# DEVELOPMENT AND EVALUATION OF A CLINICAL PRACTICE GUIDELINE TO PROMOTE EVIDENCE-BASED TREATMENT OF CHILDHOOD ATOPIC DERMATITIS IN PRIMARY CARE

by

Tiffany Anne Crawford Zook



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As members of the DNP Project Committee, we certify that we have read the DNP Project prepared by Tiffany Anne Crawford Zook entitled Development and Evaluation of a Clinical Practice Guideline to Promote Evidence-Based Treatment of Childhood Atopic Dermatitis in Primary Care and recommend that it be accepted as fulfilling the DNP Project requirement for the Degree of Doctor of Nursing Practice.

_____ Date: July 28, 2016
Gloanna Peek, PhD, RN, CPNP

_____ Date: July 28, 2016
Lorri Marie Phipps, DNP, RN, CPNP

_____ Date: July 28, 2016
Luz Wiley, DNP, RN, APRN-BC

Final approval and acceptance of this DNP Project is contingent upon the candidate's submission of the final copies of the DNP Project to the Graduate College.

I hereby certify that I have read this DNP Project prepared under my direction and recommend that it be accepted as fulfilling the DNP Project requirement.

_____ Date: July 28, 2016
DNP Project Director: Gloanna Peek, PhD, RN, CPNP

STATEMENT BY AUTHOR

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SIGNED: __Tiffany Anne Crawford Zook__

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# DEDICATION

This DNP project is dedicated to Elizabeth Eden, a talented and passionate pediatric nurse practitioner who first taught me how to provide evidence-based care for children with allergies, asthma and atopic dermatitis, while sharing pearls of wisdom that cultivated my desire to re-examine and re-shape the way primary care providers care for children with atopic dermatitis.

This DNP project is also dedicated to every young person who has the dream of becoming a nurse practitioner. Your dreams are not too great and there is no hurdle too big to overcome in following your passion.

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## ABSTRACT

Introduction and Rationale: Atopic Dermatitis (AD) is a common skin condition, characterized by markedly pruritic eczematous lesions, that most often presents in childhood. The majority of children diagnosed with AD will have mild disease and will first present with symptoms to a primary care provider (PCP), however approximately 85% of pediatricians only provide limited initial care followed by a referral to dermatology (Eichenfield et al., 2015). While there are specialty care based treatment guidelines for childhood AD, there are no guidelines available that specifically address primary care management of childhood AD.

Purpose and Objective: The primary purpose of this DNP project is to develop an evidence-based clinical practice guideline (CPG) for pediatric PCPs. The secondary purpose is to develop a corresponding atopic dermatitis action plan (ADAP) to be used by children and parents. The objective is to equip PCPs to better manage children with AD in the primary care setting and to guide patients and parents in the importance of daily control measures and in the individualized treatment plan prescribed by the PCP.

Methods: The Appraisal of Guidelines for Research & Evaluation II (AGREE II) framework and Social Cognitive Theory (SCT) serve as the theoretical frameworks for CPG and ADAP development. The American Academy of Pediatrics (AAP) process for evidence based policy setting is used as a model for key action statement development.

Results: Evaluation of the CPG was completed using the AGREE II tool, a reliable and validated tool for evaluating CPGs. Five of the six domains evaluated, yielded combined scores of at least 90%, with one domain a combined score of 63%. The overall standard deviation was 0.58, indicating an overall low level of user discrepancy Additions and revisions were made based on

the results of the AGREE II evaluation scores with specific emphasis on the lowest scoring domain.

Conclusion: This DNP Project identified the need for a CPG specific to pediatric primary care. A CPG with accompanying ADAP was developed and evaluated using the AGREE II tool. The CPG was found to meet the recommended standards and recommended for use in pediatric primary care.

# CHAPTER I: OVERVIEW

## Introduction

The purpose of this Doctor of Nursing Practice (DNP) project is to educate and equip primary care providers of children with atopic dermatitis (AD). The focus is to identify criteria to diagnose a child with AD, identify evidence-based treatments and assess the need for patient and family teaching to encourage treatment compliance, through the evaluation of current evidence. The purpose is to develop an evidence-based clinical practice guideline (CPG) for primary care providers (PCPs), and corresponding atopic dermatitis action plan (ADAP) for children and parents regarding the importance of daily care measures to control AD and prevent exacerbations. The CPG is designed to be used in pediatric primary care settings. In order to give background and understanding as to how this project came to be, a review of childhood AD including its definition, current prevalence, pathogenesis, and treatment and control recommendations will be introduced. Additionally, the significance of the project to advanced practice nursing will be discussed and definitions of terms to be used throughout the project will be provided.

## Childhood Atopic Dermatitis

AD is a chronic inflammatory skin condition that usually begins before age five, that waxes and wanes, and is associated with significant morbidity and quality of life impairment (Garg & Silverberg, 2015; Tan & Gonzalez, 2012; Wolter & Price, 2014). AD is characterized by markedly pruritic eczematous lesions distributed in a characteristic pattern with facial, neck and extensor involvement in infants/children, current or previous flexural lesions in any age group and sparing of the groin and axillary regions (Eichenfield et al., 2015; Tan & Gonzalez,

2012). Regarding diagnostic criteria, essential features include: pruritis, eczematous dermatitis (acute, subacute or chronic), typical morphology and age-specific patterns, and a chronic or relapsing history; important features (add support and are present in most cases of AD) include: early age of onset, atopy, and xerosis; associated features (suggestive of AD but too non-specific to use in defining or detecting AD in research studies) include: atypical vascular responses, keratosis pilaris/pityriasis alba/hyperlinear palms/ichtyosis, ocular or periorbital changes, other regional findings, and perifollicular accentuation/lichenification/prurigo; and exclusionary conditions (must be excluded to definitively diagnose AD) include: scabies, psoriasis, ichthyoses, seborrheic dermatitis, contact dermatitis, cutaneous T-cell lymphoma, photosensitivity dermatoses, immune deficiency diseases, and erythroderma of other causes (Eichenfield et al., 2015; Krakowski, Eichenfield, & Dohill, 2008).

The incidence of AD has increased from approximately 5% of children aged 0-17 years between 1997-1999, to an estimated 12.5% in 2009-2011 (Eichenfield et al., 2015). In 65% of children affected, disease onset occurs before the age of one, and before the age of five for 85% of children, making it a significant and relevant area of disease management for primary care providers (Tollefson & Bruckner, 2014).

Although not entirely clear, it is thought that the pathogenesis of AD is a combination of genetics, immune dysfunction and environmental factors (Tollefson & Bruckner, 2014; Wolter & Price, 2014). It is theorized that the skin barrier becomes genetically compromised and allows for penetration of environmental factors resulting in immune dysregulation (Wolter & Price, 2014). This trio of factors are often modeled in one of two ways: inside-out or outside-in. The inside-out model theorizes that the epidermal changes seen in AD are the result of constitutive

immunologic abnormalities that lead to an altered skin barrier through the activation of T helper type (Th2) immune-cell associated cytokine responses and subsequent promotion of a defective skin barrier that allows for passage of antigens that lead to a more rapid immunologic response (Margolis et al., 2015). The outside-in model holds that a dysfunctional skin barrier facilitates the transfer of external exposures which in-turn elicits AD symptoms, all due to immunologic activation through the passing of a model antigen through a constitutively defective skin barrier and high total serum IgE levels (Margolis, et al., 2015).

Regardless of the pathway, AD has a strong genetic component. In terms of genetics, the recently discovered Filaggrin gene (filament-aggregating protein, FLG) mutation has helped to explain interruptions and deficiencies in the skin barrier seen in patients with AD (Lawton, 2014). Filaggrin acts as a waterproof barrier between the outermost layer of skin and keratinocytes, therefore FLG mutations, found in up to 10% of individuals with European ancestry, are positively associated with persistent and severe AD. The defective barrier that results from FLG mutations, in turn allows for penetration of environmental triggers, such as micoorganisms, allergens and irritants, to thus be introduced to the immune system and finally impact the pathogenesis of AD (Bergmann, Caubet, Boguneiwicz, & Eigenmann, 2013). Though strongly correlated and responsible for AD exacerbations, food allergies have not been found to be an etiology of AD, despite much hypothesizing to the contrary (Bergmann et al., 2013).

Treatment of AD is generally aimed at control and prevention of acute exacerbation with a strong focus on basic management including proper skin care, antiseptic measures, and trigger avoidance (Eichenfield et al., 2015). Proper skin care includes liberal use of emollient moisturizer combined with regular skin hydration such as warm baths or showers using mild

soap followed by application of an emollient while skin is still damp to seal moisture. Antiseptic measures include diluted bleach baths twice weekly or more, depending upon the presence of recurrent skin infections. Trigger avoidance includes avoiding common irritants such as soaps with fragrance or dyes, temperature extremes and known allergens (Eichenfield et al., 2015). In terms of treating acute exacerbations or flares, the cornerstone of treatment is the use of topical anti-inflammatory medication to inflamed patches of eczematous lesions, with low potency topical corticosteroids (TCs) for mild flares, the use of medium potency TCs and consideration of secondary infection for moderate to severe flares, and for relapsing frequent/persistent flares, the maintenance use of TCs or topical calcineurin inhibitors (TCIs) for ongoing management (Eichenfield et al., 2015).

In terms of demographics, Horii, Simon, Liu and Sharma (2007) found that minorities, including Hispanics, Blacks and Asians accounted for much fewer visits to primary care providers in the United States (between 1997-2004), specifically for AD, than their White/Caucasian counterparts with only 20% of clinic visits made by Hispanics, compared to 51% for White/Caucasians. Simply by means of evaluating the data above it is easy to infer that there is not only a need for improved education in general, but also to minorities.

## Significance to Advanced Practice Nursing

Advanced Practice Nurses (APNs) and specifically Pediatric Nurse Practitioners (PNPs) provide high quality care to children, adolescents and their families through the use of a patient and family-centered approach that is backed by expert child and adolescent health knowledge (Martyn, Martin, Gutknecht, & Faleer, 2013). Many PNPs are ultimately practicing in primary care, either independently or alongside their MD colleagues in pediatric practices, with two of

their top four practice roles being to provide direct patient care and to provide patient and family teaching (Buerhaus, DesRoches, Dittus, & Donelan, 2014). Direct care and patient education are both identified as two of the greatest needs for patients newly diagnosed with AD and those with mild to moderate AD (Baron, Cohen, & Archer, 2012; Tidman, 2012). Lastly, randomized controlled trials have shown that the level of care provided by a nurse practitioner in terms of improvement of AD and quality of life outcomes is comparable to that provided by dermatologists, with the added advantages of improved patient satisfaction with care and improved cost-savings and cost-effectiveness (Schuttelaar, Vermeulen, Drukker, & Coenraads, 2010; Schuttelaar, Vermeulen, & Coenraads, 2011).

## Purpose

The purpose of this DNP project is to create an evidence-based CPG for the treatment of childhood AD. The CPG is intended for use by pediatric PCPs and parents of pediatric patients diagnosed with AD and was developed to be used in the primary care setting. It will include evidence based guidelines regarding diagnostic criteria, the recognition of potential triggers, the importance of the use of emollient skin care to control and prevent eczematous exacerbations, the selection of the appropriate first and second line topical treatment for eczematous flares, and criteria that necessitates referral to dermatology. As a secondary element, the CPG will include a customizable ADAP, similar to those used in the management of childhood asthma. The hope is that this CPG will help educate PCPs and that the ADAP will do the same for parents, making the burden of caring for a child with AD less cumbersome through the provision of a written and visual means of knowing and remembering what can be done to control their child's AD. The CPG and corresponding ADAP has been developed based on current research and on the

application of both the Appraisal of Guidelines for Research & Evaluation II (AGREE II) framework and social cognitive theory (SCT) with a focus on increasing self-efficacy of patients/parents/caregivers to produce a change in behavior.

## Definition of Terms

**Atopic Dermatitis**

A chronic, relapsing and often intensely pruritic inflammatory disorder of the skin, commonly referred to as eczema (Tollefson & Bruckner, 2014).

**Atopy**

Conventionally defined as a positive allergen-specific serum IgE or skin prick test to any inhalant or food allergen. Conventional definition doesn't account for temporal trends or patterns of sensitivity to other allergens and many experts are proposing expanded definitions (Lazic et al., 2013).

**Emollient**

Topical preparations that have occlusive and/or humectant effects to maintain the skin's softness and hydration (Ng, Liew, & Ang, 2015). Fats or oils in a two-phase system with one liquid being dispersed in the form of small droplets throughout another liquid, that function to soften the skin by forming an occlusive oil film on the stratum corneum (SC), or protective permeability layer of the skin, that prevents drying by evaporation from the deeper skin layers (Hon, Leung, & Barankin, 2013).

**Topical Corticosteroid (TC)**

Topical treatment, classified by potency, that provides effective control of AD flares through anti-inflammatory, anti-proliferative, immunosuppressive and vasoconstrictive actions with a resultant suppression of inflammatory cytokine release (Krakowski et al., 2008).

**Topical Calcineurin Inhibitor (TCI)**

Second-line and short-term, non-continuous use topical preparations that block the production and subsequent release of proinflammatory cytokines after antigen-specific or nonspecific activation of T cells and mast cells, used for chronic treatment of moderate to severe AD in patients > 2 years of age with healthy immune systems (Krakowski et al., 2008)

**Wet Wrap Therapy (WWT)**

Treatment for moderate to severe exacerbations used in conjunction with topical corticosteroids that increase the penetration of topical steroids into the skin and decrease itch through the following technique: soaking in a bath for 10-15 minutes, patting dry to leave moisture on the skin, applying steroid ointment to affected areas, applying thick layer of emollient moisturizer to the rest of skin, covering skin with dampened cotton clothing such as pajamas, and finally covering the wet layer with a dry layer of cotton clothing and leaving on for 3-8 hours (Tollefson & Bruckner, 2014).

**Finger-tip Unit (FTU)**

The amount of ointment expressed from a tube with a 5mm diameter opening measured from the distal skin crease to the tip of the palmar surface of an adult's index finger, equal to approximately 0.5 g and adequate for thin and even application to an area of skin the size of approximately two adult hands with fingers together (Eichenfield et al., 2015).

**Clinical Practice Guideline**

Defined by the Institute of Medicine (IOM) as "systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances (Field & Lohr, 1990)."

**Action Plan**

Written, customized plan outlining indications and amounts of specific products and medications to be used for control and treatment of AD (Tollefson & Bruckner, 2014).

## Conclusion

This chapter provided an introduction and brief overview of childhood AD including a discussion of incidence, pathogenesis and treatment. Additionally, this chapter discussed the significance of childhood AD to advanced practice nursing. The purpose of this DNP project was stated and finally, definitions of terms were provided.

# CHAPTER II: BACKGROUND

## Introduction

Chapter II will elaborate on the background that serves as the foundation for this DNP project. Beginning with an overview of the literature review, the chapter continues with a detailed description of AD including a discussion of risk factors and issues, including the genetics of AD, the role of food allergies and implications for quality of life. The chapter is wrapped up following a survey of the recommendations for control and treatment including the roles of skin care, antiseptic measures, trigger avoidance, acute exacerbation treatment and patient/parent education.

## Search Strategy of Literature Review

A comprehensive literature review was completed using the PubMed, CINAHL, Google Scholar and Cochrane Library search engines. Specific search criteria were used and included: published within the last five years, English, and humans. Specific search terms were also used. Terms related to childhood atopic dermatitis were used and combined several ways to optimize search results. “Childhood atopic dermatitis” and “Atopic Dermatitis” were the main search terms and were combined individually with other terms, including: clinical practice guideline, eczema, treatment, emollients, prevention, epidemiology, primary care, food allergy, nurse practitioner, clinical practice guideline, written action plan, patient teaching. Additional searches using the above search engines were performed during the writing process to find additional supporting evidence.

## Childhood Atopic Dermatitis Risk Factors and Issues

### Genetics

Twin studies have shown that approximately 80% of AD can be attributed to genetic factors, and genome-wide studies have identified numerous genetic susceptibility loci in patients with AD, with many being within or close to genes that are critical to immunity, namely, Th2-mediated inflammation, and skin barrier function (Lyons, Milner, & Stone, 2015). Additionally, there are heritable atopic syndromes (included in the differential diagnosis of AD) that have led to better understanding of the pathogenesis of AD, with loss of barrier integrity and immune cell dysfunction being characterized as necessary for disease development (Lyons et al., 2015). Skin barrier defects include: ichthyosis vulgaris, netherton syndrome, peeling skin syndrome type B, and SAM syndrome, and immune pathway defects include: autosomal dominant hyper-IgE syndrome, autosomal recessive hyper-IgE syndromes, Wiskott-Aldrich syndrome, IPEX syndrome, Omenn syndrome, and Atypical Complete DiGeorge syndrome (Lyons et al., 2015)

**Immune pathway defects.** There are several immune abnormalities identified in AD, including increased Th2 inflammation and allergic sensitization, sustained wound healing inflammation, and impaired innate immunity (Levin, Fallon Friedlander, & Del Rosso, 2013). Increases in Th2 inflammation leads to the following changes in the skin: increases in IL-4 that adversely affects skin barrier function by decreasing ceramide production, reducing loricrin synthesis, downregulating desmoglein-3 expression and decreasing FLG expression; increases in IL-13 that stimulates IgE and CCL18 production; and decreases in antimicrobial peptides (AMPs) that lead to a predisposition for staphylococcal colonization and subsequent increased risk of infection and continued elevations in IgE and allergic sensitization (Levin et al., 2013). In

terms of sustained wound healing, an inflammatory response is evident in AD that includes inflammation, proliferation of progenitor cells leading to epidermal hyperplasia, and tissue remodeling that results in epidermal intercellular edema (Levin et al., 2013). Lastly, innate immune dysfunction and subsequent increase in colonization and infection in AD is mediated by a decreased recognition of microbes, leading to increased colonization of microbes and increased IgE, along with decreased defense against microbes, both of which lead to increases in infection (Levin et al., 2013).

**Skin barrier dysfunction.** As had been briefly described in chapter one, there is growing support for the "outside-in" model, or the idea that there is an abnormality in the skin's permeability barrier that causes the skin manifestations of AD. The following reasons are cited: severity of disease phenotype and the extent of the permeability barrier abnormality are parallel; uninvolved skin and healed skin sites that are clear for more than five years continue to demonstrate barrier abnormalities; emollient therapy is found to be effective; and replacement therapy that targets the most prevalent lipid abnormalities accounting for barrier abnormality, correct the abnormality and is effective as anti-inflammatory therapy (Elias, 2008).

The FLG gene, is the most commonly reported gene variant associated with the prevalence and persistence of AD and with skin barrier dysfunction. Interestingly, FLG mutations are common in individuals with European and Asian ancestry, but rarely seen in those with African ancestry (Margolis et al., 2015). FLG deficiency leads to decreased SC hydration, increased transcutaneous water loss and a resultant skin barrier dysfunction that enhances antigen penetration (Elias, 2008). It also terminates the release of Natural Moisturizing Factor (NMF), leading to decreased water retention and skin dehydration (Lyons et al., 2015). Other

explanations for skin barrier dysfunction include: corneodesmosin (CDSN) and desmoglein-1 (DSG1) dysfunction; autosomal recessive mutations in serine protease inhibitor Kasal-type 5 (SPINK5) that lead to the loss of lympho-epithelial Kazal-type-related inhibitor (LEKTI) resulting in the increased skin permeability that is present in Netherton Syndrome; and genetic variants in KLK7 (Kallikrein family proteases) (Lyons, et al., 2015).

**Outside-inside-outside pathogenic loop.** Although greater evidence points to a barrier-initiated etiology for AD, studies also suggest that Th2-generated cytokines may further potentiate the severity of AD through increases in IL-4 and subsequent impeding of barrier recovery after acute insults to the barrier (Elias, 2008). The negative effects of IL-4 support an acquired mechanism for compromised barrier function that is first stimulated by primary inherited barrier abnormalities and ultimately leads to a further compromised permeability barrier, thus completing an outside-inside-outside pathogenesis loop as depicted in figure 1 (Elias, 2008).

