

Topical Treatment of Atopic Dermatitis: An Adherence-Based Appraisal of the AAD Guidelines

Max Oscherwitz BS,^a Aditi Gadre MS,^b Anna Martino BS,^a
Matthew Zirwas MD,^c Steven Feldman MD PhD^{a,d,e,f}

^aCenter for Dermatology Research, Department of Dermatology, Wake Forest University School of Medicine, Winston-Salem, NC

^bGeorgetown University School of Medicine, Washington, DC

^cDOCS Dermatology, Director, Clinical Trials and Dermatitis Center, Columbus OH

^dDepartment of Pathology, Wake Forest University School of Medicine, Winston-Salem, NC

^eDepartment of Social Sciences & Health Policy, Wake Forest University School of Medicine, Winston-Salem, NC

^fDepartment of Dermatology, University of Southern Denmark, Odense, Denmark

INTRODUCTION

Atopic dermatitis (AD) places a financial and illness burden on children and adults and is the most common chronic inflammatory skin disease.¹ In July of 2023, the American Academy of Dermatology (AAD) released carefully crafted, evidence-based AD treatment guidelines providing strong recommendations for moisturizers, topical calcineurin inhibitors (TCIs), topical corticosteroids (TCS), topical phosphodiesterase (PDE)-4 inhibitors, and topical Janus kinase (JAK) inhibitors.² The guidelines also included conditional recommendations encouraging bathing and wet wrap therapy while avoiding topical antimicrobials, antiseptics, and antihistamines.³ While these interventions address the multifactorial etiology of AD, including immune system hyperreactivity and epidermal dysfunction contributing to the disease, they may also be complex, impractical, and counterproductive.^{1,3}

The TCS recommended in the guidelines are effective for treating AD, providing rapid symptomatic resolution, especially in acute flares.² However, some patients may not be optimal candidates for TCS. Although full-body application of TCS may benefit hospitalized patients with extensive disease, this regimen is impractical for daily use in moderate-to-severe AD. Patients or their caretakers are responsible for maintaining topical treatment in an outpatient setting, unlike in an inpatient environment, where trained personnel apply therapies at scheduled intervals. The large amount of time and the application frequency associated with widespread topical use inconvenience patients and may contribute to medication non-adherence.⁸ Other contributing factors to non-adherence include concern about the potential adverse effects of medications, limited patient education, forgetfulness, and provider mistrust.⁸ Adherence to AD treatment regimens also varies over time. In just the first three days of medication initiation, there is a 60% decline in the application of TCS therapy.⁹ Furthermore, patients frequently do not fill prescriptions for AD treatments; in other conditions, patients were less likely to fill two prescriptions than to fill a single prescription.¹⁰

The updated guidelines also emphasize lifestyle modifications such as wet wrap therapy and bleach baths to supplement additive treatments. However, it is challenging to achieve adherence to even a single treatment, much less to broad lifestyle changes. For example, among adult patients with hypertension, four out of five are aware of the benefits of lifestyle modification. Still, only one in five adhere to non-pharmacologic lifestyle modifications such as dietary changes.⁴ The use of pharmacologic interventions is higher but still disappointing, with less than half of patients with type 2 diabetes or hypertension taking their respective medications as prescribed.^{5,6}

Moreover, AD treatments impose a financial burden on patients. The guidelines conditionally recommend using emollients, which are not typically covered by insurance. Assuming 1.5 grams can treat approximately 3% of body surface area (BSA), a single full-body application would require at least 45 grams. Over one month, patients would use 1,350 grams of moisturizer for treatment. If the average price of a moisturizer is \$0.94 for 45 grams, this equates to approximately \$338.40 per year spent on moisturizer.^{11,12} Consequently, this shifts costs to patients, disproportionately affecting those with lower socioeconomic status.

