjective symptoms are quantified by the patient on a visual analog scale (0–10) for each pruritus and sleep loss (C). The total score is calculated as $A/5 + 7B/2 + C$ .	Total score (0–72) = lesional intensity multiplied by the body surface area involved in that region and summed across regions.	–

**Abbreviations:** EASI, Eczema Area and Severity Index; IGA/PGA, Investigator's Global Assessment and Physician's Global Assessment; SCORAD, SCORing atopic dermatitis index.

application in trials related to AD, and they include the Peak Pruritus NRS for itch, the POEM for complete AD manifestations, and the DLQI for health-related QoL.<sup>23</sup> However, none of these PROMs provide complete information about the control of the disease.<sup>23</sup>

Quantifying a patient's QoL associated with disease severity is quite essential because this measurement provides extra information to the traditional objective AD severity scores. Further, there is a correlation between the objective domains of AD severity scores and the subjective domains of the QoL measures.<sup>22</sup>

DLQI is an effective and easily implementable tool, encompassing a 10-item questionnaire, with each of the 10 questions being quantified on a 4-point scale, which aids in assessing the impact of AD on routine daily activities, such as work, social activities, intimacy, and the QoL.<sup>18</sup>

The POEM is an important patient-reported tool that measures the AD symptom severity. This eczema-specific tool evaluates seven symptoms, including xerosis, sleep deprivation, bleeding, skin flaking, weeping/oozing, broken skin, and itch experienced over the prior week. This patient-centered tool has the following advantages: simplicity, easy

interpretation, completion of questionnaires before visiting their dermatologists, and less time consuming, that is, it hardly takes 1–2 minutes for most patients to complete this test.<sup>18,22</sup> However, cross-cultural validity, measurement errors, reliability, and lack of proper evaluation strategies to assess symptom severity are the disadvantages that raise major problems about the application of this tool in daily hospital practice.<sup>22</sup>

### Consensus Statement 3

DLQI is the preferred tool to evaluate the burden of AD on the QoL of patients.

### Approach for Chronic Disease Control: Atopic Dermatitis Control Tool

The experts examined the studies conducted by Pariser et al, Chopra et al, and Simpson et al during the discussion.<sup>22–24</sup> The characteristic features of uncontrolled AD include persistent itch, insomnia, functional impairment, depression, anxiety, reduced morbidity, and work unproductiveness. An important factor of disease burden in the case of uncontrolled AD is a paucity of long-term disease control when compared to controlled AD. Therefore, achieving adequate long-term disease control by performing assessments is an important parameter as a part of guidance in the management of AD in healthcare settings.<sup>24</sup> Regarding measurements that assess control over flares, there is no evidence that whether another instrument particular to flares or the same scoring systems, such as POEM and DLQI, which assess signs, symptoms, and QoL, is used for capturing long-term disease control.<sup>22</sup> To overcome the current gaps in the assessment of patient-perceived disease control, a novel PROM-designed tool is developed, known as the Atopic Dermatitis Control Tool (ADCT), to assess disease control. It is a patient's self-assessment tool that can be easily scored and interpreted and would enhance valid patient–physician communication about disease control, thereby enhancing decision-making criteria for the management of AD.<sup>23</sup>

According to the findings of the study by Simpson et al, real-world data confirmed that the ADCT is a reliable and valid tool for evaluating patient-perceived AD disease control and may impart an effective communication tool between patients and healthcare professionals on AD disease control in clinical and nonclinical practices.<sup>23</sup>

### Consensus Statement 4

ADCT may be considered an efficient measure to assess patient-perceived long-term AD control.

### Preference of Guidelines for the Management of AD

The core committee discussed the American and European guidelines (refer to [Table 3](#))<sup>3</sup> and reached a consensus recommendation.

### American (JTF and AAD) Guidelines on Treatment Selection Methods for AD

On comparing JTF and AAD guidelines, the following key points were elucidated:<sup>19</sup>

- Moisturizers are the front-line, basic, nonpharmacologic treatment strategies for the management of both acute and proactive AD and their application is usually recommended after bathing.
- When nonpharmacologic interventions fail, TCS is recommended as the front-line therapy and should be used with caution in patients with thin skin.
- TCIs are alternatives to patients showing an increased risk of adverse events with TCS. They are specifically beneficial in sensitive areas, such as the skin folds and face.
- Topical antimicrobial bleach baths, that is, 0.005% sodium hypochlorite, are recommended two times a week in patients at a greater risk of skin infections.
- Phototherapy is recommended for unmanageable AD or for patients who are refractory to topical regimens. The use of narrow-band ultraviolet B is preferred.
- Systemic immunosuppressants are recommended in severe AD patients who were unmanageable with topical regimens and phototherapy.