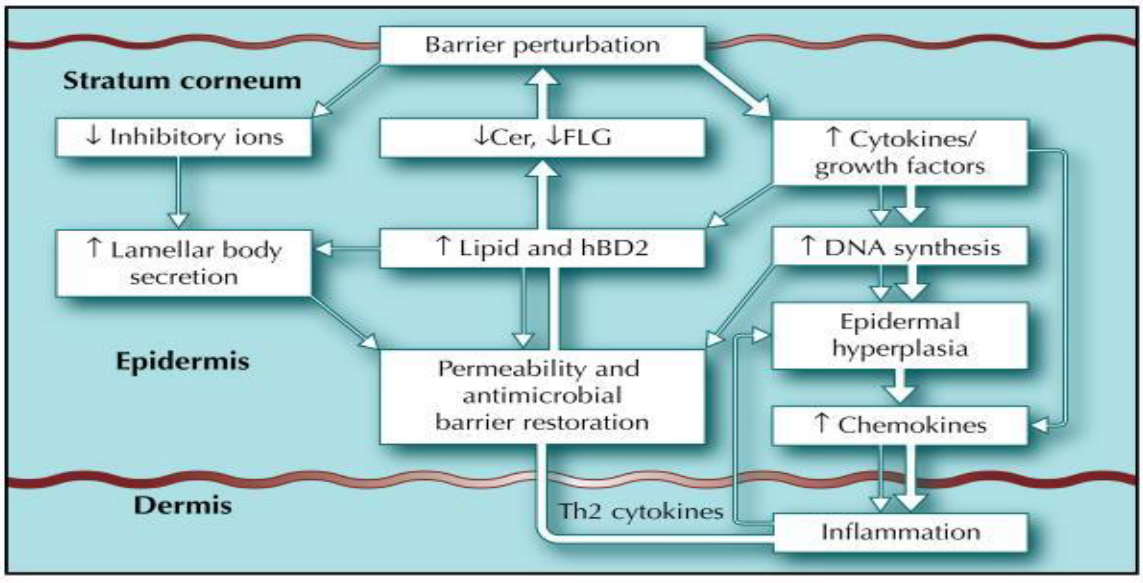



FIGURE 1: Outside-Inside-Outside Pathogenic Loop (Elias, 2008)

**Food Allergies**

It has been well established that the presence of food allergies (FA) is higher in children with AD, with 15-30% of AD patients also having food allergies (Ricci et al., 2014). Cow's milk hen's egg, wheat, soy, peanut, tree nuts and fish account for greater than 90% of FA in children with AD, with cow's milk, hen's egg, peanut and soy being most prevalent in infants and wheat, fish, shellfish and tree nuts being most common in older children (Bergmann et al., 2013). In the late 1970's the idea of using elimination diets to improve AD was first introduced and further expanded over the next several decades to the inclusion of oral food challenge (OFC) testing following elimination diets with additional evaluation of basophil histamine release in those that had positive challenge tests, to lastly, a 1998 study that was considered to be "true and unbiased" because of its use of patients with AD not referred to an allergist, that found that 37% of patients with moderate to severe AD also had OFC confirmed FAs (Bergmann et al., 2013).

Three different patterns of reactions have been observed in patients with AD following an OFC, including immediate-type, delayed-type, and immediate-type followed by an eczematous delayed-type reaction (Bergmann et al., 2013). An immediate-type reaction is usually noneczematous, IgE-mediated and occur within 2 hours of exposure producing urticarial, flushing and pruritis along with the possibility of other gastrointestinal, respiratory or anaphylactic reactions, whereas a delayed-type reaction typically occurs 6-48 hours following OFC, is non-IgE-mediated and is expressed as eczematous reactions on predilection sides of AD (Bergmann et al., 2013).

The following points are important to consider when evaluating the link between AD and FA: AD and FA are associated, but FA does not cause AD; foods may trigger AD exacerbations;

IgE measurement and allergy skin testing have been shown to be poor measures in the identification of foods that may be triggering flares of AD; FA is more prevalent and likely to be correlated with AD in infants and younger children with severe AD; foods should not be eliminated from the diet of a child with AD without determining a specific clinical outcome and plan for reintroduction; foods should be re-introduced within 3-4 weeks of removal from the diet if there is no clinical effect; and OFC is the most effective and appropriate way to identify a food as a trigger for AD (Campbell, 2012). Figure 2 provides a recommended algorithm for evaluation of FA in patients with AD.

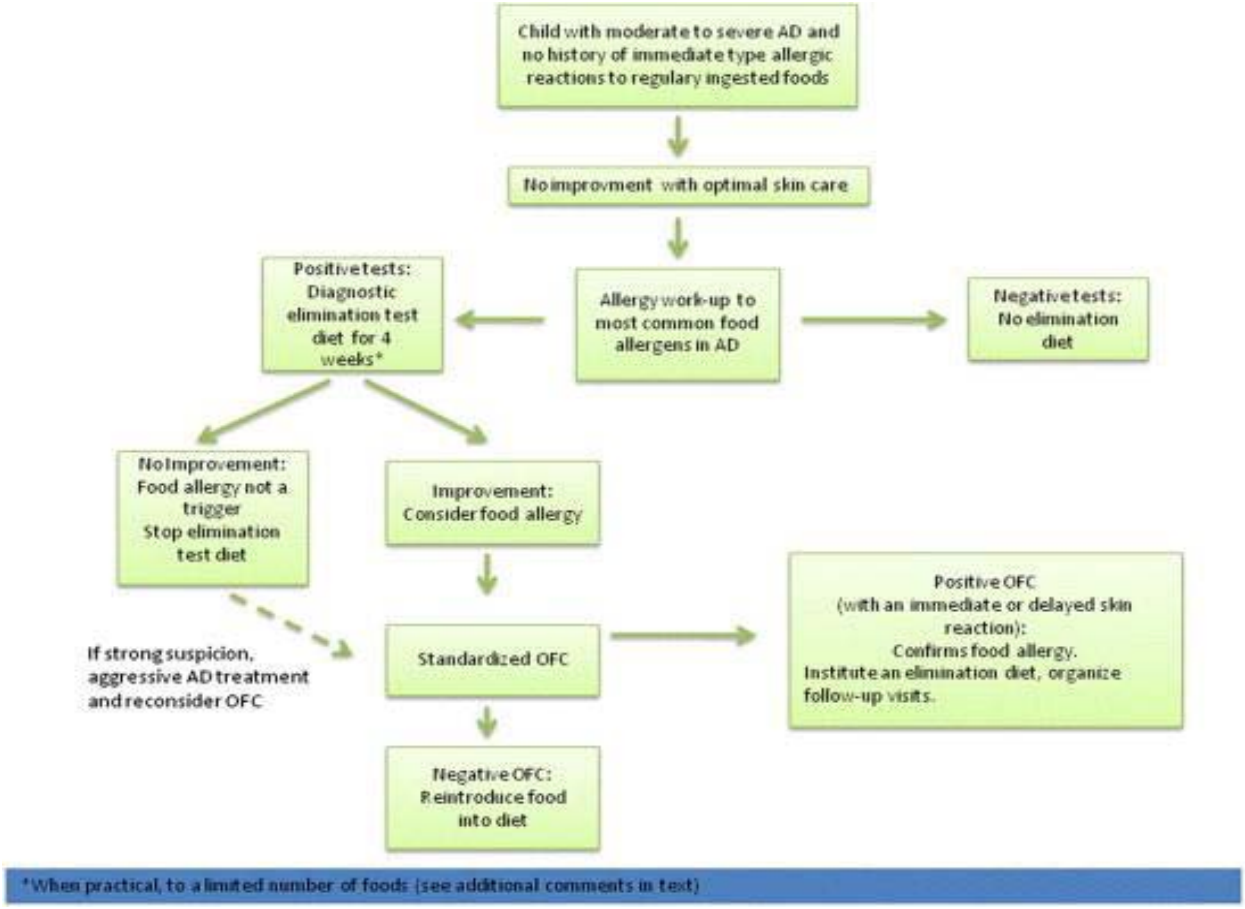



FIGURE 2: Algorithm for Evaluation of Food Allergy in Patients With Atopic Dermatitis (Bergmann et al., 2013)

**Quality of Life and Emotional Effects**

AD is a difficult condition that frequently affects quality of life (QOL) and often leads one or more of the following: child and parental sleep disturbances, behavioral symptoms, poor self-esteem**,** parent-child conflict, activity restriction and depression (Chamlin & Chren, 2010; Lewis-Jones, 2006; Tollefson & Bruckner, 2014). Because itching and subsequent scratching is one of the cardinal symptoms of AD, sleep is disturbed in 60% of children affected, leading to physical and mental exhaustion, mood disturbances, and impaired school performance in children and fatigue and impaired work performance in parents (Lewis-Jones, 2006). Delayed onset to sleep, multiple night awakenings and reduced sleep efficiency are all documented sleep dysfunctions in children with AD and often persist even during disease remissions due to the fact that the abnormalities may become learned sleep patterns (Chamlin & Chren, 2010). Specifically for parents of younger children or toddlers with AD, co-sleeping is often employed as a means to improve sleep through the prevention of awakenings and holding the child's hand to prevent scratching, but it actually does the opposite and leads to decreased parental quality of sleep and subsequent decreased daytime productivity (Chamlin & Chren, 2010).

Behavioral and emotional issues are also inherent to a diagnosis of AD. Younger children exhibit irritability, fussiness, increased crying, clinginess, fearfulness, frustration and wanting to be held more frequently (Chamlin & Chren, 2010). In older children social and school life are affected through appearance discomfort, limitations in ability to participate in sports, feelings of social isolation, peer-group rejection and teasing that corporately lead to loss of confidence, mood changes and depression (Lewis-Jones, 2006). Additionally, AD has significant effects on overall family life beyond behavioral and emotional issues, some of which include financial

losses through missed work to care for the child with AD, everyday routines such as increased laundry, house cleaning and food preparation for children with AD who also have food allergies, and lifestyle restrictions such as limitations in diet, not being able to have pets, and avoidance of certain household products (Lewis-Jones, 2006).

## Recommendations for Control and Treatment

Many children with AD first present to their pediatric health care provider (HCP) for diagnosis and management, and can be well-managed by their HCP without the necessity of being referred to a specialist, provided that the HCP is informed of and familiar with current recommendations (Eichenfield et al., 2015). To provide guidance for PCPs, Eichenfield et al. (2015) evaluated recommendations from the following organizations in order to more clearly and concisely provide an evidence-based model for primary care: American Academy of Dermatology (AAD), American College of Allergy, Asthma, and Immunology (ACAAI), American Academy of Allergy, Asthma, and Immunology (AAAAI), European Academy of Allergology and Clinical Immunology (EAACI), and European Dermatology Forum (EDF). This model will serve as the basis for the following recommendations with additional evidence based literature to support each step in management. Regardless of severity, there are fundamental management strategies for AD care that should be employed for every patient, including hydration and emollient skin care, antiseptic measures, trigger avoidance and treatment of acute exacerbations (Eichenfield et al., 2015).

### Emollient Skin Care

Daily skin care with a combination of skin hydration and an emollient moisturizer is the cornerstone of control treatment and prevention of acute exacerbation for patients with AD. With

the goal to repair and maintain a functional skin barrier, maintenance skin care is foundational to the management of patients with AD and not only includes the use of emollients but also the practice of routine bathing and skin soaking (Tollefson & Bruckner, 2014). Though there isn't complete agreement among experts as to how often bathing should take place, soaking baths allow the skin to soak in moisture and can be beneficial daily, as long as it is followed by emollient application immediately afterwards, preferably when the skin is still damp and hasn't had the opportunity to dry out (Tollefson & Bruckner, 2014). Daily bathing in lukewarm water for 10-15 minutes with minimal use of soap, provides an important means to remove bacteria, gently exfoliate and improve hydration (Wolter & Price, 2014). The use of soap is also debated, as soap can cause skin irritation and washing the skin with soap can increase skin pH for at least 90 minutes and subsequently leads to impairment in barrier function, therefore it is recommended that hypoallergenic soaps with very minimal ingredients be used in very small amounts (Oszukowska et al., 2015).

Following a soaking bath, immediate application of an emollient moisturizer allows for a "sealing-in" of the moisture soaked in from bathing. Oszukowska et al. (2015) notes that emollients contain lipids such as animal fats, vegetable oils, waxes, mineral hydrocarbons and cocoa butter and often are enriched with substances such as ceramides, phospholipids, waxes, squalenes, free fatty acids and cholesterol. The authors further explain that emollients work in two ways: to hydrate the epidermal stratum corneum in combination with the presence of water-binding ingredients; and by reduction in trans-epidermal water loss through inherent occlusal action. Furthermore, the epidermis is penetrated and water binds with the following common ingredients in emollients: urea, pyrolidone carboxylic acid, hyaluronic acid, glycerol, and lactic

acid, followed by the sealing of the epidermal barrier by the following components: fruit acids, animal fats, vegetable oils, waxes, lactic acid, and lipids (Oszukowska et al., 2015).

Emollients should be applied head to toe to all skin, regardless of locations of eczematous lesions and are important in not only lubricating the skin, but in the alleviation of discomfort associated with xerosis and in the repair of the skin barrier, ultimately leading to a reduction in the quantity and potency of topical corticosteroid or other pharmacologic treatment needed (Tollefson & Bruckner, 2014). There are a large variety of commercially available emollients and most parents/patients will have to try multiple to discern what offers the best relief and feel for the child (Eichenfield et al., 2015).

**Antiseptic Measures**

Because of the widely studied and agreed upon fact that the skin of patients with AD has a tendency to be colonized by *Staphylococcus aureus* (SA), not only in the areas of eczematous lesions but also in uninfected areas such as the anterior nares, axillae and perianal region, antiseptic treatment is a growing area of study and clinical recommendation (Lee & Van Bever, 2014). The use of sodium hypocholorite (bleach) baths have been found to an effective, readily accessible, inexpensive and well-tolerated means to reduce or eradicate the incidence of SA cutaneous infections (Barnes & Greive, 2013). The recommended process includes the following 2-3 times weekly: filling bathtub completely with lukewarm water; add 0.25-0.5 cup (depending on tub size) of common bleach solution (6%) to water; stir to ensure that bleach is completely diluted; have patient soak for 5-10 minutes; thoroughly rinse skin with lukewarm, fresh water; and finally, as soon as rinsed off, apply emollient to damp skin head to toe (Barnes & Greive, 2013).

**Avoidance of Environmental Triggers**

Patient-specific triggers may be unavoidable, but attempts to minimize or completely avoid common triggers such as aeroallergens, environmental allergens, infections, harsh soaps and detergents, fragrances, rough or non-breathable clothing fabrics, excess saliva, sweat and psychosocial stress, can be helpful (Tollefson & Bruckner, 2014). It is important for providers to also keep in mind that typical or relevant allergens vary by age group, with younger children being more likely to have food allergy and older children being more likely to have aero allergies (Eichenfield et al., 2015). Environmental triggers are numerous and avoiding them completely in unrealistic and not likely possible, however there are general measures that can be taken to potentially decrease exposure, such as using mattress covers, low-pile carpet (particularly in sleeping areas), having non-dander-producing pets, keeping the home environment clean and free of dust, and using soap, detergent and cleaning products that are hypoallergenic and fragrance-free (Caubet & Eigenmann, 2010; Krakowski et al., 2008).

Regarding identification of specific allergies, it is not recommended that providers offer routine allergy testing, as the predictive value of positive tests is low (Eichenfield et al., 2015). However, Caubet and Eigenmann (2010) note that when specific aero or environmental allergies are strongly suspected, allergy skin-prick testing along with specific IgE can be of use to confirm the allergen and to inform treatment such as avoidance or in some cases specific immunotherapy (SIT). The same authors note that SIT may play a larger role in the future for patients with AD, as it currently plays for patients with allergic rhinitis and asthma.

**Acute Exacerbation Treatment**

Once a patient has eczematous lesions, treatment shifts from prevention and control to acute lesional treatment, as flares rarely respond to moisturization alone, with topical steroids serving as first-line treatment, and TCIs as second-line treatment alongside adjunct medications to treat and minimize itching (Tollefson & Bruckner, 2014). Eichenfield et al. (2015) points out that it is widely agreed upon that treatment should be directed at severity of disease, and has developed an algorhythm to guide treatment, as shown in figure 3.

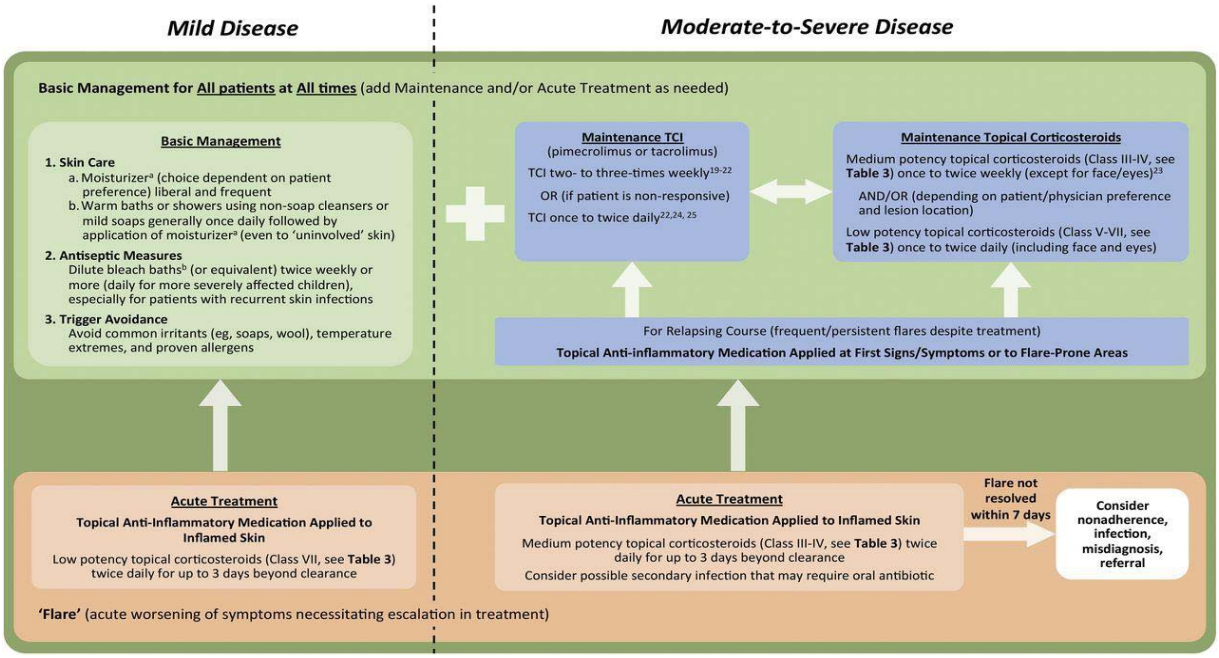



FIGURE 3: Proposed Treatment Model/Eczema Action Plan for Pediatricians and Other Primary Care Providers (Eichenfield et al., 2015).

**Topical Corticosteroids (TCs).** TCs have been used for more than 40 years, are effective and safe when used appropriately, and are available in varying strengths allowing for stepped treatment and treatment individualization based on severity of lesions (Tollefson & Bruckner). The mainstay of lesional treatment, topical CSs decrease inflammation and subsequently reduce

severity and duration of flares, improve sleep and reduce bacterial colonization (Wolter, 2014). Classified from class VII to class I, topical CSs divided according to their potency, ranging from low potent (class VII) to super potent (class I), with class I medications being 1800 times more potent than class VII medications (Tollefson & Bruckner, 2014) Table 1 gives examples of topical CS preparations according to class.

TABLE 1: Topical Steroids by Potency and Class. Adapted from Tollefson & Bruckner, 2014

| CLASS | GENERIC NAME |
|---|---|
| **VERY HIGH Potency I** | Diflorasone diacetate 0.05% ointment<br>Fluocinonide 0.1% cream<br>Halobetasol propionate 0.05% ointment and cream<br>Clobetasol propionate 0.05% Cream and Ointment |
| **HIGH Potency II** | Betamethasone dipropionate 0.05% ointment and cream<br>Desoximetasone 0.25% cream<br>Fluocinonide 0.05% cream and ointment<br>Mometasone furoate 0.1% ointment<br>Budesonide 0.025% cream |
| **MODERATE Potency III** | Desoximetasone 0.05% cream<br>Betamethasone valerate 0.1 % ointment<br>Fluticasone propionate 0.005% ointment<br>Triamcinolone acetonide 0.5% cream<br>Diflorasone diacetate 0.05% cream |
| **MODERATE Potency IV** | Betamethasone valerate 0.12% foam<br>Fluocinolone acetonide 0.025% ointment<br>Hydrocortisone valerate 0.2% ointment<br>Mometasone furoate 0.1% cream and lotion<br>Triamcinolone acetonide 0.1% cream |
| **MODERATE Potency V** | Betamethasone valerate 0.1% cream<br>Fluocinolone acetonide 0.01% cream<br>Fluocinolone acetonide 0.025% cream<br>Hydrocortisone butyrate 0.1% ointment, cream, lotion<br>Triamcinolone 0.025% ointment |
| **LOW Potency VI** | Triamcinolone acetonide 0.025% cream<br>Flurandrenolide 0.025% cream<br>Fluocinolone acetonide 0.01% oil<br>Desonide 0.05% ointment, cream, lotion, hydrogel, foam<br>Alclometasone dipropionate 0.05% ointment |
| **LOW Potency VII** | Hydrocortisone 0.5% and 1% ointment, cream<br>Hydrocortisone 2.5% ointment, cream, lotion |

Along with class it is important to consider the type of preparation, in terms of whether it is a lotion, cream, or ointment, because different preparations offer different levels of occlusion and potency, with ointments being the most potent and occlusive, creams more potent than lotions and lotions the least potent (Lyons et al., 2015). Lyons et al. (2015) further notes that ointments are most often preferred, given that they provide a more occlusive barrier to maintain skin hydration, facilitate improved absorption of the CS itself and contain fewer preservatives.

Selection of potency is dependent upon severity of flare and historical success with the particular choice of CS. As shown in figure 3, mild flares should be treated with a low potency (class VI-VII) CS twice daily for up to three days following resolution of lesions, along with continuing control and preventive measures (Eichenfield et al., 2015). Given the wide range of options in each potency category it can often be challenging for PCPs to know which to use, and it is for this reason that it is recommended that PCPs choose a handful (2-3) from the low and moderate potency categories to be their "go-to" choices for everyday practice and treatment (Tollefson & Bruckner, 2014). For moderate to severe disease, Eichenfield et al. (2015) recommends that PCPs select medium potency CSs (class III-IV) for use twice daily for up to three days beyond clearance, consideration of secondary infection that may require antibiotic treatment, and consideration of nonadherence, misdiagnosis, infection or a referral for a flare that does not resolve within seven days. Topical CSs can also be used for maintenance therapy in patients that have chronic and relapsing disease, and are typically recommended for use daily if low potency or once to twice weekly if moderate potency (Eichenfield et al., 2015).

Although topical CSs are frequently prescribed and usually well tolerated, it is important to consider potential adverse effects and to make it a practice to educate and monitor for these

effects while managing pediatric patients with AD. Possible adverse effects include cutaneous atrophy, striae, telangiectasia, systemic absorption that may lead to adrenal suppression, local intraocular hypertension or cataracts around the eyes, and perioral dermatitis (Tollefson & Bruckner, 2014). Although there is some systemic exposure through the use of topical CSs, and there are known systemic complications that have been reported, they are very rare when the medication is used properly and monitored (Krakowski et al., 2008).

**Wet-Wrap Therapy (WWT).** As an addition to the use of topical CSs for moderate severity flares, WWT is a modality that is recommended and may enhance treatment. WWT is the use of a double layer of tubular bandages or gauze, with the first layer being moist and the second layer being dry (Andersen, Thyssen, & Maiback, 2015). Prior to application of the wet layer, the child soaks in a warm bath for 10-15 minutes, pats dry so that there is still moisture present on the skin, and applies emollients and/or topical CSs to lesional areas and emollients to the whole body surface if treating whole body (Andersen et al., 2015; Nicol, Boguneiwicz, Strand, & Klinnert, 2014) Once the first layer of moist lukewarm bandages or tubular cotton-based garments is in place, a top dry layer is applied with the addition of blankets as needed to maintain warmth, and the layers are left on for a period of several hours or overnight if the child falls asleep after application (Andersen et al., 2015; Nicol et al., 2014). Though studies are limited and have focused on this being an intervention for severe to refractory AD, there is a study that found that supervised WWT was not only an effective treatment for moderate to severe AD but also was effective in maintaining improvement in AD severity for one month after discharge, and allowed for management without the need for systemic immunosuppressive therapy (Nicol et al., 2014).

**Topical Calcineurin Inhibitors (TCIs).** Relatively new to treatment of AD, TCI's are topical immunosuppressive medications that function to inhibit T-cell function through the selective blocking of cytokine transcription, with the two formulations approved for AD being tacrolimus 0.03% and 0.1% ointments and pimecrolimus 1% cream (Lyons et al., 2015; Tollefson & Bruckner, 2014). In terms of the Eichenfield et al. (2015) recommendations for PCPs, TCI's are recommended also to play a role in maintenance or "proactive" therapy to be applied to normal appearing skin in flare-prone areas 2-3 times weekly or at first signs of a flare. Clinical trials have demonstrated effectiveness in using TCIs for maintenance treatment 2-3 times weekly or if non-responsive to that, 1-2 times daily (Eichenfield et al., 2015). Among the benefits to using TCIs is that their use does not result in skin atrophy and thus is a good option for eyelid and facial lesions, and that they may be useful as long-term anti-inflammatory treatment geared at decreasing exposure to steroids (Lyons et al., 2015). The only commonly identified side effect to TCIs is transient burning, however it usually subsides within a few days of use (Lyons et al., 2015).

**Itch control.** Itch is inherent to AD and often one of the most debilitating factors for children to deal with, leading to poor sleep, decreased quality of life, and increased risk of hyperactivity-impulsivity disorders (Eichenfield et al., 2015). While potentially effective in controlling allergic factors that contribute to AD, little evidence has been found to support the effectiveness of antihistamines on AD associated itch (Lio, Lee, LeBovidge, Timmons, & Schneider, 2014). Longer-acting oral antihistamines that are more sedating may be helpful to promote sleep and prevent the nighttime scratch-wake cycle but do not have a direct effect on AD (Wolter & Price, 2014)

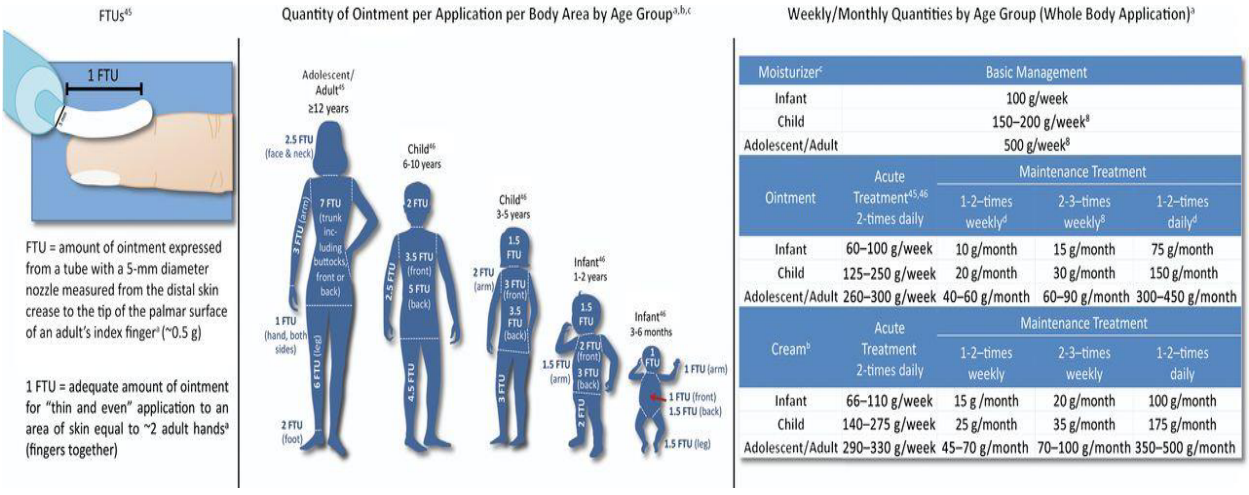
**Parent and Patient Education**

As has been expanded upon above, AD is a complex condition that requires ongoing management, acute treatment and daily, sometimes around the clock, attention to skin-care needs, and is a condition that often has profound effects on overall QOL. Due to the complexity of AD, overstrain, lack of information, lack of confidence and helplessness in how to manage the condition leads to suboptimal management of the disease and increased use of healthcare resources (Staab et al., 2006). In their German study that was one of the first of its kind to evaluate structured educational programs for children with AD and their families, Staab et al. (2006) found that age-related educational programs were significantly more effective in the long term management of AD than conventional treatment alone. The educational sessions were conducted by members of a multidisciplinary team including nurses, pediatricians, dermatologists, psychologists and dieticians, and educational topics addressed were: basic medical information about AD and relaxation techniques; stress management, dealing with itching and sleep disturbances; trigger avoidance and daily skin care; stage related treatment of symptoms including unconventional therapies; general nutrition and food allergies in AD; and issues of coping, self-care and daily routine (Staab et al., 2006). In the study all outcome measures, improved severity of eczema, improved subjective severity, improved itch and improved QOL for parents of younger children, were met, demonstrating the value of structured education.

Since the seminal work of Staab et al. (2006), additional studies have been completed and have continued to find that there is significant improvement in the control of AD in children receiving education (Mason et al., 2013). Mason et al. (2013) cited previous studies specifically

with regards to emollient use, one in which found an 800% increase in the use of emollients and corresponding 89% reduction in severity of AD following dermatology clinic-based specialist nurse-led education. Mason and colleagues (2013) also underscored the importance of a comprehensive approach to support and education that not only included verbal and visual teaching, but also printed educational materials.

Unfortunately, many PCPs do not have the staff resources, time or monetary resources to provide a comprehensive patient-directed educational program. Eichenfield et al. (2015) cites the need to provide the following in terms of patient/family education in the primary care setting: a written treatment plan that includes proper skin care instructions, antiseptic measures, trigger avoidance and pharmacologic treatment; follow-up and modification of the written plan (if needed) at each clinic visit with the MD, nurse or other medical staff; and focus on each visit being an opportunity to provide reinforcement of teaching and to correct misconceptions or barriers to care.




| Moisturizer[c] | Basic Management |
|---|---|
| Infant | 100 g/week |
| Child | 150–200 g/week[g] |
| Adolescent/Adult | 500 g/week[g] |

| Ointment | Acute Treatment[45,46] 2-times daily | Maintenance Treatment 1-2–times weekly[d] | 2-3–times weekly[g] | 1-2–times daily[d] |
|---|---|---|---|---|
| Infant | 60–100 g/week | 10 g/month | 15 g/month | 75 g/month |
| Child | 125–250 g/week | 20 g/month | 30 g/month | 150 g/month |
| Adolescent/Adult | 260–300 g/week | 40–60 g/month | 60–90 g/month | 300–450 g/month |

| Cream[b] | Acute Treatment 2-times daily | Maintenance Treatment 1-2–times weekly | 2-3–times weekly | 1-2–times daily |
|---|---|---|---|---|
| Infant | 66–110 g/week | 15 g /month | 20 g/month | 100 g/month |
| Child | 140–275 g/week | 25 g/month | 35 g/month | 175 g/month |
| Adolescent/Adult | 290–330 g/week | 45–70 g/month | 70–100 g/month | 350–500 g/month |

FIGURE 4: Topical Application Amounts with FTU Description (Eichenfield et al., 2015)

He further stresses the importance of patient/parent instruction regarding the quantity of topical medication and/or emollient to use for each application and per day/week/month with emphasis on use of the fingertip unit (FTU) as a means to measure topical medication (figure 4).

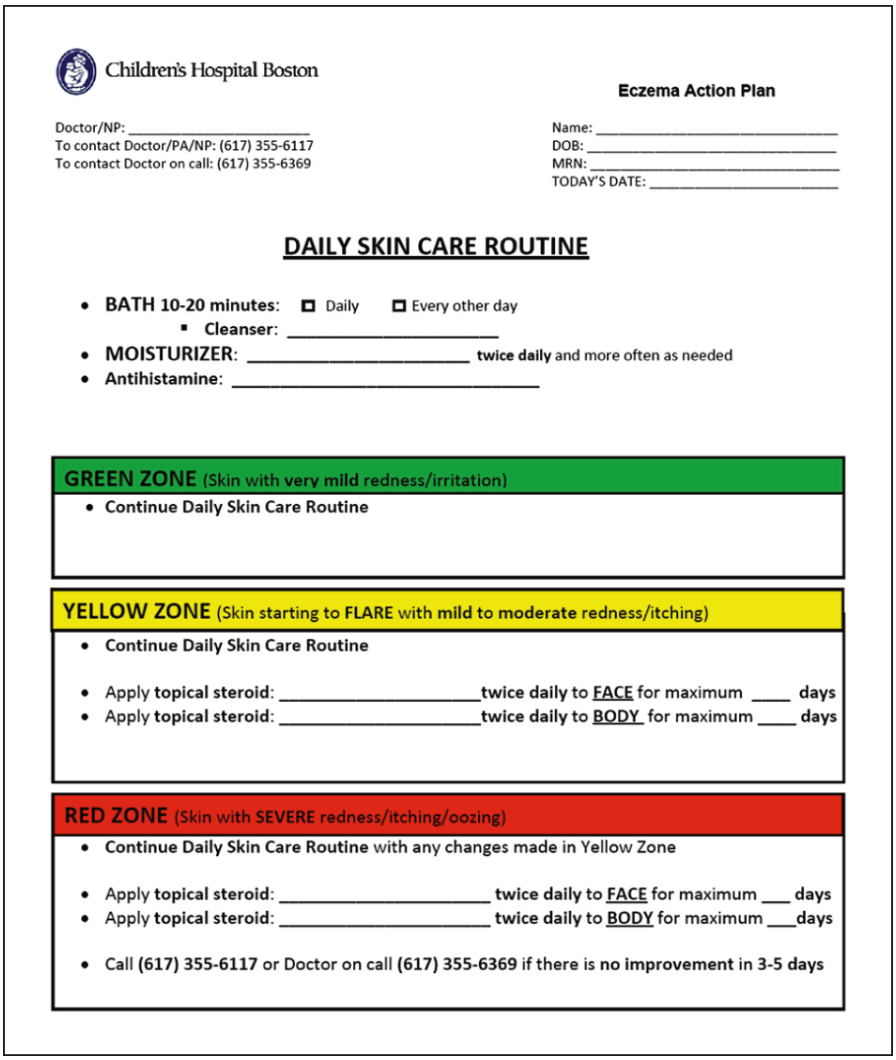
**Individualized Written Action Plans**

Defined as a written set of instructions to assist patients and their caregivers in managing a condition that come in various forms, but serve a common purpose to provide parents with a written plan to guide them through management of their child's chronic illness between health-care visits, written action plans (WAPs) have been shown to be useful in the management of asthma for many years (Ntuen et al., 2010). Similar to asthma, AD is a waxing and waning chronic disease that is marked by frequently evolving treatment plans that are often complex and require instruction for control and prevention, as well as for acute flare management (Rork et al., 2012). Although there is still limited data, there is growing evidence that the use of WAPs in AD management is helpful to parents, clarifies treatment instructions and overall improves AD as a result of their use (Rork et al., 2012).

Two recent controlled trials, one randomized (Shi et al., 2013) and one nonrandomized (Duhovic et al., 2014), both revealed positive data in favor of the use of eczema action plans (EAP). Ninety percent of the Duhovic et al. (2014) experimental arm that received and EAP rated the intervention as useful or very useful. In the Shi et al. (2013) trial, the EAP group demonstrated improvement in AD recognition, prevention and management with step-wise treatment, visualization and daily reminders found to be the EAP elements that were most beneficial. The data is encouraging, but indicates that there is a need for future studies to broaden

the body of evidence supporting the use of WAPs in the care of children with AD (Sauder et al., 2016).

There is not a specific, universal template for a WAP geared to patients with AD, however Children's Hospital of Boston developed an EAP (figure 5) that is modeled after an asthma action plan with the use of green, yellow and red to indicate very mild/no symptoms, mild to moderate symptoms/flare, and severe symptoms, respectively (Rork et al., 2012).



Children's Hospital Boston

**Eczema Action Plan**

Doctor/NP: _____
To contact Doctor/PA/NP: (617) 355-6117
To contact Doctor on call: (617) 355-6369

Name: _____
DOB: _____
MRN: _____
TODAY'S DATE: _____

**DAILY SKIN CARE ROUTINE**

- **BATH 10-20 minutes:** ☐ Daily ☐ Every other day
  - **Cleanser:** _____
- **MOISTURIZER:** _____ **twice daily** and more often as needed
- **Antihistamine:** _____

**GREEN ZONE** (Skin with very mild redness/irritation)

- **Continue Daily Skin Care Routine**

**YELLOW ZONE** (Skin starting to **FLARE** with **mild to moderate** redness/itching)

- **Continue Daily Skin Care Routine**
- Apply **topical steroid:** _____ **twice daily to FACE** for maximum ____ **days**
- Apply **topical steroid:** _____ **twice daily to BODY** for maximum ____ **days**

**RED ZONE** (Skin with **SEVERE** redness/itching/oozing)

- **Continue Daily Skin Care Routine** with any changes made in Yellow Zone
- Apply **topical steroid:** _____ **twice daily to FACE** for maximum ___ **days**
- Apply **topical steroid:** _____ **twice daily to BODY** for maximum ___**days**
- Call **(617) 355-6117** or Doctor on call **(617) 355-6369** if there is **no improvement** in **3-5 days**

FIGURE 5: Children's Boston Eczema Action Plan. Copied with permission from Rork et al., 2012.

Though the study design used self-report rather than a validated measuring instrument, 86% of parents in this study reported that it was helpful and clarified which medications to use during a flare, and 68% of parents whose child's eczema improved attributed it to the use of the EAP (Rork et al., 2012). Given the encouraging data and the fact that there is a lack of evidence using any type of written educational intervention with Spanish and English-speaking Mexican-American children and their families, a WAP will be incorporated into the educational brochure being developed for this project.

## Conclusion

This chapter has provided a literature review with explanation of search strategy and expounds upon two major topics: AD risk factors and issues, and recommendations for control and treatment. Furthermore, this chapter has given an evidence-based, comprehensive framework for the establishment of the CPG.

# CHAPTER III: METHODS

## Introduction

Chapter three will focus on the need for a CPG with ADAP directed at pediatric PCPs, pediatric patients with AD and their parents, with the purpose of providing evidence-based guidelines to include: diagnostic criteria for AD, use of emollient skin care to control and prevent eczematous exacerbations, selection of the appropriate first and second line topical treatment for eczematous flares, value of adjunctive treatments, recognition of potential triggers, criteria that necessitates referral to dermatology, and patient and family tailored education. The CPG will include a corresponding ADAP that can be customized for each patient/family to guide them in the importance of proactive control measures to prevent acute exacerbations of eczematous lesions.

The Appraisal of Guidelines for Research & Evaluation II (AGREE II) framework, developed to assess the quality of guidelines, provide methodological strategy for development of guidelines and to inform what information and how information should be reported in guidelines, was used to guide CPG development (Brouwers et al., 2010a). Social Cognitive Theory (SCT) is the health behavior model that was used to guide the development of the ADAP. This chapter will provide an overview of AGREE II with an overview of each dimension, and an overview of SCT along with definitions of each dimension of SCT as applied to the ADAP. Using the guidance of AGREE II and SCT, a clinical practice guideline and corresponding ADAP was created to be used in pediatric primary practice to inform the above patient demographic of the importance of preventive and control measures in childhood AD.

**Need for Pediatric Clinical Practice Guidelines and Education**

Given that the majority (~67%) of children diagnosed with AD will have mild disease, and that the majority will first present to their pediatric PCP, this is a condition that should be able to be more than adequately managed in primary care, however, ~85% of pediatricians refer patients to dermatologists and only provide limited initial care (Eichenfield et al., 2015). Tollefson and Bruckner (2014) note that considerable variability persists in clinical practice, despite the fact that there have been consensus guidelines and practice parameters published, and further note that inconsistencies in treatment approaches leads to frustration for both PCPs and families. The literature indicates that, despite multiple specialty specific guidelines, there is a need for treatment guidelines specific to the management of AD in the primary care setting. Furthermore, clarity on the part of the PCP in setting treatment and treatment outcome expectations leads to better parental compliance and less frustration (Tollefson & Bruckner, 2014).