**Table 3** European Task Force on Atopic Dermatitis (ETFAD) of the EADV 2020 guidelines

Forms of AD	Treatment in Adults	Treatment in Children
<b>Baseline:</b> basic therapy	Patient education, emollients, oil bathing practices, or avoidance of irritants and allergens.	Patient education, emollients, oil bathing practices, or avoidance of irritants and allergens.
<b>Mild:</b> SCORAD less than 25	Reactive therapy with topical glucocorticosteroid class II <sup>a</sup> or depending on local cofactors: topical calcineurin inhibitors <sup>a</sup> , antiseptics including silver <sup>a</sup> , silver-coated textiles, or topical crisaborole <sup>b</sup> .	Reactive therapy with topical glucocorticosteroid class II <sup>a</sup> or based on cofactors in local region: topical calcineurin inhibitors <sup>a</sup> , antiseptics including silver <sup>a</sup> , silver-coated textiles, or topical crisaborole <sup>b</sup> .
<b>Moderate:</b> SCORAD 25–50	Proactive therapy with topical tacrolimus <sup>a</sup> or class II or III topical glucocorticosteroids <sup>b</sup> , wet wrap therapy, UV therapy (UVB 311 nm and medium-dose UVA), psychosomatic counseling, or climate therapy.	Proactive therapy with topical tacrolimus <sup>a</sup> or class II or III topical glucocorticosteroids <sup>b</sup> , wet wrap therapy, UV therapy (UVB 311 nm), psychosomatic counseling, or climate therapy.
<b>Severe:</b> SCORAD greater than 50	Hospital admission with the following first choice of therapy: a short course of cyclosporine A <sup>a</sup> or dupilumab <sup>a</sup> . The additional therapeutic options include: a short course of oral glucocorticosteroids <sup>a</sup> ; longer course of systemic immunosuppression: methotrexate <sup>b</sup> , azathioprine or mycophenolate mofetil <sup>b</sup> ; PUVA; and alitretinoin <sup>b</sup> .	Hospital admission with the following first choice of therapy: dupilumab <sup>a</sup> . The additional therapeutic options include: a course of systemic immunosuppression: cyclosporine A <sup>b</sup> , methotrexate <sup>b</sup> , azathioprine, or mycophenolate mofetil <sup>b</sup> .

**Notes:** Antiseptics or antibiotics are recommended in cases of superinfection. <sup>a</sup>Licensed drugs; <sup>b</sup>off-label treatment drugs. Adapted from: Wollenberg A, Christen-Zäch S, Taieb A, et al. ETFAD/EADV Eczema task force 2020 position paper on diagnosis and treatment of atopic dermatitis in adults and children. *J Eur Acad Dermatol Venerol.* 2020;34:2717–2744. doi:10.1111/jdv.16892. © 2020 The Authors. Journal of the European Academy of Dermatology and Venereology published by John Wiley & Sons Ltd on behalf of European Academy of Dermatology and Venereology. Creative Commons Attribution-NonCommercial License (<https://creativecommons.org/licenses/by-nc/4.0/>.)

**Abbreviations:** AD, atopic dermatitis; EADV, European Academy of Dermatology and Venereology; UV, ultraviolet; SCORAD, SCORing atopic dermatitis index.

- Systemic corticosteroids are not advised for the management of chronic AD. However, atopic flares may develop with a short course of these agents after discontinuation.
- In patients with confirmed infection, systemic antibiotics are recommended, and systemic antivirals are recommended in patients with eczema herpeticum.

## Consensus Statement 5

In the absence of national or institutional guidelines, reference could be made to the European guidelines in the management of AD.

## Preference of Treatment Strategies in Patients Refractory to Topical Treatment

Studies by Megna et al and Deleuran et al were analyzed to understand the optimal systemic therapy after topical treatment or in combination with topical treatment for AD management.<sup>25,26</sup> Methotrexate, corticosteroids, mycophenolate mofetil, cyclosporine, and azathioprine are the nonbiologic immunosuppressants used in the management of AD in adults; these agents exhibit their immunosuppressive actions by lowering the Th2 cell (inflammatory cell) count and cytokine expression. In both adults and children, cyclosporine is a widely recommended choice for acute treatment of severe refractory AD as well as for maintenance AD therapy.<sup>25</sup> In addition to cyclosporine, other agents such as methotrexate, azathioprine, and mycophenolate mofetil may be suggested for the management of recurrent and severe AD.<sup>25</sup> Treatment with dupilumab shows a stable and favorable profile with respect to efficacy and safety and can be a solution for an unmet clinical need in AD patients.<sup>26</sup>

## Consensus Statement 6

In AD patients who are uncontrolled with topical or systemic therapies, the preferred systemic agent for use either alone or in combination with topical treatments are dupilumab\*, cyclosporine, methotrexate, phototherapy, or other available systemic treatments<sup>#</sup>.

\*Dupilumab is the only approved biologic treatment by the Saudi Food and Drug Authority for treating moderate-to-severe AD patients after topical treatment.

Of note, the meeting was held before the approval of a newer agent (baricitinib).