As noted in chapter two, the need to maintain an intact skin barrier by means of regular use of emollients, antiseptic measures, trigger avoidance, and the use of topical CSs and/or TCIs when indicated, is well established in the literature. With attention to control and flare prevention through close adherence to skin care recommendations, PCPs can facilitate the control of AD and minimization of acute flares (Eichenfield et al., 2015; Lyons et al., 2015). That said, treatment is often time consuming, complex and costly with management posing an ongoing challenge for parents and caregivers, especially given the increased incidence of co-morbidities, such as asthma, allergic rhinitis and severe food allergy, that also require attention and management (Mitchell, Fraser, Ramsbotham, Morawska, & Yates, 2015). Santer et al. (2012) note that poor adherence most often is the etiology of treatment failure for the following reasons:

therapy being too time consuming, poor understanding of topical preparations, fear of TC side effects, and child refusal of therapy.

Unfortunately, the burdens of treatment compliance often result in poor treatment adherence (Mitchell et al., 2015). Medications are often not kept up with or even picked up from the pharmacy (Mitchell et al., 2015) Storm, Andersen, Benfeldt and Serup (2008) found that nearly 48% of prescriptions for children attending a dermatology outpatient clinic remained unfilled and that even when a clinic has the ability to directly supply medications to parents and provide regular follow-up, adherence rates can be as low as 32% (Mitchell et al., 2015). Furthermore, Mitchell et al. (2015) mention that a failure of therapy or apparent lack of response to traditional therapy following a good initial response, may be attributed to decreased adherence to the AD treatment plan, rather than an increasing resistance to topical medications. Adherence is a facet of treatment that underscores successful management of AD and that needs continual attention.

One of the most crucial components of ensuring ongoing success in treatment adherence, is ongoing patient education and treatment plan reinforcement (Santer et al., 2012). This idea was validated by the National Institute for Health and Clinical Excellence (NICE) guideline on atopic eczema in children, that attributed poor adherence and treatment failure to a lack of education about therapy (Santer et al., 2012). Increased emphasis on patient/family education along with the provision of a specific treatment plan are recommended and all treatment plans should include a scheduled follow-up within a couple of weeks to assess patient/parent comfort with the plan and adherence to treatment (Eichenfield et al., 2015). In two qualitative studies evaluating the experiences of caregivers of children with AD, it was noted in both studies, that there was a

lack of understanding of the importance of and/or rationale for emollient use and that regular adherence could potentially provide control of AD and prevention of acute exacerbations (Santer et al., 2012; Santer et al., 2013). Both of the same studies also found that treatment adherence was positively associated with a strong relationship with the child's healthcare provider (Santer et al., 2012; Santer et al., 2013). Though written materials are only one facet of patient and family education, the literature clearly indicates a need for better education, and a concise CPG with accompanying ADAP such as that developed in this project serves not only to provide written and visual reinforcement but also has the potential to enhance the patient provider relationship through explanation and individualization of the included ADAP.

## Frameworks

### Appraisal of Guidelines for Research & Evaluation

The AGREE II framework was established as a response and re-edit to the AGREE instrument, first released in 2003 with key changes including: refinement of the purpose, response scale and items of the instrument; and a revised and extended user's manual with additional information linked to each item making it easier for the appraiser to use the instrument (Brouwers et al., 2010a). As of 2010, AGREE II had been used to evaluate several hundred guidelines and can be used not only to appraise guidelines but also as a framework for the creation of CPG's, protocols, procedural documents and reporting templates (Brouwers, 2010a). AGREE II specifically allows appraisers to evaluate CPG's in six specific domains: scope and purpose, stakeholder involvement, rigour of development, clarity of presentation, applicability and editorial independence.(Brouwers et al., 2010a).

**Scope and purpose.** Domain 1 addresses the scope and purpose of the CPG (Brouwers et al., 2010a). Specifically, this domain of the framework is designed to address the specificity of the CPG objectives, the specificity of the health questions covered in the CPG and the specificity of the target population of the CPG (Brouwers et al., 2010a). Each of these elements is typically found in the following section of the CPG, respectively: introduction/purpose, questions and target population.

**Stakeholder involvement.** Domain 2 addresses all stakeholders to which the CPG pertains (Brouwers et al., 2010a). Specifically, this is designed to provide clarity as to the inclusion of all relevant professional groups in the development of the CPG, the inclusion of views and preferences of the target population in the CPG and lastly the clear definition of the target users for the CPG (Brouwers et al., 2010a). Specific sections that include the above elements include methods, target population perspectives, and target user respectively.

**Rigour of development.** Domain 3 is one of the larger domains that seeks to address the methods, research base and overall scientific rigor of the CPG (Brouwers et al., 2010a). Specifically, this domain addresses eight important components that include the following: use of systematic elements to search for evidence; clear description of criteria for evidence selection; clear description of the strengths and limitations of the body of evidence used to create the CPG; clear description of the methods for formulating the recommendations; consideration of the health benefits, side effects, and risks in formulating the recommendations; inclusion of an explicit link between the recommendation and supporting evidence; external review by experts prior to its publication; and provision of a procedure for updating the CPG (Brouwers et al., 2010a). The following sections typically contain the above elements, respectively: literature

search strategy, inclusion/exclusion criteria, evidence tables, methods/guideline development process, discussion/recommendations, recommendations and evidence, methods and guideline update.

**Clarity of presentation.** Domain 4 moves forward to address the language, structure and format of the guideline (Brouwers et al., 2010a). The specific components addressed are the specificity with which each recommendation is written, the clear presentation of different options for management of the health condition addressed by the CPG, and the presence of easily identifiable key recommendations (Brouwers et al., 2010a). Clarity of presentation components are typically found in the recommendations, treatment summary and key recommendations sections, respectively.

**Applicability.** Domain 5 pertains to the potential barriers and facilitators to implementation of the CPG, strategies to improve uptake and resource issues inherent to application of the CPG (Brouwers et al., 2010a). In terms of applicability, the framework seeks to answer the following questions: are the facilitators and barriers to application of the CPG described?; is there advise and/or tools for how the recommendations can be put into practice provided?; have the potential resource implications to applying the recommendations been considered?; and have monitoring and/or auditing criteria for the guideline been included in the CPG? (Brouwers et al., 2010a). These questions are typically addressed in following sections of the guideline, respectively: guideline utilization, implementation, cost effectiveness, and quality indicators.

**Editorial independence.** Domain 6 is concerned with making sure that recommendations are formulated free of competing interests or bias (Brouwers et al., 2010a). The following elements are specifically addressed: assurance that the views of the funding body have not influenced the

content of the guideline; and the inclusion and recording of any/all competing interests included in the guideline development group (Brouwers et al., 2010a). Both of these elements are typically found in the funding source and conflict of interest sections of the CPG respectively.

**Social Cognitive Theory**

In the 1970's, a time that focus had been largely placed on learning through the consequences of one's behavior, Albert Bandura demonstrated that trial and error could be circumvented through social modeling of knowledge and competencies (Luszczynska & Schwarzer, 2005). By 1986, Bandura had fully developed his theory, social cognitive theory (SCT), proposing that a personal sense of control facilitates behavioral change, in that, people generally become more willing to take action and commit to the decision to solve a problem, when they believe that they can take action to do it in and of their own personal initiative (Luszczynska & Schwarzer, 2005). In terms of modeling SCT there are several factors that influence behavior: perceived self-efficacy, outcome expectancies (physical, social, self-evaluative), goals, and sociostructural factors (facilitators, impediments), all of which interplay throughout the behavior change process (Luszczynska & Schwarzer, 2005). Figure 6 illustrates this interplay. Bandura (1998) proposes that patients with higher perceived self-efficacy, functional social support, outcome expectancies and knowledge about the proposed treatment will demonstrate greater adherence to treatment.

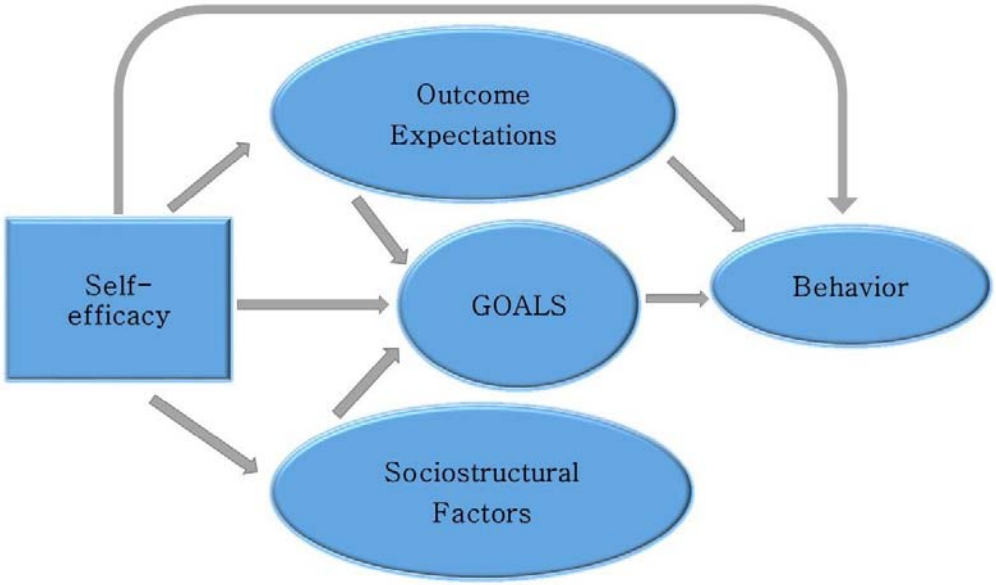



FIGURE 6: Social Cognitive Theory – Adapted from Bandura (2004) Health promotion by social cognitive means.

**Behavior.** *Behavior* is simply the desired outcome or result of the goal that has been set. Through the lens of SCT, a behavior can be evaluated retrospectively, by looking at the behavior and evaluating each of the determinants to discover what impacted the final result, or can be used proactively as the desired end-point or outcome, by which each of the constructs of SCT can be enlisted to seek the positive outcome (Bandura, 2004). With regard to the implementation of a clinical practice guideline specific to primary care, the *behavior* would be successful implementation and regular use of the clinical practice guideline by PCPs. With regard to the care of a child with AD using the complex treatment regimens that are prescribed for control and prevention of exacerbation, the *behavior* would be successful adherence to the prescribed treatment and could be made as specific as needed in tailoring patient education needs.

**Perceived self-efficacy.** *Perceived self-efficacy* is the belief in one's own capabilities to organize and execute plans and subsequent actions required to attain a desired action (Bandura,

1998) It is the impetus of action, as there is little incentive to persevere through difficulty and set-backs, unless there is a belief on a person's own behalf that they can produce the desired effects (Bandura, 1998). With regard to health and health-related behavior, evidence has shown that the belief in one's own self-efficacy in gaining control over a health-related behavior plays an important role in overall health status and functioning, and that the stronger the perceived self-efficacy, the more likely people are to make and sustain the efforts needed to take on and continue with health-promoting behavior (Bandura, 1998). Self-efficacy is rooted in the following different sources: personal accomplishment or mastery; vicarious experience; verbal persuasion by others; and emotional arousal through the absence of apprehension in a difficult situation (Bandura, 1997).

With regard to the care of a child with AD and the complex treatment regimens that are prescribed for control and prevention of exacerbation, *perceived self-efficacy* applies to the PCP through his/her belief that the implementation of a clinical practice guideline will benefit practice and lead to greater outcomes. In terms of the patient/caregiver, *perceived self-efficacy* applies to the belief that he/she is able to undertake the instructed skin care regimen in order to yield a healthier skin barrier. A caregiver/patient's perceived self-efficacy is reinforced through acts such as a demonstration and successful return demonstration of how to apply emollients or topical CS treatment or feeling good about oneself after successfully maintaining the child's clear skin without a flare of eczematous lesions. A caregiver or parent with a higher perceived self-efficacy is going to more willingly adopt and follow-through with the desired treatment plan, whereas a caregiver with lower perceived self-efficacy is going to need much more guidance,

teaching and positive reinforcement to get to the point of feeling that they can successfully adopt and adhere to a complex treatment plan, such as those required for children with AD.

**Goals.** Goals are fundamental to the process of adopting a desired behavior, and serve as self-incentives and guides to health behaviors (Luszczynska & Schwarzer, 2005). Under the constructs of SCT, goals can further be distinguished as distal goals and proximal goals, with proximal goals serving to regulate the amount of invested effort and to guide action, and distal goals functioning to orient in a broader sense (Bandura, 1998). Goals independently contribute to performance or behavior, but are tied to self-efficacy beliefs, in terms of goal setting and whether substandard performance ends up in an attitude of being defeated and demoralized or serves to motivate the person to greater effort (Bandura, 1998). For example, a person with higher self-efficacy, seeking to improve his/her overall health by adopting an exercise plan following previously failed attempts, will set higher, more challenging goals than a person with lower self-efficacy, who may be completely inhibited by his/her past failures and thus not set a goal or set a very low goal.

With regard to the care of a child with AD and the complex treatment regimens that are prescribed for control and prevention of exacerbation, goals can be multi-faceted and tailored to the individual needs of the patient. For example, a parent/patient may be very compliant with the use of topical CSs when eczematous patches first appear, but may struggle to maintain regular use of emollients in order to control or prevent flares, so an appropriate goal could be made regarding regular emollient use. Of course, there should always be the distal goal of maintaining a healthy skin barrier, which is a broader goal that informs the proximal goals that are specific to the patient/parent's individualized needs.

**Outcome expectations.** *Outcome expectations* are social, physical and self-evaluative outcomes expected of behavior, are dependent on an individuals' efficacy beliefs and act as incentives for following through with the behavior (Anderson, Winett, & Wojcik, 2007). *Outcome expectations* can also refer to the perception of possible consequences of one's action. *Social outcome expectations* are the anticipated social responses after a change in behavior, *physical outcome expectations* refer to the anticipation of what will happen and be experienced after behavior change takes place and include short and long-term effects of the change, and lastly, *self-evaluative outcome expectations* or the anticipation of experiences, such as being proud of oneself or feeling ashamed (Luszczynska & Schwarzer, 2005).

With regard to the care of a child with AD and the complex treatment regimens that are prescribed for control and prevention of exacerbation, *social outcome expectations* include improved interpersonal relationships that result from better sleep on behalf of patient and parent secondary to a decrease in exacerbations and less nighttime itching. *Physical outcome expectations* include less pain, itch, discomfort secondary to improved treatment adherence. Lastly, *self-evaluative outcomes* include improved ability to be social and improved patient self-esteem that results from treatment adherence and subsequent decrease in the visible lesions that make patients self-conscious and cause emotional distress.

**Sociostructural factors.** *Sociostructural factors* are defined as the barriers or opportunities that are found in living conditions, health systems, political, economic or environmental systems, and can be further divided into *impeding factors* and/or *facilitating factors* (Bandura, 1997). Making changes would be easy if there weren't obstacles or impediments to overcome, with some of the impediments being personal obstacles that deter performance of healthful behavior

(Bandura, 2004). The interplay between perceived self-efficacy and impediments to successful performance is important in considering behavioral changes, such as the self-efficacy needed to make sure a person sticks to an exercise routine in the face of impediments such as fatigue, more interesting things to do, etc… (Bandura, 1998).

With regard to the care of a child with AD and the complex treatment regimens that are prescribed for control and prevention of exacerbation, sociostructural factors play an important role. There are many impediments that affect successful treatment adherence, some of which include, competing commitments in the daily routine and care of siblings, parental and child fatigue, refusal of the child to cooperate with treatment without throwing a fit, and making the time in the midst of busy schedules needed to complete all of the recommended steps in the skin-care regimen. On the other hand there are also opportunities that positively affect adherence to treatment for children with AD and may include, the wide availability of all of the resources necessary to treat AD, the presence of a helpful co-parent or family member willing to help with daily skin care, or a cooperative child willing comply with treatment.

## Clinical Practice Guideline Development

### Target User

The target user for this CPG is the pediatric primary care provider practicing in a primary care outpatient clinic, as noted in chapters one and two. It may also be of use for nursing and ancillary staff working on the primary care team and for parents/caregivers who desire to have an evidence-based understanding of what is being recommended for their child with AD.

**Formulation of Key Action Statements**

The American Academy of Pediatrics (AAP) process for evidence based policy setting was used as the format for formulating each key action statement with the inclusion of their three recommended steps for formulate a recommendation: first, determination of evidence quality in support of the proposed recommendation; second, evaluation of the balance between anticipated harm and benefit of carrying out the recommendation; and third, assigning a recommendation strength (Marcuse & Shiffman, 2004). Determination of evidence quality is the evaluation of the type of research study and the rigor of the investigator's adherence to methodologic principles with high quality evidence being well conducted randomized controlled trials (RCT) in a comparable population and low quality evidence being derived from case report and expert opinion (Marcuse & Shiffman, 2004). Assessment of the balance between benefit and harm associated with adhering to a guideline recommendation is important in that, the stronger the proportion of benefit over harm is determined to be, the easier it is to justify classification as a stronger recommendation (Marcuse & Shiffman, 2004). Lastly, assignment of recommendation strength comes from the combination of the evidence quality and the balance between harm and benefit, as depicted in figure 7, and is classified as a strong recommendation, a recommendation, an option or as no recommendation, with a strong recommendation indicating that the benefits clearly exceed the harm and that the quality of evidence is excellent, a recommendation indicating that the benefits exceed the harms, but that the evidence base is not as strong, an option indicating that the evidence quality is suspect or that studies have not demonstrated a clear advantage or disadvantage, and no recommendation indicating that there is both a lack of evidence and unclear balance between benefit and harm (Marcuse & Shiffman, 2004).

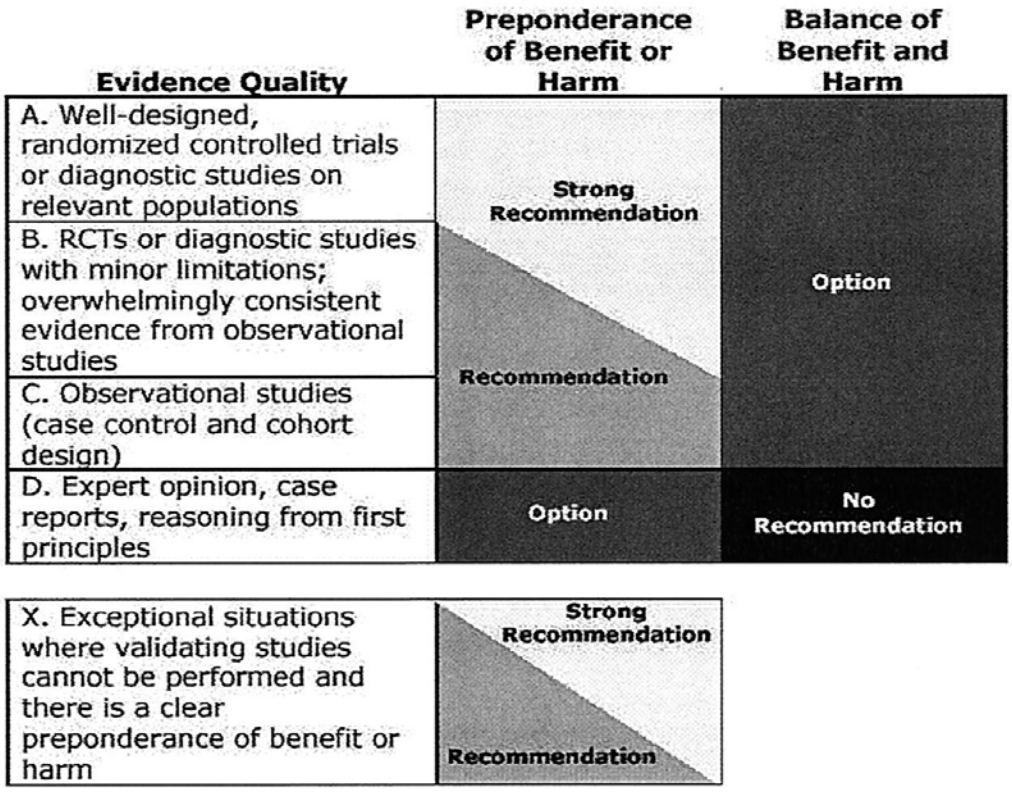



FIGURE 7: Relationship of Evidence Quality and Benefit-Harm Balance in Determining the Level of Recommendation. (Marcuse & Shiffman, 2004).