#Other available systemic treatments may include mycophenolate mofetil or oral corticosteroids. Other approved systemic biologics or small molecules were not approved in Saudi Arabia till the date of the consensus meeting held on October 8, 2020.

## Discussion

AD is a long-term, pruritic, relapsing, systemic inflammatory cutaneous disorder that has a pronounced effect in children and has a comparatively less pronounced effect in adults. Underdiagnosis and lack of region-specific guidelines on the diagnostic and management approaches of AD are the major barriers to the effective treatment of AD in the KSA region. An expert committee meeting was convened to understand the current barriers in the diagnosis and treatment of AD in the KSA region to provide optimal care to AD patients. An expert committee meeting has two benefits. First, the findings from published literature can be generated into recommendations quickly, which is different from clinical studies that are usually associated with greater time consumption. Second, ratification of recommendations can be concurrently done with the expert panel members.

In this study, concerns raised during discussions were facilitated to generate consensus statements, which were validated by the expert panel. These consensus recommendations provide new directions in the diagnosis and management of AD in adults in KSA.

Our experts agreed regarding the definition of AD based on the AAD guidelines, the use of an objective tool, the EASI or SCORAD index, as well as the use of a subjective tool, DLQI, to quantify disease severity, and the use of European guidelines in the management of AD in the KSA region. They also agreed that among patients with AD who are refractory to topical or systemic treatments, the preferred systemic agents for management, either alone or in combination with topical treatments, are dupilumab, cyclosporine, methotrexate, phototherapy, mycophenolate mofetil, or oral corticosteroids. These recommendations aid other dermatologists in the management of AD and would improve patients' QoL in the KSA region.

To our understanding, this is the first endeavor to utilize guidance from experts and published literature to propose consensus statements as recommendations for enhancing the diagnosis and effectiveness of AD therapy in the KSA region. This study imparts a balanced consensus that involves the perspectives of both physicians and patients, furnishing a sound basis for the diagnosis and treatment of AD in KSA.

Physicians still lack awareness about the disease at a critical level, which is one of the important issues that must be resolved in KSA. Flourishing physicians' knowledge about the diagnosis and management of AD would assist them with the appropriate background to enhance an effective management strategy for the maximization of persistence and adherence. Various communication strategies are recommended to increase awareness about AD among physicians, encompassing symposiums and social initiatives in the primary care settings, like free topical assessments, to improve physicians' understanding of AD. Besides, the developed recommendations from the current expert consensus would be the best and most appropriate option for physicians to enhance their knowledge about the complete picture of AD.

Despite increasing awareness of diagnostic and treatment strategies for physicians, there is a need for future research to recognize specific patient outcomes. This would also involve furthering patient interactions and understanding patients' perceptions of the information provided at the time of treatment initiation and their attitude to therapy. The scope of this understanding would help in achieving the results of the current expert consensus through effective clinical outcomes by enabling individualized patient-tailored treatment as personalized therapy is essential for an effective treatment algorithm.

## Conclusion

Our consensus concluded that unsatisfactory guidelines hamper AD diagnosis and management, and these conclusions are in alignment with the perception of experts. To date, no regional guidelines are available in the KSA region, and these

**Box 1** Expert Recommendations

1. The AAD definition may be applied to guide the clinical practice at the regional level.
  2. Either EASI or SCORAD is the recommended tool that can be used in practice as per the physician's clinical judgement.
  3. The use of DLQI assessment tool is recommended to evaluate the burden of AD on QoL of patients.
  4. ADCT may be considered as an efficient measure to assess patient-perceived, long-term AD control and management.
  5. In the absence of national or institutional guidelines, reference could be made to the European guidelines in the management of AD.
  6. In patients with AD, who are uncontrolled with topical treatment or systemic therapies, the preferred systemic agents for use, either alone or in combination with topical treatments, are dupilumab\*, cyclosporine, methotrexate, phototherapy, or other available systemic treatments#.
- \*Dupilumab is the only approved biologic treatment by the SFDA Health Authority in Saudi Arabia for managing moderate-to-severe AD patients following topical treatment. Of note, the meeting was held before the approval of a newer agent (baricitinib).
- #Other available systemic treatments may include mycophenolate mofetil or oral corticosteroids. Other approved systemic biologics or small molecules were not approved in Saudi Arabia till the date of the consensus meeting held on October 8, 2020.

**Abbreviations:** AAD, American Association of Dermatology; ADCT, Atopic Dermatitis Control Tool; AD, atopic dermatitis; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; QoL, quality of life; SCORAD, SCORing Atopic Dermatitis index; SFDA, Saudi Food and Drug Authority.

expert consensus recommendations would form a standard document for the effective treatment of AD in adults in the KSA region.

Our experts believe that effective diagnostic and treatment strategies play a potent role in patient management. Therefore, we recommend focusing on future research in AD to develop novel therapeutic options, which are clinically effective with good patient-reported outcomes (Box 1).

## Research Ethics and Consent

This is a Review article and hence ethics committee approval is not applicable.

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## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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