**Literature Inclusion/Exclusion Criteria**

The general strategy for reviewing the literature is outlined in chapter two.

**External Review**

In addition to the reviewers who will appraise the CPG with the use of the AGREE II tool, it will be reviewed by the DNP committee of the primary author of the CPG, consisting of two DNP-prepared NPs and one PhD-prepared NP. Should additional publication be sought, the primary author will see the review of a larger committee of experts.

## Clinical Practice Guideline Implementation

CPGs facilitate the translation of best evidence into best practice and promote quality by: reducing variations in care delivery; improving accuracy in diagnoses; discouraging ineffective interventions; and by promoting safe, effective treatments (Rosenfeld & Shiffman, 2009). CPGs should be quality driven, evidence-based, action-ready, efficient, use transparent methodology, and demonstrate multi-disciplinary applicability and validity (Rosenfeld & Shiffman, 2009). Furthermore, guidelines benefit patients through improved outcomes, fewer interventions that are ineffective, consistency in care, and by creating secondary education and implementation materials such as the proposed ADAP (Rosenfeld & Shiffman, 2009).

Limited health literacy, or "the degree to which individuals have the capacity to obtain, process, and understand basic health information" has a profound impact on people of all demographics (USDHHS, 2010). Among the goals set forth in the National Action Plan to Improve Health Literacy, are the goals to develop and distribute health and safety information that is accurate, accessible and actionable, and to support efforts to provide culturally and linguistically appropriate health information services in the community (USDHHS, 2010).

The use of educational tools has been found to improve knowledge and understanding of health information and awareness of the potential consequences of not adhering to treatment plans (Gebhard, Goske, Salisbury, Leopard, & Hater, 2015; Taddio et al., 2013; Warland, 2013). Written educational materials are best used when the information is presented in a clear, concise manner with simple design and plain language (Ryan et al., 2014).

A CPG with accompanying ADAP was created with the purposes of providing concise, evidence-based information about the treatment and control of childhood AD for use by pediatric

PCPs, and of giving patients and parents an interactive tool to promote treatment adherence. Guiding the development of the CPG and ADAP, the AGREE II framework and SCT were used to inform the content and presentation of the CPG, and the design and content of the ADAP, and will be discussed in greater detail in Chapter 4.

## Conclusion

This chapter discussed the importance of a clinical practice guideline and parent and patient education as a means to improve adherence to treatment plans for childhood AD. SCT and AGREE II were introduced as the theoretical framework guiding the development of the clinical practice guideline and ADAP. Each of the domains of AGREE II were defined and applied to the context of CPG development. Each of the determinants fundamental to the understanding of SCT, were defined and applied to the context of care management of children with AD. Following the descriptions of each framework, CPG development is described, including the target user, key action statement formulation, literature inclusion/exclusion criteria, and external review. Lastly, a brief introduction to the value of clinical practice guidelines and accompanying patient/parent education as tools to educate patients and their families was provided.

# CHAPTER IV: CLINICAL PRACTICE GUIDELINE

## Introduction

Chapter four will present the clinical practice guideline developed for pediatric PCPs to use in primary care for the treatment of children with AD. Brief descriptions of the objective, target population and questions that led to the formulation of the key action statements will be provided. Key action statements will be provided and broken into the following five categories: diagnosis, prevention/control, treatment, patient/parent education and referral criteria. A brief overview of each category will be provided with an overview of evidence. Following each key action statement, will be an evidence profile with the following list of constructs: aggregate evidence quality, benefit, harm, cost, benefit-harm assessment, value judgements, intentional vagueness, role of patient preferences and exclusions and discussion of the evidence (Marcuse & Shiffman, 2004; Rosenfeld & Shiffman, 2009). Guideline utilization and implementation will be discussed at the end of the CPG. Following the CPG, the proposed ADAP will be presented.

### Objective

The objective of the following CPG is to provide pediatric PCPs with specific, evidence-based guidelines for the diagnosis, prevention of exacerbation, and treatment for childhood AD, the provision of patient/family teaching and criteria for specialist referral. A secondary goal is to decrease long-term disease sequelae, improve quality of life and increase patient/parent understanding of treatment and treatment goals.

### Population

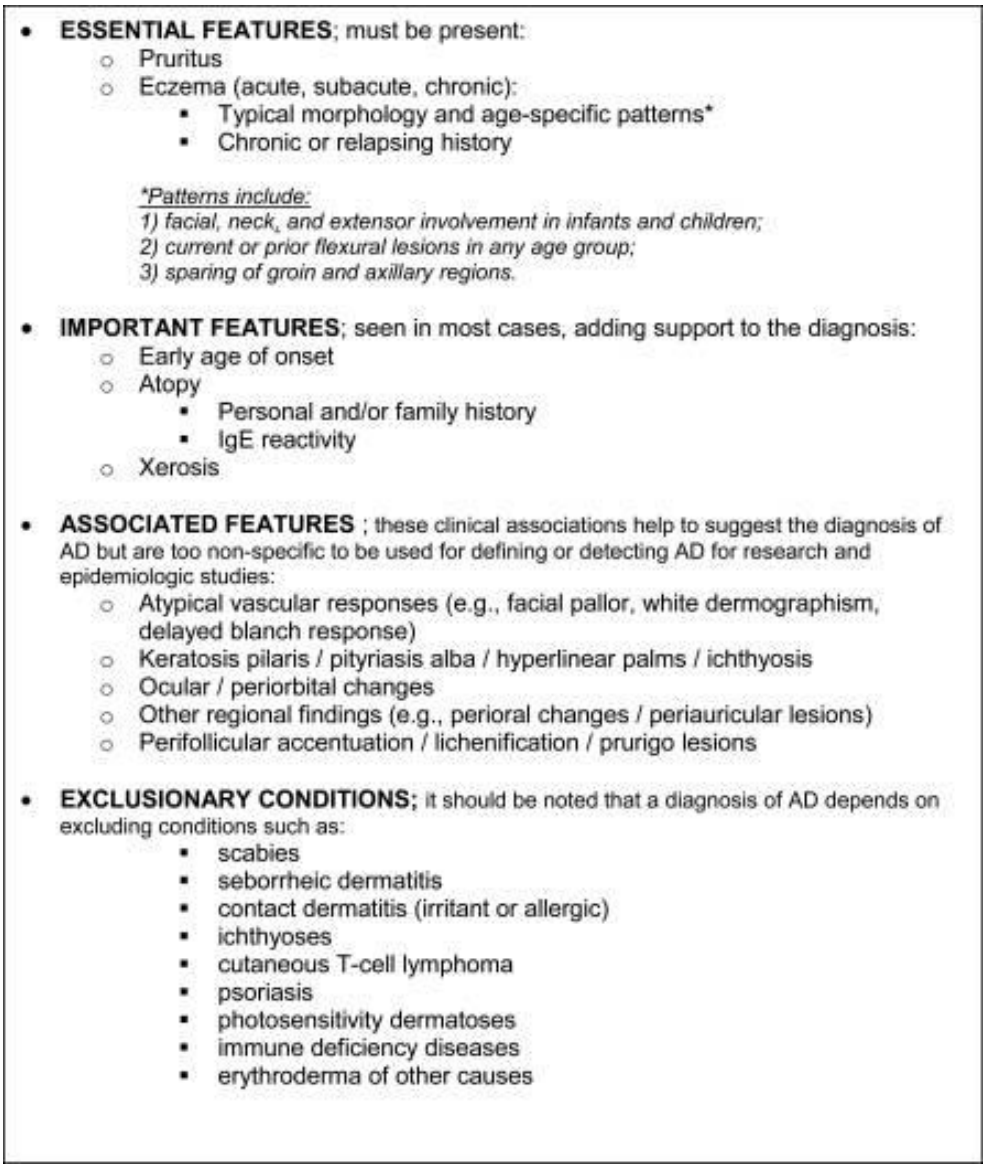
The following CPG is intended for use in the diagnosis and treatment of pediatric patients, ages 0-18 years old, male and female, being managed by a pediatric PCP in the primary care

setting. Pediatric PCPs in the primary care setting may include physicians, nurse practitioners and physician assistants who specifically care for pediatric patients as defined above.

## Key Action Statements

### Diagnosis of Childhood AD

Childhood AD encompasses a wide variety and spectrum of skin manifestations in terms of presentation, severity and distribution that has resulted in disagreement about its definition among clinicians (Brenninkmeijer, Schram, Leeflang, Bos & Spuls, 2008). It is important to differentiate AD from other red, scaly skin conditions such as seborrheic dermatitis or allergic contact dermatitis (Eichenfield et al., 2014a). Though diagnostic criteria exist, nearly a quarter of clinical trials for AD do not specify diagnostic criteria (Brenninkmeijer et al., 2008). When used, The Hanifin and Rajka diagnostic criteria and the UK Working Party diagnostic criteria are two largely accepted sets of diagnostic criteria that have both been validated in studies and tested in different populations (Chalmers et al., 2007; Eichenfield et al., 2014a; Firooz et al., 1999; Gu et al., 2001; Saeki et al., 2007; Samochocki & Delewska, 2012; Williams, Burney, Pembroke & Hay, 1994; Williams, Burney, Pembroke, & Hay, 1996). The American Academy of Dermatology (AAD) 2003 consensus conference recommended a revised version of the Hanifin and Rajka criteria (figure 8) because of its applicability to a full range of ages, including infants, given that the UK Working Party diagnostic criteria does not apply to children below the age of two (Eichenfield, Hanifin, Luger, Stevens, & Pride, 2003).



- **ESSENTIAL FEATURES**; must be present:
  - Pruritus
  - Eczema (acute, subacute, chronic):
    - Typical morphology and age-specific patterns*
    - Chronic or relapsing history

  *Patterns include:*
  *1) facial, neck, and extensor involvement in infants and children;*
  *2) current or prior flexural lesions in any age group;*
  *3) sparing of groin and axillary regions.*

- **IMPORTANT FEATURES**; seen in most cases, adding support to the diagnosis:
  - Early age of onset
  - Atopy
    - Personal and/or family history
    - IgE reactivity
  - Xerosis

- **ASSOCIATED FEATURES** ; these clinical associations help to suggest the diagnosis of AD but are too non-specific to be used for defining or detecting AD for research and epidemiologic studies:
  - Atypical vascular responses (e.g., facial pallor, white dermographism, delayed blanch response)
  - Keratosis pilaris / pityriasis alba / hyperlinear palms / ichthyosis
  - Ocular / periorbital changes
  - Other regional findings (e.g., perioral changes / periauricular lesions)
  - Perifollicular accentuation / lichenification / prurigo lesions

- **EXCLUSIONARY CONDITIONS;** it should be noted that a diagnosis of AD depends on excluding conditions such as:
  - scabies
  - seborrheic dermatitis
  - contact dermatitis (irritant or allergic)
  - ichthyoses
  - cutaneous T-cell lymphoma
  - psoriasis
  - photosensitivity dermatoses
  - immune deficiency diseases
  - erythroderma of other causes

FIGURE 8: Revised Hanifin and Rajka criteria adapted from Eichenfield et al. (2003) and published in Eichenfield et al. (2014). Used with permission from the Journal of the American Academy of Dermatology.

**Key Action Statement 1. Clinicians should use the revised Hanifin and Rajka diagnostic criteria to diagnose atopic dermatitis in a child age 0-17 who presents to the primary care setting with pruritic eczematous lesions distributed in a characteristic pattern with facial, neck and extensor involvement.**

TABLE 2: Key Action Statement Profile: KAS 1

| **Aggregate evidence quality** | **Grade C** |
|---|---|
| **Benefits** | Reduction in incorrect diagnosis and unnecessary treatment. Increases incidence of correct diagnosis of not only AD, but of other conditions that may be incorrectly diagnosed as AD. Promotes the use of a standardized, evidence-based method for diagnosis. |
| **Risks, harm, cost** | No risk or harm; possible cost in training providers. |
| **Benefits-harms assessment** | Preponderance of benefit |
| **Value judgements** | High value placed on the importance of a set of diagnostic criteria. |
| **Intentional vagueness** | None |
| **Role of patient preferences** | None |
| **Exclusions** | None |
| **Strength** | **Recommendation** |

***Discussion.*** Evidence for this key action statement is almost exclusively ascertained from case-controlled and cross-sectional studies which accounts for it being classified as Grade C in terms of research rigor. Three studies in particular validate the utility of the Hanifin and Rajka diagnostic criteria, through a comparison to the U.K. diagnostic criteria (De, Kanwar, & Handa, 2006; Samochocki & Delewska, 2012; Williams et al., 1994). De et al. (2006) found that the Hanifin and Rajka criteria (sensitivity 96%, specificity 93.75%, positive predictive value [PPV] 97% and negative predictive value [NPV] 91.84%) was statistically superior to the UK working party diagnostic criteria (sensitivity 86%, specificity 95.83%, PPV 97.75% and NPV 76.67%). Williams et al. (1994) found that use of the Hanifin and Rajka criteria resulted in a sensitivity of 93.1%, a specificity of 77.6, PPV of 83.1% and NPV of 90.5, and while impressive, this particular study yielded slightly better results for the UK working group criteria that resulted in a sensitivity of 87.9%, specificity of 92.8%, PPV of 93.6% and NPV of 86.7%. Lastly,

Samochocki and Dejewska (2012) concluded that the Hanifin and Rajka criteria was still the gold standard, however found that the UK working group criteria were useful in the diagnosis of children four years and older, with results demonstrating that 153 of the 173 children diagnosed with AD by means of the Hanifin-Rajka criteria were also diagnosed positive by the UK working group criteria. While limited in number of studies the above validates the utility of the Hanifin and Rajka diagnostic criteria.

Regarding the remainder of the evidence profile, there is really no risk of harm, but rather a preponderance of benefit over harm. If any cost at all, it would only be needed to provide paid time for training in the use of the criteria. Lastly, there are really no exclusions, because the Hanifin and Rajka criteria are designed to be used for all ages of infant and children.

**Prevention/Control of Childhood AD**

Arguably, the cornerstone of providing care for children with AD is a strong focus on the prevention and control of eczematous flares. The most important goals in the management of AD are to improve quality of life and to prevent complications while minimizing potential medication side effects, with optimal control being most effectively achieved through hydration, restoration of the skin barrier and control of inflammation (Lyons et al., 2015). Two important aspects of prevention and control that should be addressed in primary care and included in the treatment plan of all children with AD, are the daily use of topical moisturizer skin-care and assessment and avoidance of known AD triggers that potentiate the itch-scratch cycle (Eichenfield et al., 2015; Schneider et al., 2013). The following two key action statements specifically address their inclusion in the treatment plan.

**Key Action Statement 2a. Clinicians should include topical moisturizer daily skin care in the treatment plan for children diagnosed with AD with the purpose of preventing and controlling eczematous lesion flares.**

TABLE 3: Key Action Statement Profile: KAS 2a

| Aggregate evidence quality | Grade A |
|---|---|
| **Benefits** | Combat xerosis and transdermal water loss. Lessen pruritus, erythema, fissuring and lichenification. Decrease amount of prescription anti-inflammatory treatments needed for disease control. Prevent flares. |
| **Risks, harm, cost** | Potential adverse effects. Variable efficacy of individual selection of agent. Cost of emollient |
| **Benefits-harms assessment** | Preponderance of benefit over harm |
| **Value judgements** | None |
| **Intentional vagueness** | No specific name or brand of emollient added related to the number of options available. |
| **Role of patient preferences** | Limited only to discussion of specific emollient to use. |
| **Exclusions** | None |
| **Strength** | Strong Recommendation |

***Discussion.*** Evidence for the use of daily topical moisturizer skin care is abundant and of high quality. Topical moisturizer skin care includes emollients such as glycol and glyceryl stearate and soy sterols, that lubricate and soften skin, occlusive agents such as petrolatum and mineral oil, that form a layer that prevents the evaporation of water, and humectants such as glycerol, lactic acid and urea, that attract and hold water (Eichenfield et al., 2014b). It is well studied and well agreed upon that regular use of moisturizer skin care combats xerosis and prevents water loss from the skin (Eichenfield et al., 2014b; Lee, Son & Cho, 2016).

In terms of rigor, randomized control trials (RCT) have shown that daily use of moisturizers decreases pruritus, erythema, fissuring and lichenification (Breternitz, Kowatzki,

Langenauer, Elsner & Fluhr, 2008; Grimalt, Mengeaud & Cambazard, 2007; Korting, Schollmann, Cholcha & Wolff, 2010). The RCT described by Breternitz et al. (2008) found that glycerol-based emollients increased SC hydration and decreased severity of xerosis. Korting et al. (2010) specifically evaluated pale sulfonated shale oil (PSSO) using a RCT and found an overall decrease in erythema, crusts, excoriations, itch, lichenification and scale in children from 0-12 years old. RCTs have also demonstrated that emollient use leads to a steroid-sparing effect and subsequent decreased use of TCs (Grimalt et al., 2007; Msika et al., 2008; Tan, Suresh, Tey, Chiam & Goon, 2010). Grimalt et al. (2007) detail a 6 week trial evaluating infants under 12 months old with inflammatory lesions being treated with moderate and/or high potency TCs with randomization to a control group and a study group that had emollients added to the TC treatment, that resulted in a significant reduction in TC need and consumption. Additionally, Tan et al. (2010) and Msika et al. (2008) conducted RCTs that found a steroid-sparing effect with the use of a triclosan-containing emollient and a 2% Sunflower Oleodistillate emollient respectively.

Though this is a strong recommendation, there is a minimal risk of adverse effect to the chosen topical moisturizer and there is potential for varied efficacy, as there will be patients that will have greater need for a more occlusive product, whereas others will respond well to an emollient. In terms of cost, over the counter moisturizers that fall into the emollient, humectant or occlusive categories are often more expensive, which is a potential burden for patients/parents. Additionally, there is intentional vagueness in the exclusion of specific brands/names of moisturizers due to the overwhelming number of options, therefore it is up to the individual clinician to use discretion in determining specific recommendations for specific

patients. Due to all of the above evidence and factors, this key action statement meets criteria to be a strong recommendation.

**Key Action Statement 2b. Clinicians should recommend avoidance of common irritants that trigger xerosis and the itch-scratch cycle such as: abrasive occlusive, tight clothing; harsh laundry detergents; soaps without a neutral pH, and known harsh chemicals.**

TABLE 4: Key Action Statement: KAS 2b

| Aggregate evidence quality | Grade C |
|---|---|
| **Benefits** | Less skin irritation, reduction of the itch-scratch cycle |
| **Risks, harm, cost** | Low possibility of reaction, even to milder products. Cost in purchase of hypoallergenic products that often are more expensive. |
| **Benefits-harms assessment** | Preponderance of benefit over harm |
| **Value judgements** | None |
| **Intentional vagueness** | None |
| **Role of patient preferences** | None |
| **Exclusions** | None |
| **Strength** | Recommendation |

***Discussion.*** Patients with AD have a lower threshold for skin irritation than patients who do not have AD, and for this reason it is important to give attention to identifying and minimizing irritants that can trigger the itch-scratch cycle such as harsh soaps and detergents, harsh household chemicals and abrasive clothing (Lee et al., 2016; Schneider et al., 2013). Toiletries and astringents that contain alcohol and sodium laurel sulfate (SLS) are drying and should be avoided, and patients/parents should choose soaps that have a neutral pH and minimal defatting activity such as Dove, Neutrogena, Aveeno, CeraVe, Eucerin, Vanicream, and Cetaphil (Schneider et al., 2013). Additionally, clothing should be open-weave, cotton-blend and loose fitting, and should be laundered with a mild liquid detergent prior to wearing due to the common

presence of formaldehyde and other chemicals in the fabric (Lee et al., 2016; Schneider et al., 2013).

With regard to evidence, Nassif, Chan, Storrs and Hanifin (1994) conducted and observational study that showed greater irritant response in atopic study patients with active flares, when exposed to SLS, hypothesizing that intrinsic hyper-reactivity in the inflammatory cells of atopic individuals predisposes to a lowered threshold or irritant responsiveness. Similarly, two non-randomized control studies published by Tabata, Tagami and Kligman (1998) found that exposure to SLS led to stronger and longer lasting SC damage through diffusional water loss and lower levels of intercellular lipid ceramides, and that the reaction to SLS was similar to that found in the native disease and in patch test reaction to specific allergens. An observational case-report study of children 0-15 that involved the use of daily electronic diaries and portable data loggers, found that wool clothing, shampoo and the physical state of sweating were all associated with both "bother" and "scratch" symptoms (Langan, Silcocks & Williams, 2009). With regard to clothing, data, including a controlled study, has revealed that occlusive fibers such as polyester and nylon have the potential to worsen AD and that exposure to rough fiber such as wool can cause mechanical irritation and exacerbation of AD (Bendsoe, Bjornberg & Asnes, 1987; Diepgen, Stabler & Hornstein, 1990; Langan et al., 2009; Mobolaji-Lawal & Nedorost, 2015; Yao, Tokura, Li, Newton & Gohel, 2006).

There are very few risks, if any to this key recommendation. It is possible that patients could react, even to the milder substances and there are costs involved in choosing milder products. Many hypoallergenic products and preferable fabrics are more expensive than synthetics and this may become a barrier for parents/patient. Generally, though, this is a

recommendation with very little possibility for harm and one that is very straightforward for the clinician to use in clinical practice.

**Treatment of Acute Eczematous Lesions in Childhood AD**

Even with the best moisturizing skin care compliance and trigger avoidance, the majority of children will experience at least one flare that requires additional pharmacological treatment, with mild to moderate flares marked by itching, erythema, mild excoriations, papules, dry scaly patches and/or lichenification and severe flares marked by persistent itching, substantial erythema, extensive excoriations, oozing/crusting and/or lichenification (Krakowski et al., 2008). Topical corticosteroids (TC) are the gold standard and mainstay of first-line treatment for acute flares. They decrease inflammation and pruritus, prevent bacterial colonization, and should be used with attention to potency (Lyons et al., 2015). In children, it is particularly important to start with the lowest potency that will be effective, to give attention to stepping-up and stepping-down as severity necessitates, and to select the appropriate potency for body part (Lyons et al., 2015). For children with moderate to severe AD, there is another class of topical treatment, topical calcineurin inhibitors (TCI). TCIs have shown effectiveness for both daily use alongside for following unsuccessful TC treatment and for proactive or maintenance therapy to be used regularly to normal appearing skin in flare prone areas and/or applied at the first sign of a flare (Eichenfield et al., 2015). A benefit to the use of TCIs is that they are associated with less side-effects and can be used long-term with less risk than with TCs. Lastly, wet wrap therapy (WWT) is an additional treatment for acute flares in patients with moderate to severe AD and involves the application of a wet tubular bandage, gauze or occlusive cotton garment to skin that has been treated with moisturizers and/or diluted TS, followed by the addition of a dry top layer that are

both left on the skin for a period of hours and repeated daily or twice daily for a period of time to speed response and recovery from moderate to severe eczematous flares (Nicol et al., 2014).

**Key Action Statement 3a. Clinicians should prescribe topical corticosteroids with specific attention to selection of appropriate potency for severity of eczematous lesion, as first line treatment for acute eczematous lesions**

TABLE 5: Key Action Statement Profile: KAS 3a

| Aggregate evidence quality | Grade A |
|---|---|
| **Benefits** | Relief and resolution of eczematous lesions. Itch and pain relief. Easy mode of application. No systemic therapy needed. Ability to step-up or step-down treatment |
| **Risks, harm, cost** | Risk of relatively mild treatment side-effects and of incorrect application that could lead to under or over treatment and corresponding mild adverse effects. No associated cost. |
| **Benefits-harms assessment** | Preponderance of benefit over harm |
| **Value judgements** | High value placed on the prompt and effective resolution of symptoms. |
| **Intentional vagueness** | None |
| **Role of patient preferences** | Minimal |
| **Exclusions** | Patients with allergy or hypersensitivity to TCs. Refractory lesions. |
| **Strength** | Strong Recommendation |

***Discussion.*** The body of evidence supporting the use of TCs as first-line treatment for AD is robust and well validated with more than 110 different RCTs performed as of 2014 (Eichenfield et al., 2014b). In a systematic review of treatments for atopic eczema, Hoare, Li Wan Po and Williams (2001) cited 13 level I studies that showed effectiveness of TC over placebo, ranging from the years 1967-1997, with at least four of the 13 studies including children in their study participants and six studies that didn't specify. There are also more recent RCTs that further validate their value, as well (Eichenfield et al., 2014b; Ring et al., 2012; Schneider et al., 2013).

Ring et al. (2012) further highlighted studies supporting the importance of potency selection in correlation with severity of lesions, and also noted the importance of not sparing TCs during acute flares, along with baseline, daily emollient skin care combined with early anti-inflammatory intervention to stabilize before the flare becomes treatment-intensive.

Benefits ascribed to the use of TCs as first-line treatment are the resolution and relief of eczematous lesions along with itch and pain relief. Topical treatment provides a relatively easy mode of treatment without the need for systemic therapy. TCs are also available in varying potencies allowing treatment to be tailored according to severity. Though the benefits greatly outweigh the potential for harm, there are risks of adverse effects with longer term use and that are increased with over-application, including purpura, striae and skin atrophy (Eichenfield et al., 2014b). Additionally, under-application could lead to ineffective treatment and prolonged presence of eczematous lesions, however the fact that it is a topical preparation allows for ease in adjustment of the amount being used.

Regarding value judgements, there is high value placed on the ability to rapidly and effectively resolve symptoms. Lastly, there is no intentional vagueness, or role of patient preferences, and the only exclusion would be patients who have shown allergy or hypersensitivity to TCs and patients who are refractory to TC treatment. All of the above lends support to this being designated as a strong recommendation.

**Key Action Statement 3b. Clinicians should prescribe topical calcineurin inhibitors for patients age 2-17 with moderate to severe persistent atopic dermatitis as second-line treatment when no longer responding to TC's, to be used daily for short time-periods (< 12 weeks) to treat acute eczematous lesions, or for longer time-periods (up to one year),**

**several days weekly in commonly affected areas as a means to provide long-term treatment and prevention of eczematous flares.**

TABLE 6: Key Action Statement Profile: KAS 3b

| Aggregate evidence quality | Grade A |
|---|---|
| **Benefits** | Treatment alternative to TCs. Less side effects than TCs. Ability to be used as a long term treatment. High treatment efficacy. Low discontinuation rates. Reduction in bacterial colonization |
| **Risks, harm, cost** | Minimal risk of application site skin irritation, Oldest data available is 10 years old causing less long-term certainty. No associated cost |
| **Benefits-harms assessment** | Preponderance of benefit over harm |
| **Value judgements** | High value placed on avoidance of common high potency TC side effects and on potential for longer term treatment. |
| **Intentional vagueness** | None |
| **Role of patient preferences** | None |
| **Exclusions** | Patients with allergy or hypersensitivity to TCIs. Patients less than 2 years old |
| **Strength** | Strong Recommendation |

***Discussion.*** Although this key action statement begins to get more specific and to delve into the treatment of moderate to severe eczematous flares, it is relevant to primary care, in that there will be instances that a patient is refractory or not achieving complete resolution of eczematous lesions, despite the use of moderate to high potency TCs. Rather than that patient having to wait the time it takes for a specialist referral, it is reasonable for PCPs to initiate TCI treatment while the patient awaits the specialist evaluation. Likewise, this same type of patient may need intermittent care should they not be able to get back in to see the specialist in a timely manner, and the ability to manage treatment with TCIs will be of dual benefit to the patient and to the specialist who is juggling many patients and a packed schedule allowing for a collaborative

model of care. The second reason this is relevant to primary care, is that PCPs will likely receive their patients back from specialty care receiving long term TCI treatment and should be familiar with its use and value, again, for collaborative management.

The rigor of research regarding the short-term use of both tacrolimus and pimecrolimus for the treatment of moderate to severe AD is strong with multiple double blind, randomized, vehicle-controlled studies to support their effectiveness (Kalavala & Dohil, 2011). Boguniewicz et al. (1998) detail a double-blind, vehicle controlled trial in which children age 7-16 years were treated twice daily with either tacrolimus or pimecrolimus against those treated with the vehicle and found to have 67% and 70% response rates respectively compared to 38% in the vehicle group. Likewise, Paller, Eichenfield, Leung, Stewart and Appell (2001) conducted a 12-week RCT for children 2-15 years old that demonstrated a 90% clinical improvement rate and success with both TCIs against the control vehicle agent. Two additional RCTs found success in cohorts aged 1-17 years (Eichenfield et al., 2002).

Regarding the use of TCI's for long-term (up to 12 months) use with the purpose of flare prevention, data is also robust. Three long-term RCTs and one long-term non-comparative study, in particular found that there was reduced need for TCs. longer median time to first flare, reduced incidence of flares, and progressive improvement that was maintained for the full 12-month trial, respectively (Kapp et al., 2002; Remitz et al., 2007; Wahn et al., 2002; Zuberbier & Brautigam, 2008).

Benefits of the use of TCIs for moderate to severe AD include: less side-effects than TCs, the ability to be used as long-term treatment, high treatment efficacy, the fact that they are an alternative to TCs, low discontinuation rates and reduction in rates of bacterial colonization. All

of these benefits make TCIs a compelling choice for second-line treatment and support their recommendation for use. Though few, risks may include: low rate of application site skin irritation and the fact that the oldest study data available is less than 15 years old leading to less long-term certainty of benefit (Kalavala & Dohil, 2011). There is no associated cost to this key action statement.

Regarding value judgements, a high value attributed to the avoidance of high potency TC side effects and the potential for successful longer term treatment should be expected with this recommendation. There is no intentional vagueness or role of patient preferences, and the only exclusions would be patients with allergy or hypersensitivity to TCIs and patients less than 2 years old. Although there are studies that validate the use of TCIs in infants and children less than 2 years old, for the purposes of primary care the judgement was made to take that discernment out of the hands of PCPs who are not specialized in dermatology, allergy or immunology. All of the above support the classification of this being a strong recommendation.

**Key Action Statement 3c. Clinicians should recommend the use of wet-wrap therapy, with or without the concurrent use of a topical steroid, for moderate to severe or refractory childhood atopic dermatitis with the intent to minimize the need for systemic immunosuppressive therapy.**

TABLE 7: Key Action Statement Profile: KAS 3c

| Aggregate evidence quality | Grade B |
|---|---|
| **Benefits** | Quickly reduces AD severity. Effective in severe and refractory disease. Allows for increased penetration of topical agent; provides a physical barrier against scratching. |
| **Risks, harm, cost** | Risk of HPA axis suppression if over used or used with higher potency TC, although short courses have not been associated with prolonged adrenal suppression. Higher risk of infection when combined with higher-potency topical steroid, but data is minimal and conflicting as to actual occurrence. Cost of supplies (tubular bandage, gauze, cotton garments). |
| **Benefits-harms assessment** | Preponderance of benefit over harm |
| **Value judgements** | High value ascribed to likelihood of success for patients with severe or refractory lesions |
| **Intentional vagueness** | "With or without" is used so that the clinician can use discernment on an individual patient basis. |
| **Role of patient preferences** | Shared decision making given that WWT involves substantial work on the part of the parent and patient outside of clinic setting. |
| **Exclusions** | Patients with mild AD |
| **Strength** | Recommendation |

***Discussion.*** WWT, the practice of covering the skin (prepped with a moisturizing product alone or with TC's to lesions) with a wet layer of cotton clothing, tubular bandage or gauze followed by a second dry layer of clothing, is an excellent option for the quick reduction in AD severity for patients with severe flares, moderate to severe persistent AD and/or refractory AD (Eichenfield et al., 2014b). In the largest study (observational cohort) evaluating WWT for pediatric patients with moderate to severe AD with the use of a validated outcomes tool, Nicol et al. (2014) found that WWT in a supervised setting, with the use of diluted TCs, for a two week period of time resulted in the avoidance of systemic immunotherapy and maintenance of

improvement for at least one month following completion. Although this study was completed in a controlled in-patient setting, its quality and results allow for the potential of translation to primary care and the home setting. Janmohamed et al. (2014) completed a prospective, randomized, double blind, placebo-controlled study comparing the effectiveness with WWT with emollients versus WWT with diluted corticosteroids and found that both were successful with the diluted corticosteroid group improving faster and was only limited by a small study group. Lastly, there have been at least 15 other studies that have validated the effectiveness of WWT, but limited by their variability in size, differences in procedural details and scoring tools (Abeck, Brockow, Mempel, Fesq & Ring, 1999; Devillers, de Waard-van der Spek, Mulder & Oranje, 2002; Nicol et al., 2014; Pei, Chan & Ho, 2008; Wolkerstorfer et al., 2000).

With respect to potential risks of the use of WWT, the risk of HPA axis suppression if over used with higher potency TC has been documented, however data is minimal and has noted that there isn't as much risk when shorter courses or diluted TCs are used (Eichenfield et al., 2014b; Pei et al., 2001; Wolkerstorfer et al., 2000). A higher risk of infection when combined with higher-potency topical steroid, has been documented, but data is out of date, minimal and conflicting as to actual occurrence (Eichenfield et al., 2014b; Hindly, Galloway, Murray & Gardener, 2006; Schnopp et al., 2002). In terms of cost, there are costs to consider associated with the need for more supplies than with other treatments, such as tubular bandage, gauze, and/or cotton garments.

Lastly, value judgement and the role of patient preferences play a role in this key action statement. There is going to be a higher value placed on this recommendation due to the high potential for success in patients who have not had treatment success or for whom the burden of

trying to attain disease control has been high. Likewise, the role of patient preferences will also play a larger role due to the amount of effort and commitment needed on the part of the patient/parent to complete the very complex and involved treatment.

**Patient/Parent Education for Childhood AD**

Patient/parent education is an essential aspect of treating children with AD and should be made a priority in the time spent with children and their respective caregivers. Adherence to treatment is of paramount importance for successful management of AD and is often impacted by patient motivation, understanding of treatment, sense of empowerment and control, and trust in the treatment regimen (Ntuen et al., 2010). In order to foster education and empowerment of patients/parents, it is important to spend time at every visit reviewing the treatment plan, answering questions and making necessary adjustments (Eichenfield et al., 2015). In addition to the preceding action statements, two interventions that are particularly helpful to the primary care provider are: the instruction in use of the finger-tip unit (FTU) for measurement of topical agents, which not only lends to better clarity in medication administration, but also helps foster compliance by caregivers/patients who may have fears regarding the use of too much; and the use of written action plans (WAP), which provide an interactive way to communicate the treatment plan to better foster compliance and clarity in instruction (Eichenfield et al., 2015; Ntuen et al., 2010; Sidbury et al., 2014)

**Key Action Statement 4a. Clinicians should use the fingertip unit to instruct parents/caregivers of patients age 0-17, how to quantify the amount of topical medication to use for each application.**

TABLE 8: Key Action Statement Profile: KAS 4a

| Aggregate evidence quality | Grade B |
|---|---|
| **Benefits** | Clarity in prescribing directions. Avoidance of over using topical medications. Easing fears of parents ("steroid phobia") that they will over-use topical steroids. |
| **Risks, harm, cost** | Very mild risk of parents/patients incorrectly completing performing the task. No cost |
| **Benefits-harms assessment** | Preponderance of benefit over harm |
| **Value judgements** | High value ascribed to the avoidance of harm from overtreatment |
| **Intentional vagueness** | None |
| **Role of patient preferences** | None |
| **Exclusions** | None |
| **Strength** | Strong Recommendation |

***Discussion.*** Proper measurement of topical treatment has long been an issue for patients and more often than not, they are not using enough, out of fear of using too much. The measurement method that has become the most widely accepted is the fingertip unit (FTU), devised over two decades ago to help doctors and patients obtain a better understanding of the amount of topical agents to use for specific body areas (Bewley, 2009). Defined as the amount of cream or ointment expressed from a standard 5mm diameter tube tip applied from the distal skin crease to the tip of the patient's index finger and is equal to approximately 500 mg and is sufficient to cover two adult palms (Kalavala, Mills, Long & Finlay, 2007). In a seminal study, Long, Mills and Finlay (1998) devised simple guidelines for topical therapy for children that were based on the following four principles: first, the adult FTU; second, Lund and Browder's method to estimate the surface area of burns, on which the "rule of 9's" is based; third, standard growth charts for children; and fourth, standard nomograms for the calculation of body surface area (BSA) in children. The resulting recommendations of the Long et al., (1998) study are depicted

in chapter 2, figure 4 as adapted by Eichenfield et al., 2015. Though, not entirely clear how rigorous the study designs were, Nelson, Miller, Fleischer, Balkrishnan and Feldman (2006) also made similar conclusions with a greater focus on the calculation of BSA for each patient.

Benefits of using this recommendation are significant and include the provision of clarity in prescribing directions, avoidance of topical medication over-use and the easing of fears of parents with "steroid phobia" who think they will use too much TC and subsequently under dose. There is only one very mild risk in patients/parents incorrectly completing the task, leading to the determination that the benefit far outweighs the potential for harm. There is no cost associated with the recommendation, nor is there any intentional vagueness, role of patient preferences or exclusions. There is a value judgement in that there is a high value ascribed to the avoidance of harm from overtreatment of TCs on behalf of patients/parents. This, therefore, encompasses a strong recommendation.

**Key Action Statement 4b. Clinicians should include individualized written patient/parent education in the overall treatment plan for patients with childhood AD, such as an individual written action plan.**

TABLE 9: Key Action Statement Profile: KAS 4b

| Aggregate evidence quality | Grade B |
|---|---|
| **Benefits** | Clearly communicated treatment information. Personally tailored to each individual patient. Encouragement of compliance |
| **Risks, harm, cost** | Small risk of not understanding the verbal explanation of the plan and then being confused when referring to written plan. Cost of supplies to produce and print at each visit. |
| **Benefits-harms assessment** | Preponderance of benefit over harm. |
| **Value judgements** | None |
| **Intentional vagueness** | The use of "such as" to give liberty in type of written individualized education that can be provided |
| **Role of patient preferences** | Minimal |
| **Exclusions** | Patients/caregivers who are illiterate |
| **Strength** | Recommendation |

***Discussion.*** As noted in chapter II, WAPs have been shown to be useful in the management of asthma for many years (Ntuen et al., 2010). Similar in nature to asthma, AD is a waxing and waning chronic disease that is marked by frequently evolving treatment plans that are often complex and require instruction for control and prevention, as well as for acute flare management (Rork et al., 2012). Although there is still limited data, there is growing evidence that the use of WAPs in AD management is helpful to parents, clarifies treatment instructions and overall improves AD as a result of their use (Rork et al., 2012).

Shi et al. (2013) and Duhovic et al., (2014) recently evaluated the use of WAPs for patients with eczema and found positive data in favor of the use of EAPs. Ninety percent of the Duhovic et al. (2014) experimental arm that received and an EAP, rated the intervention as useful or very useful. In the Shi et al. (2013) trial, the EAP group demonstrated improvement in AD recognition, prevention and management, with step-wise treatment, visualization and daily

reminders found to be the most beneficial elements of the EAP. The data is encouraging, but limited, and indicates that there is a need for future studies to broaden the body of evidence supporting the use of WAPs in the care of children with AD (Sauder et al., 2016).

The benefits of the use of individual WAPs include: clarity in the communication of treatment information/plan, ability to personally tailor the WAP to each individual patient and the encouragement of treatment compliance. The only risk is that of the patient/parent not understanding the in-office verbal explanation of the treatment plan depicted in the WAP, leading to later confusion as to which explanation is correct. The only associated cost would be that of supplies to produce and print the WAPs at each patient visit for AD. There is no value judgement and minimal role of patient preferences. The only intentional vagueness is the use of "such as" with the intent to give the clinician liberty in the type of written individualized education to be provided and the only exclusion would be parents/patients who are illiterate. The above summary leads to this being designated as a recommendation.

## Guideline Implementation/Utilization

The intention behind the creation of this CPG is make it available to implement it as widely and as desired as possible among pediatric PCPs, first locally in the metro Phoenix area and later at the state level and beyond.

## Funding/Conflict of Interest

The creation of this CPG was the work of a Doctor of Nurse Practice project and there has been no funding, nor receipt of grants towards its development. There are no competing interests that may affect the editorial independence of the work.

## Proposed ADAP

The proposed ADAP has been created to provide a model for pediatric PCPs to use and/or follow in the implementation of their own ADAP to satisfy CPG key action statement 4b. The recommendations of both Shi et al. (2013) and Duhovic et al., (2014) have been considered in its creation. A rendering of the proposed ADAP is found in Appendix B. Included in the ADAP are the following elements: title; space for demographic information; date initiated/updated; the patient's approximate FTU measurements for topical treatment based on age; a green column for well controlled AD, including a brief description of skin appearance and focus, along with instructions for daily care; a yellow column for mild to moderate AD, including a brief description of skin appearance and focus of care, along with instructions for daily care; and lastly a red column for moderate to severe AD including a brief description of skin appearance and focus of care, along with instructions for daily care. As discussed in chapter III, SCT has been used as the theoretical framework for the ADAP with strong consideration of the importance of the perceived self-efficacy of patients and/or families/caregivers.

## Conclusion

This chapter started with a description of the objective of the CPG and the target population respectively. The proposed CPG was then presented with key action statements in the following areas of childhood AD management: diagnosis of childhood AD, prevention/control of childhood AD, treatment of acute eczematous lesions in childhood AD, and patient/parent education for childhood AD. Each key action statement included the statement, a key action statement profile and a discussion. Following the key action statements, guideline

implementation/utilization and funding/conflict of interest are addressed. Lastly, the proposed ADAP is described

# CHAPTER V: EVALUATION

## Introduction

The following chapter discusses the evaluation of the CPG using the validated AGREE II evaluation tool. Three separate appraisers systematically evaluated the CPG using the online "My AGREE Plus" platform. A valid and reliable tool, AGREE II is comprised of 23 items divided into six separate domains designed to assess the methodological rigor, variability in quality and transparency in which a CPG is developed (Brouwers et al., 2010[1]). The individual and combined results will be discussed and evaluated, along with the limitations of the evaluation. Following the results and limitations, recommendations for revision will be discussed. Finally, this chapter provides a discussion of future implications of the DNP project.

## AGREE II

First published in 2003, the original AGREE instrument was developed by the AGREE Collaboration, a group of international guideline developers with the objective to develop a tool to assess the quality of guidelines (The AGREE Collaboration, 2003). Quality of guidelines was defined by the AGREE Collaboration as: the confidence that the potential biases of guideline development have been addressed adequately and that the recommendations are both internally and externally valid, and are feasible for practice (The AGREE Collaboration, 2003). Consisting of 23 items distributed through the following domains: scope and purpose, stakeholder involvement, rigour of development, clarity of presentation, applicability and editorial independence, the original AGREE instrument was translated into multiple languages and cited by numerous publications prior to its revision (Brouwers et al., 2010a). As a response to the need for refinement of the original tool, the AGREE Next Steps Research Consortium undertook

two studies that resulted in the refined AGREE II tool with improvement to the tool's usability, validity and reliability, while maintaining the same six domains of focus (Brouwers et al., 2010b; Brouwers et al., 2010c). The AGREE II tool scoring sheet with all domains and all 23 items can be found in Appendix C.

It is recommended that at least two appraisers and preferably four appraisers rate each guideline and takes on average 1.5 hours to complete provided that the appraiser have basic knowledge of the principles of evidence-based decision making and healthcare methodology (Brouwers et al., 2010a). While not required by AGREE II, content-specific expertise on the topic of a guideline may improve the ease of interpreting findings (Brouwers et al., 2010a). For the purposes of this project, three appraisers out of four who were asked, agreed to participate. The three appraisers have the following backgrounds: appraiser 1 is a PhD prepared doctoral nursing professor with extensive knowledge of evidence-based practice and nursing research; appraiser 2 is a Masters-prepared PNP with nearly five years of clinical practice in pediatric allergy/immunology and extensive knowledge of childhood atopic dermatitis; and appraiser 3 is a recently graduated DNP prepared family nurse practitioner currently working in primary care with pediatric as well as adult patients and a solid knowledge base in evidence-based practice and research. Each appraiser was invited to use the my AGREE plus website to complete their appraisal, which allowed for scores to be calculated automatically.

**AGREE II Results**

The AGREE II tool is designed not only to give individual scores to each of the 23 statements, but also to provide an overall domain score for each of the six domains that averages all of the appraiser responses (Brouwers et al., 2010a). Appendix D contains the results as

depicted by the Seven-point AGREE II Score Calculator obtained through the Capacity Enhancement Program (CEP), a partner organization to the AGREE Collaboration (CEP, 2012). This resource was found to be more useful for the purposes of this project, than the raw data with domain scores as provided by the my AGREE plus website, because of the provision of the statements alongside the scores, along with average standard deviations and indicators of higher discrepancies that necessitate revision or evaluation.

Three appraiser scores for domains one through six were 96%, 91%, 90%, 91%, 63% and 100% respectively with standard deviations (SD) below 2 for all domains except for domain 5 which yielded an SD of 2.42, indicative of a high level of discrepancy. The overall guideline assessment yielded an SD of 0.58, an overall low discrepancy level. Two of the three appraisers responded "yes" to the statement "I would recommend this guideline for use," and one responded "yes with modifications.

The tool allows for comments following each of the 23 statements which were compiled by the My AGREE Plus platform. Aside from positive comments the following recommendations/critiques were offered in each of the following domains: for domain 1 (Scope and Purpose), item 2, concern about the subjective nature of skin assessment was raised stating that there may be some unanticipated issues; for domain 2 (Stakeholder Involvement), item 5, the issue of the views and preferences of the target population is raised with the question as to whether or not they will be delivered as the CPG is put into practice; for domain 3 (Rigour of Development), item 9, one of the appraisers notes that they did not see a specific section where strengths and limitations were delineated; for domain 4 (Clarity of Presentation), item 17, one of the appraisers notes that, "the CPG is very difficult to read and sort out information. After

reading a few times, I found what I think are key recommendations"; for domain 5, item 18, it was noted by two appraisers that this information was lacking or could be more complete; for domain 5, item 19, it was noted by one appraiser that it could be strengthened through the provision of a one page summary table of all of the recommendations; and lastly, for domain 5, item 21, one appraiser stated that more information was needed about how the guideline will be implemented and how its use will be monitored.

Overall, domain five, applicability, proved to be the weakest of the six domains and the one with to most recommendation for improvement and with the most overt omissions. Although the outlying score in domain five did not affect the overall score and SD, the CPG will be strengthened by addressing these issues and making clear additions of the information.

**Limitations**

While a validated and reliable tool, the AGREE II tool is not without limitations. The items and domains in the tool do not address the clinical appropriateness or the validity of the recommendations themselves, but rather focus on the methodologic issues relevant to guideline development and reporting. (Brouwers et al., 2010a). Additionally, Brouwers et al. (2010) note that rigorous development and explicit reporting do not guarantee optimal and/or acceptable recommendations or better health outcomes for patients.

In addition to limitations in the structure of the evaluation tool, there are limitations in how the information is presented that are inherent to this being a DNP project rather than solely a CPG being prepared for publication without much of the expounded upon material that potentially makes it difficult to easily identify the elements in each item of the AGREE II tool. Furthermore, a significant limitation is that this CPG is being created by one individual, rather

than a team of experts, as recommended by Rosenfeld and Shiffman (2009) in their principles of guideline development that include "convening and running guideline development groups" as a step in the development of an evidence-based guideline. Though there will be external review by the DNP project committee in addition to the evaluation completed by three outside appraisers, the CPG is exclusively developed by one person.

**Recommendations for Revision**

In response to the applicability domain results of the AGREE II evaluation and the comments made by the appraisers, a revised CPG with the addition of sections detailing the procedure for updating the guideline, and detailing the Facilitators and Barriers to Guideline Application, have been added. The revised CPG is contained in appendix E. In addition, Appendix A was added with a simplified version of the CPG without the introductory and discussion sections for each key action statement. While the key action statement profile tables could have been left out to further simplify the deconstructed CPG, the value of having the information left with the key recommendations over-rode the concerns of being cumbersome. With regard to the suggestion to have the recommendations laminated for providers, the addition of the ADAP for use in practice was thought to sufficiently fulfill this need on the end of the patient/parent, though could be considered for future revisions to further benefit the provider.

**Discussion & Future Implications**

This project was initiated through the completion of a comprehensive literature review of childhood AD with emphasis on diagnosis, evidence-based treatment, patient/parent education and preventive care. Through the literature review, a gap was discovered in the availability of a CPG specifically geared towards care of the child with AD that is being managed in the primary

care setting, as opposed to a specialist setting. Because of this, the goal of the project was to create a CPG for use in pediatric primary care with emphasis upon patient/family education in addition to diagnosis and treatment and the provision of an ADAP for implementation by PCPs. The CPG and ADAP were developed with the guidance of the AGREE II framework and SCT respectively. Once the CPG was developed, it was evaluated using the AGREE II evaluation tool. Minor revisions and additions were indicated and made, in evaluation of the AGREE II results and appraiser comments.

This project could be further strengthened through the formation of a committee of experts to offer review and revision at agreed upon intervals. It would also be useful to conduct several Plan Do Study Act (PDSA) cycles to quickly evaluate its utility in live practice with patients and providers. The use of PDSA cycles has been effective in quality improvement projects, such as that described by Tartaglia, Campbell, Shaniuk, & McClead (2013). With the goal of improved compliance with adherence to AAP guidelines for the inpatient management of neonatal hyperbilirubin, the use of PDSA cycles resulted in a 30% increase in guideline compliance from 60.5% to 90.4% over a 12 month period (Tartaglia et al., 2013). Lastly, it would be useful to elicit the thoughts/opinions/experiences of patients/parents who are using the ADAP and/or being treated according to the CPG for further revision and strengthening from the patient/parent perspective.

## Conclusion

The incidence of AD has increased to an estimated 12.5% of children between the age of 0-17 years, as of 2009-2011 (Eichenfield et al., 2015). Because the majority of children will be initially diagnosed before age five, the diagnosis, treatment, management and education of

patients with childhood is a significant and relevant area of disease management for primary care providers (Tollefson & Bruckner, 2014). The combination of the role that primary care pediatric nurse practitioners play in the care of children, and the fact that RCTs have shown that the level of care provided by a nurse practitioner in terms of improvement of AD and quality of life outcomes is comparable to that provided by dermatologists, with the added advantages of improved patient satisfaction with care and improved cost-savings and cost-effectiveness, there is great value to the addition of this CPG and ADAP to the body of pediatric primary care research (Schuttelaar et al., 2010; Schuttelaar et al., 2011). DNPs are equipped with the necessary skills and commitment to evidence-based practice to successfully implement a CPG and ADAP for the care of children with AD.

# APPENDIX A

## CLINICAL PRACTICE GUIDELINE

## Atopic Dermatitis Clinical Practice Guideline for Pediatric PCPs

### Objective

The objective of the following CPG is to provide pediatric PCPs with specific, evidence-based guidelines for the diagnosis, prevention of exacerbation, and treatment for childhood AD, the provision of patient/family teaching and criteria for specialist referral. A secondary goal is to decrease long-term disease sequelae, improve quality of life and increase patient/parent understanding of treatment and treatment goals.

### Population

The following CPG is intended for use in the diagnosis and treatment of pediatric patients, ages 0-18 years old, male and female, being managed by a pediatric PCP in the primary care setting. Pediatric PCPs in the primary care setting may include physicians, nurse practitioners and physician assistants who specifically care for pediatric patients as defined above.

**Key Action Statement 1**

**Clinicians should use the revised Hanifin and Rajka diagnostic criteria to diagnose atopic dermatitis in a child age 0-17 who presents to the primary care setting with pruritic eczematous lesions distributed in a characteristic pattern with facial, neck and extensor involvement.**

Key Action Statement Profile: KAS 1

| **Aggregate evidence quality** | **Grade C** |
|---|---|
| **Benefits** | Reduction in incorrect diagnosis and unnecessary treatment. Increases incidence of correct diagnosis of not only AD, but of other conditions that may be incorrectly diagnosed as AD. Promotes the use of a standardized, evidence-based method for diagnosis. |
| **Risks, harm, cost** | No risk or harm; possible cost in training providers. |
| **Benefits-harms assessment** | Preponderance of benefit |
| **Value judgements** | High value placed on the importance of a set of diagnostic criteria. |
| **Intentional vagueness** | None |
| **Role of patient preferences** | None |
| **Exclusions** | None |
| **Strength** | **Recommendation** |

**Key Action Statement 2a.**

**Clinicians should include topical moisturizer daily skin care in the treatment plan for children diagnosed with AD with the purpose of preventing and controlling eczematous lesion flares.**

Key Action Statement Profile: KAS 2a

| **Aggregate evidence quality** | **Grade A** |
|---|---|
| **Benefits** | Combat xerosis and transdermal water loss. Lessen pruritis, erythema, fissuring and lichenification. Decrease amount of prescription anti-inflammatory treatments needed for disease control. Prevent flares. |
| **Risks, harm, cost** | Potential adverse effects. Variable efficacy of individual selection of agent. Cost of emollient |
| **Benefits-harms assessment** | Preponderance of benefit over harm |
| **Value judgements** | None |
| **Intentional vagueness** | No specific name or brand of emollient added related to the number of options available. |
| **Role of patient preferences** | Limited only to discussion of specific emollient to use. |
| **Exclusions** | None |
| **Strength** | Strong Recommendation |

**Key Action Statement 2b.**

**Clinicians should recommend avoidance of common irritants that trigger xerosis and the itch-scratch cycle such as: abrasive occlusive, tight clothing; harsh laundry detergents; soaps without a neutral pH, and known harsh chemicals.**

TABLE 4: Key Action Statement: KAS 2b

| **Aggregate evidence quality** | **Grade C** |
|---|---|
| **Benefits** | Less skin irritation, reduction of the itch-scratch cycle |
| **Risks, harm, cost** | Low possibility of reaction, even to milder products. Cost in purchase of hypoallergenic products that often are more expensive. |
| **Benefits-harms assessment** | Preponderance of benefit over harm |
| **Value judgements** | None |
| **Intentional vagueness** | None |
| **Role of patient preferences** | None |
| **Exclusions** | None |
| **Strength** | Recommendation |

**Key Action Statement 3a.**

**Clinicians should prescribe topical corticosteroids with specific attention to selection of appropriate potency for severity of eczematous lesion, as first line treatment for acute eczematous lesions**

Key Action Statement Profile: KAS 3a

| **Aggregate evidence quality** | **Grade A** |
|---|---|
| **Benefits** | Relief and resolution of eczematous lesions. Itch and pain relief. Easy mode of application. No systemic therapy needed. Ability to step-up or step-down treatment |
| **Risks, harm, cost** | Risk of relatively mild treatment side-effects and of incorrect application that could lead to under or over treatment and corresponding mild adverse effects. No associated cost. |
| **Benefits-harms assessment** | Preponderance of benefit over harm |
| **Value judgements** | High value placed on the prompt and effective resolution of symptoms. |
| **Intentional vagueness** | None |
| **Role of patient preferences** | Minimal |
| **Exclusions** | Patients with allergy or hypersensitivity to TCs. Refractory lesions. |
| **Strength** | Strong Recommendation |

**Key Action Statement 3b.**

**Clinicians should prescribe topical calcineurin inhibitors for patients age 2-17 with moderate to severe persistent atopic dermatitis as second-line treatment, as a means to provide short or long term treatment, and to prevent the long-term incidence of eczematous flares.**

Key Action Statement Profile: KAS 3b

| **Aggregate evidence quality** | **Grade A** |
|---|---|
| **Benefits** | Treatment alternative to TCs. Less side effects than TCs. Ability to be used as a long term treatment. High treatment efficacy. Low discontinuation rates. Reduction in bacterial colonization |
| **Risks, harm, cost** | Minimal risk of application site skin irritation, Oldest data available is 10 years old causing less long-term certainty. No associated cost |
| **Benefits-harms assessment** | Preponderance of benefit over harm |
| **Value judgements** | High value placed on avoidance of common |

| | |
|---|---|
| | high potency TC side effects and on potential for longer term treatment. |
| **Intentional vagueness** | None |
| **Role of patient preferences** | None |
| **Exclusions** | Patients with allergy or hypersensitivity to TCIs. Patients less than 2 years old |
| **Strength** | Strong Recommendation |

**Key Action Statement 3c.**

**Clinicians should recommend the use of wet-wrap therapy, with or without the concurrent use of a topical steroid, for moderate to severe or refractory childhood atopic dermatitis with the intent to minimize the need for systemic immunosuppressive therapy.**

TABLE 7: Key Action Statement Profile: KAS 3c

| **Aggregate evidence quality** | **Grade B** |
|---|---|
| **Benefits** | Quickly reduces AD severity. Effective in severe and refractory disease. Allows for increased penetration of topical agent; provides a physical barrier against scratching. |
| **Risks, harm, cost** | Risk of HPA axis suppression if over used or used with higher potency TC, although short courses have not been associated with prolonged adrenal suppression. Higher risk of infection when combined with higher-potency topical steroid, but data is minimal and conflicting as to actual occurrence. Cost of supplies (tubular bandage, gauze, cotton garments). |
| **Benefits-harms assessment** | Preponderance of benefit over harm |
| **Value judgements** | High value ascribed to likelihood of success for patients with severe or refractory lesions |
| **Intentional vagueness** | "With or without" is used so that the clinician can use discernment on an individual patient basis. |
| **Role of patient preferences** | Shared decision making given that WWT involves substantial work on the part of the parent and patient outside of clinic setting. |
| **Exclusions** | Patients with mild AD |
| **Strength** | Recommendation |

**Recommendation 4a. Clinicians should use the fingertip unit to instruct parents/caregivers of patients age 0-17, how to quantify the amount of topical medication to use for each application.**

TABLE 8: Key Action Statement Profile: KAS 4a

| Aggregate evidence quality | Grade B |
|---|---|
| **Benefits** | Clarity in prescribing directions. Avoidance of over using topical medications. Easing fears of parents ("steroid phobia") that they will over-use topical steroids. |
| **Risks, harm, cost** | Very mild risk of parents/patients incorrectly completing performing the task. No cost |
| **Benefits-harms assessment** | Preponderance of benefit over harm |
| **Value judgements** | High value ascribed to the avoidance of harm from overtreatment |
| **Intentional vagueness** | None |
| **Role of patient preferences** | None |
| **Exclusions** | None |
| **Strength** | Strong Recommendation |

**Recommendation 4b. Clinicians should include individualized written patient/parent education in the overall treatment plan for patients with childhood AD, such as an individual written action plan.**

TABLE 10: Key Action Statement Profile: KAS 4b

| Aggregate evidence quality | Grade B |
|---|---|
| **Benefits** | Clearly communicated treatment information. Personally tailored to each individual patient. Encouragement of compliance |
| **Risks, harm, cost** | Small risk of not understanding the verbal explanation of the plan and then being confused when referring to written plan. Cost of supplies to produce and print at each visit. |
| **Benefits-harms assessment** | Preponderance of benefit over harm. |
| **Value judgements** | None |
| **Intentional vagueness** | The use of "such as" to give liberty in type of written individualized education that can be provided |
| **Role of patient preferences** | Minimal |
| **Exclusions** | Patients/caregivers who are illiterate |
| **Strength** | Recommendation |

## Guideline Implementation/Utilization

The intention behind the creation of this CPG is make it available to implement it as widely and as desired as possible among pediatric PCPs, first locally in the metro Phoenix area and later at the state level and beyond. Add information about putting the guidelines into practice

## Funding/Conflict of Interest

The creation of this CPG was the work of a Doctor of Nurse Practice project and there has been no funding, nor receipt of grants towards its development. There are no competing interests that may affect the editorial independence of the work

# APPENDIX B

## ATOPIC DERMATITIS ACTION PLAN

# ATOPIC DERMATITIS ACTION PLAN

**Date:**_____

**Patient Name:**_____ **Date of birth:**_____

**Healthcare Provider Name:**_____ **Phone:**_____

**Fingertip Units (FTU) to be used with topical steroids:**

*face/neck*_____ *each arm*_____ *each leg*_____ *torso/abdomen (front)*_____ *back/buttocks*_____

## WELL CONTROLLED

**No eczematous lesions**

Focus on:
Daily moisturizing
skin care &
trigger avoidance

**Daily Skin Care Routine**

Check your child's skin care daily looking and feeling for signs of rash and avoid known triggers.

**Bath**: Have your child bathe or shower daily for 10-15 minutes. Use a mild cleanser on armpits, groin, feet and to any other areas with visible dirt. *Recommended cleansers*: Dove Sensitive Skin unscented bar soap, Cetaphil, Cerave, Aveeno Baby Eczema.

**Moisturizer:** Apply moisturizer to your child's entire body twice daily. Once, immediately following bath/shower: pat dry leaving skin damp and immediately apply moisturizer. *Recommended moisturizers*: Cetaphil, Cerave, Aveeno Baby Eczema, Eucerin Eczema, Vanicream

## MILD to MODERATE SYMPTOMS

**Mild to moderate rash, redness and itching**

Focus on:
Controlling the flare
with short course
topical steroid

**Continue Daily Skin Care**

**Apply topical steroid:**

_____

twice daily to affected areas of face, neck, ears, groin before moisturizer.

**Apply topical steroid:**

_____

twice daily to affected areas of arms, legs, hands, feet, abdomen and back before moisturizer.

**Apply topical steroid for no more than 14 days in a row.**

*** If rash persists after 10-14 days of treatment, call clinic for further instructions.

## MODERATE to SEVERE SYMPTOMS

**Moderate to severe rash, redness, itching, oozing**

Focus on:
Stronger treatment of
flare, wet wraps,
1st line treatment

**Continue Daily Skin Care**

**Apply topical steroid/calcineurin inhibitor:**

_____

twice daily to affected areas of face, neck, ears groin.

**Apply topical steroid/calcineurin inhibitor:**

_____

twice daily to affected areas of arms, legs, hands, feet, abdomen and back.

**Start wet wrap therapy:** if no pustules or yellow crusting or oozing.

**Apply topical antibiotic:**

_____

to pustules, yellow crusting or oozing areas

**Apply topical steroid for no more than 14 days in a row.**

*** If rash persists after 10-14 days of treatment, call clinic for further instructions.

# APPENDIX C

## AGREE II SCORE SHEET

## AGREE II Score Sheet

| Domain | Item | AGREE II Rating | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | 1 *Strongly Disagree* | 2 | 3 | 4 | 5 | 6 | 7 *Strongly Agree* |
| Scope and purpose | 1. The overall objective(s) of the guideline is (are) specifically described. | | | | | | | |
| | 2. The health question(s) covered by the guideline is (are) specifically described. | | | | | | | |
| | 3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described. | | | | | | | |
| Stakeholder involvement | 4. The guideline development group includes individuals from all the relevant professional groups. | | | | | | | |
| | 5. The views and preferences of the target population (patients, public, etc.) have been sought. | | | | | | | |
| | 6. The target users of the guideline are clearly defined. | | | | | | | |
| Rigor of development | 7. Systematic methods were used to search for evidence. | | | | | | | |
| | 8. The criteria for selecting the evidence are clearly described. | | | | | | | |
| | 9. The strengths and limitations of the body of evidence are clearly described. | | | | | | | |
| | 10. The methods for formulating the recommendations are clearly described. | | | | | | | |
| | 11. The health benefits, side effects and risks have been considered in formulating the recommendations. | | | | | | | |
| | 12. There is an explicit link between the recommendations and the supporting evidence. | | | | | | | |
| | 13. The guideline has been externally reviewed by experts prior to its publication. | | | | | | | |
| | 14. A procedure for updating the guideline is provided. | | | | | | | |
| Clarity of presentation | 15. The recommendations are specific and unambiguous. | | | | | | | |
| | 16. The different options for management of the condition or health issue are clearly presented. | | | | | | | |
| | 17. Key recommendations are easily identifiable. | | | | | | | |
| Applicability | 18. The guideline describes facilitators and barriers to its application. | | | | | | | |
| | 19. The guideline provides advice and/or tools on how the recommendations can be put into practice. | | | | | | | |
| | 20. The potential resource implications of applying the recommendations have been considered. | | | | | | | |
| | 21. The guideline presents monitoring and/ or auditing criteria. | | | | | | | |
| Editorial independence | 22. The views of the funding body have not influenced the content of the guideline. | | | | | | | |
| | 23. Competing interests of guideline development group members have been recorded and addressed. | | | | | | | |
| Overall Guideline Assessment | 1. Rate the overall quality of this guideline. | 1 *Lowest possible quality* | 2 | 3 | 4 | 5 | 6 | 7 *Highest possible quality* |
| **Overall Guideline Assessment** | **2. I would recommend this guideline for use.** | *Yes* | *Yes, with modifications* | | | | | *No* |
| | | | | | | | | |

# APPENDIX D

## AGREE II SEVEN POINT SCORE CALCULATOR RESULTS

# Seven-point AGREE II Score Calculator

**You must fill in ALL of the Question ratings from an appraiser for the Domain score to be accurate.** **Note: Please use the AGREE II User's Manual for full instructions.*

| Total # of Appraisers | Appraiser | | | | |
|---|---|---|---|---|---|
| 3 | 1 | 2 | 3 | 4 | |
| **Domain 1 - Scope and Purpose** | | | | | |
| **Q1** - The overall objective(s) of the guideline is (are) specifically described. | 6 | 7 | 7 | | 20 |
| **Q2** - The health question(s) covered by the guideline is (are) specifically described. | 6 | 7 | 7 | | 20 |
| **Q3** - The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described. | 7 | 7 | 7 | | 21 |
| | 19 | 21 | 21 | Caution: Empty Cells | **61** |
| | | | | **Domain 1 Score for 3 Appraiser(s):** | 96% |
| **Domain 2 - Stakeholder Involvement** | | | | | |
| **Q4** - The guideline development group includes individuals from all relevant professional groups. | 7 | 7 | 6 | | 20 |
| **Q5** - The views and preferences of the target population (patients, public, etc.) have been sought. | 5 | 7 | 5 | | 17 |
| **Q6** - The target users of the guideline are clearly defined. | 7 | 7 | 7 | | 21 |
| | 19 | 21 | 18 | Caution: Empty Cells | **58** |
| | | | | **Domain 2 Score for 3 Appraiser(s):** | 91% |
| **Domain 3 - Rigour of Development** | | | | | |
| **Q7** - Systematic methods were used to search for evidence. | 7 | 7 | 7 | | 21 |
| **Q8** - The criteria for selecting the evidence are clearly described. | 7 | 7 | 6 | | 20 |
| **Q9** - The strengths and limitations of the body of evidence are clearly described. | 4 | 7 | 7 | | 18 |
| **Q10** - The methods for formulating the recommendations are clearly described. | 6 | 7 | 7 | | 20 |
| **Q11** - The health benefits, side efects, and risks have been considered in formulating the recommendations. | 7 | 7 | 7 | | 21 |
| **Q12** - There is an explicit link between the recommendations and the supporting evidence. | 7 | 7 | 7 | | 21 |
| **Q13** - The guideline has been externally reviewed by experts prior to its publication. | 7 | 7 | 5 | | 19 |
| **Q14** - A procedure for updating the guideline is provided. | 1 | 7 | 6 | | 14 |
| | 46 | 56 | 52 | Caution: Empty Cells | **154** |
| | | | | **Domain 3 Score for 3 Appraiser(s):** | 90% |

| | | | | | |
|---|---|---|---|---|---|
| **Domain 4 - Clarity of Presentation** | | | | | |
| **Q15** - The recommendations are specific and unambiguous. | 6 | 7 | 7 | | 20 |
| **Q16** - The different options for management of the condition or health issue are clearly presented. | 6 | 7 | 7 | | 20 |
| **Q17** - Key recommendations are easily identifiable | 4 | 7 | 7 | | 18 |
| | 16 | 21 | 21 | Caution: Empty Cells | **58** |
| | | | **Domain 4 Score for 3 Appraiser(s):** | | 91% |
| **Domain 5 - Applicability** | | | | | |
| **Q18** - The guideline describes facilitators and barriers to its application. | 2 | 7 | 4 | | 13 |
| **Q19** - The guideline provides advice and/or tools on how the recommendations can be put into practice. | 2 | 7 | 5 | | 14 |
| **Q20** - The potential resource implications of applying the recommendations have been considered. | 2 | 7 | 6 | | 15 |
| **Q21** - The guideline presents monitoring and/or auditing criteria. | 5 | 7 | 3 | | 15 |
| | 11 | 28 | 18 | Caution: Empty Cells | **57** |
| | | | **Domain 5 Score for 3 Appraiser(s):** | | 63% |
| **Domain 6 - Editorial Independence** | | | | | |
| **Q22** - The views of the funding body have not influenced the content of the guideline. | 7 | 7 | 7 | | 21 |
| **Q23** - Competing interests of guideline development group members have been recorded and addressed. | 7 | 7 | 7 | | 21 |
| | 14 | 14 | 14 | Caution: Empty Cells | **42** |
| | | | **Domain 6 Score for 3 Appraiser(s):** | | 100% |
| **Overall Guideline Assessment** | | | | | |
| **1.** Rate the overall quality of this guideline. *Scoring: 1(Least Quality) - 7(Highest Quality)* | 6 | 7 | 6 | | |
| **2.** I would recommend this guideline for use. *Scoring: "Yes"; "Yes, with modifications"; "No"* | | | | | |

## DATA AUDIT

| | |
|---|---|
| # of Domains with SD that are >=1.5 and <2 SD (OS: Outlying Score, first level severity) | 0 |
| # of Domains with SD that are >=2 SD (OS2: Outlying Score, 2nd level severity) | 1 |

**Decision Rule:**
Of Domains 1-5 and the Overall Assessment
OS >=3 or OS2 >=1

**Please review the domains highlighted below**

**Average Standard Deviation of Items by Domain**

| Domain | Standard Deviation | Discrepancy Level |
|---|---|---|
| 1 | 0.38 | LOW |
| 2 | 0.58 | LOW |
| 3 | 0.91 | LOW |
| 4 | 0.96 | LOW |
| 5 | 2.42 | HIGH |
| Overall Guideline Assessment | 0.58 | LOW |

# APPENDIX E

## REVISED CLINICAL PRACTIC GUIDELINE

## Atopic Dermatitis Clinical Practice Guideline for Pediatric PCPs

### Objective

The objective of the following CPG is to provide pediatric PCPs with specific, evidence-based guidelines for the diagnosis, prevention of exacerbation, and treatment for childhood AD, the provision of patient/family teaching and criteria for specialist referral. A secondary goal is to decrease long-term disease sequelae, improve quality of life and increase patient/parent understanding of treatment and treatment goals.

### Population

The following CPG is intended for use in the diagnosis and treatment of pediatric patients, ages 0-18 years old, male and female, being managed by a pediatric PCP in the primary care setting. Pediatric PCPs in the primary care setting may include physicians, nurse practitioners and physician assistants who specifically care for pediatric patients as defined above.

**Key Action Statement 1**

**Clinicians should use the revised Hanifin and Rajka diagnostic criteria to diagnose atopic dermatitis in a child age 0-17 who presents to the primary care setting with pruritic eczematous lesions distributed in a characteristic pattern with facial, neck and extensor involvement.**

Key Action Statement Profile: KAS 1

| **Aggregate evidence quality** | **Grade C** |
|---|---|
| **Benefits** | Reduction in incorrect diagnosis and unnecessary treatment. Increases incidence of correct diagnosis of not only AD, but of other conditions that may be incorrectly diagnosed as AD. Promotes the use of a standardized, evidence-based method for diagnosis. |
| **Risks, harm, cost** | No risk or harm; possible cost in training providers. |
| **Benefits-harms assessment** | Preponderance of benefit |
| **Value judgements** | High value placed on the importance of a set of diagnostic criteria. |
| **Intentional vagueness** | None |
| **Role of patient preferences** | None |
| **Exclusions** | None |
| **Strength** | **Recommendation** |

**Key Action Statement 2a.**

**Clinicians should include topical moisturizer daily skin care in the treatment plan for children diagnosed with AD with the purpose of preventing and controlling eczematous lesion flares.**

Key Action Statement Profile: KAS 2a

| **Aggregate evidence quality** | **Grade A** |
|---|---|
| **Benefits** | Combat xerosis and transdermal water loss. Lessen pruritis, erythema, fissuring and lichenification. Decrease amount of prescription anti-inflammatory treatments needed for disease control. Prevent flares. |
| **Risks, harm, cost** | Potential adverse effects. Variable efficacy of individual selection of agent. Cost of emollient |
| **Benefits-harms assessment** | Preponderance of benefit over harm |
| **Value judgements** | None |
| **Intentional vagueness** | No specific name or brand of emollient added related to the number of options available. |
| **Role of patient preferences** | Limited only to discussion of specific emollient to use. |
| **Exclusions** | None |
| **Strength** | Strong Recommendation |

**Key Action Statement 2b.**

**Clinicians should recommend avoidance of common irritants that trigger xerosis and the itch-scratch cycle such as: abrasive occlusive, tight clothing; harsh laundry detergents; soaps without a neutral pH, and known harsh chemicals.**

TABLE 4: Key Action Statement: KAS 2b

| **Aggregate evidence quality** | **Grade C** |
|---|---|
| **Benefits** | Less skin irritation, reduction of the itch-scratch cycle |
| **Risks, harm, cost** | Low possibility of reaction, even to milder products. Cost in purchase of hypoallergenic products that often are more expensive. |
| **Benefits-harms assessment** | Preponderance of benefit over harm |
| **Value judgements** | None |
| **Intentional vagueness** | None |
| **Role of patient preferences** | None |
| **Exclusions** | None |
| **Strength** | Recommendation |

**Key Action Statement 3a.**

**Clinicians should prescribe topical corticosteroids with specific attention to selection of appropriate potency for severity of eczematous lesion, as first line treatment for acute eczematous lesions**

Key Action Statement Profile: KAS 3a

| **Aggregate evidence quality** | **Grade A** |
|---|---|
| **Benefits** | Relief and resolution of eczematous lesions. Itch and pain relief. Easy mode of application. No systemic therapy needed. Ability to step-up or step-down treatment |
| **Risks, harm, cost** | Risk of relatively mild treatment side-effects and of incorrect application that could lead to under or over treatment and corresponding mild adverse effects. No associated cost. |
| **Benefits-harms assessment** | Preponderance of benefit over harm |
| **Value judgements** | High value placed on the prompt and effective resolution of symptoms. |
| **Intentional vagueness** | None |
| **Role of patient preferences** | Minimal |
| **Exclusions** | Patients with allergy or hypersensitivity to TCs. Refractory lesions. |
| **Strength** | Strong Recommendation |

**Key Action Statement 3b.**

**Clinicians should prescribe topical calcineurin inhibitors for patients age 2-17 with moderate to severe persistent atopic dermatitis as second-line treatment, as a means to provide short or long term treatment, and to prevent the long-term incidence of eczematous flares.**

Key Action Statement Profile: KAS 3b

| **Aggregate evidence quality** | **Grade A** |
|---|---|
| **Benefits** | Treatment alternative to TCs. Less side effects than TCs. Ability to be used as a long term treatment. High treatment efficacy. Low discontinuation rates. Reduction in bacterial colonization |
| **Risks, harm, cost** | Minimal risk of application site skin irritation, Oldest data available is 10 years old causing less long-term certainty. No associated cost |
| **Benefits-harms assessment** | Preponderance of benefit over harm |
| **Value judgements** | High value placed on avoidance of common |

| | |
|---|---|
| | high potency TC side effects and on potential for longer term treatment. |
| **Intentional vagueness** | None |
| **Role of patient preferences** | None |
| **Exclusions** | Patients with allergy or hypersensitivity to TCIs. Patients less than 2 years old |
| **Strength** | Strong Recommendation |

**Key Action Statement 3c.**

**Clinicians should recommend the use of wet-wrap therapy, with or without the concurrent use of a topical steroid, for moderate to severe or refractory childhood atopic dermatitis with the intent to minimize the need for systemic immunosuppressive therapy.**

TABLE 7: Key Action Statement Profile: KAS 3c

| **Aggregate evidence quality** | **Grade B** |
|---|---|
| **Benefits** | Quickly reduces AD severity. Effective in severe and refractory disease. Allows for increased penetration of topical agent; provides a physical barrier against scratching. |
| **Risks, harm, cost** | Risk of HPA axis suppression if over used or used with higher potency TC, although short courses have not been associated with prolonged adrenal suppression. Higher risk of infection when combined with higher-potency topical steroid, but data is minimal and conflicting as to actual occurrence. Cost of supplies (tubular bandage, gauze, cotton garments). |
| **Benefits-harms assessment** | Preponderance of benefit over harm |
| **Value judgements** | High value ascribed to likelihood of success for patients with severe or refractory lesions |
| **Intentional vagueness** | "With or without" is used so that the clinician can use discernment on an individual patient basis. |
| **Role of patient preferences** | Shared decision making given that WWT involves substantial work on the part of the parent and patient outside of clinic setting. |
| **Exclusions** | Patients with mild AD |
| **Strength** | Recommendation |

**Recommendation 4a. Clinicians should use the fingertip unit to instruct parents/caregivers of patients age 0-17, how to quantify the amount of topical medication to use for each application.**

TABLE 8: Key Action Statement Profile: KAS 4a

| Aggregate evidence quality | Grade B |
|---|---|
| **Benefits** | Clarity in prescribing directions. Avoidance of over using topical medications. Easing fears of parents ("steroid phobia") that they will over-use topical steroids. |
| **Risks, harm, cost** | Very mild risk of parents/patients incorrectly completing performing the task. No cost |
| **Benefits-harms assessment** | Preponderance of benefit over harm |
| **Value judgements** | High value ascribed to the avoidance of harm from overtreatment |
| **Intentional vagueness** | None |
| **Role of patient preferences** | None |
| **Exclusions** | None |
| **Strength** | Strong Recommendation |

**Recommendation 4b. Clinicians should include individualized written patient/parent education in the overall treatment plan for patients with childhood AD, such as an individual written action plan.**

TABLE 10: Key Action Statement Profile: KAS 4b

| Aggregate evidence quality | Grade B |
|---|---|
| **Benefits** | Clearly communicated treatment information. Personally tailored to each individual patient. Encouragement of compliance |
| **Risks, harm, cost** | Small risk of not understanding the verbal explanation of the plan and then being confused when referring to written plan. Cost of supplies to produce and print at each visit. |
| **Benefits-harms assessment** | Preponderance of benefit over harm. |
| **Value judgements** | None |
| **Intentional vagueness** | The use of "such as" to give liberty in type of written individualized education that can be provided |
| **Role of patient preferences** | Minimal |
| **Exclusions** | Patients/caregivers who are illiterate |
| **Strength** | Recommendation |

## Guideline Implementation/Utilization

The intention behind the creation of this CPG is make it available to implement it as widely and as desired as possible among pediatric PCPs, first locally in the metro Phoenix area and later at the state level and beyond. In terms of actually putting the guidelines into practice the initiation of use of the ADAP would be one of the easiest and most beneficial ways to immediately put many of the guidelines into practice.

## Procedure for Updating the Guideline

The CPG will be evaluated every year for additions to existing evidence-based data that would have implications, positive or negative, on the existing key action statements. Ideally, it will be evaluated by a group of experts rather than solely one individual (Rosenfield & Shiffman, 2009). Lastly, the ADAP for use with patients and parents will be updated according to any changes or amendments to the CPG that would affect its existing content.

## Facilitators and Barriers to Guideline Application

Facilitators to CPG application include the established need for pediatric PCPs to have more guidance in caring for children with AD, the provision of clear concise guidelines that require less time to implement with patients and families, and inclusion of ample evidence to support each key action statement and subsequent trust and confidence inherent to having that evidence readily available (Eichenfield et al., 2015). Barriers to guideline application include: the time to familiarize oneself with guidelines the point of comfort in implementing them into practice; and established views and philosophies regarding the treatment of childhood AD that may be contrary to or different from the CPG key action statements.

## Resource Implications to Guideline Implementation

The only anticipated resources needed to implement the CPG key action statements would be the cost of printed materials in the form of an ADAP and time needed to provide in-service and or training for PCPs.

## Funding/Conflict of Interest

The creation of this CPG was the work of a Doctor of Nurse Practice project and there has been no funding, nor receipt of grants towards its development. There are no competing interests that may affect the editorial independence of the work

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