Regimen complexity is another concern for non-adherence. The current guidelines advise daily topical (prescription or non-prescription) applications for moderate-to-severe or recalcitrant AD. However, patients are less likely to adhere to this regimen than a single topical application daily, potentially eschewing treatment altogether due to overwhelming complexity. In other words, while applying multiple topical therapies is attractive in theory to target different aspects of AD pathophysiology, this strategy risks non-adherence, effectively failing to address any aspects of pathophysiology in practice.

Although the guidelines are well-meaning and evidence-based, they may need to be more pragmatic. Given the issues of cost and adherence associated with multiple topicals, understanding the broad recommendation for emollients in all AD patients is challenging, especially considering the lack of data supporting the meaningful benefit of moisturizer use in individuals with moderate-to-severe AD.^{2,13} The current AAD guidelines strongly recommend topical emollients for all severities of atopic dermatitis. Recommending moisturizers and prescription topicals leads to reduced adherence to the prescription topicals and worse outcomes, and recommending moisturizers and prescription topicals makes the treatment regimen more complex for many patients. Taken together, these recommendations could lead to reduced adherence to prescription topicals. Since policies influence the requirements healthcare insurance companies adopt for authorization of therapies, insufficient documentation of topical emollient application may lead to the denial of systemic escalation treatment.¹⁴

Our Recommendations

In a controlled setting, proactive treatment for AD may optimize disease management and prevent flares. In a real-life practice setting, a proactive approach may not be pragmatic, as patients often do not use topical treatments even when acutely suffering from skin disease. Encouraging complex, multi-modal treatment regimens when the condition is inactive may be unrealistic at best and counterproductive at worst. Implementing a simple reactive approach to treat flaring AD with a single topical followed by cessation of therapy once symptomatic improvement occurs and then initiating therapy again for subsequent flares is more realistic and likely more effective.

Adherence remains a barrier to following recommended AD treatment. Therefore, we suggest a patient-centered approach involving simpler regimens to promote adherence (Table 1).

TABLE 1.

A Patient-Centered Approach to AD Treatment. This table provides a patient-centered approach physicians can adopt when prescribing therapy for AD and counseling patients to promote higher levels of adherence.

1.	Recommend no more than one application of topical therapy daily
2.	Prescribe a single topical therapy
3.	Use topical therapies on active disease, not proactively on clear skin
4.	Moisturizer use is optional

Given the strength of evidence for TCS use in mild disease, TCS can remain a first-line therapy when providers can prescribe a single medication. However, prescribing multiple TCS potencies for different body areas may reduce adherence due to a more significant treatment burden and the potential for confusion. We recommend against prescribing multiple topical therapies, as keeping to a single daily topical treatment is higher than adherence to two daily.^{15,16} Adding or switching to other topical therapies patients will not use will unlikely lead to a better outcome. Thus, switching to a systemic agent or including body

phototherapy when the response to initial topical treatment is inadequate may often be a prudent option.

DISCLOSURES

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REFERENCES

- Kim J, Kim BE, Leung DYM. Pathophysiology of atopic dermatitis: clinical implications. *Allergy Asthma Proc.* 2019;40(2):84-92. doi: 10.2500/aap.2019.40.4202. PMID: 30819278; PMCID: PMC6399565.
- Sidbury R, Alikhan A, Bercovitch L, et al. Guidelines of care for the management of atopic dermatitis in adults with topical therapies. *J Am Acad Dermatol.* 2023;89(1). doi: 10.1016/j.jaad.2022.12.029. PMID: 36641009.
- Langan SM, Irvine AD, Weidinger S. Atopic dermatitis. *Lancet.* 2020;396(10247):345-360. doi: 10.1016/S0140-6736(20)31286-1. Erratum in: *Lancet.* 2020;396(10253):758. PMID: 32738956.
- Andualem A, Gelaye H, Damtie Y. Adherence to lifestyle modifications and associated factors among adult hypertensive patients attending chronic follow-up units of Dessie Referral Hospital, North East Ethiopia, 2020. *Integr Blood Press Control.* 2020;13:145-156. doi: 10.2147/IBPC.S275575. PMID: 33122940; PMCID: PMC7591036.
- Mitiku Y, Belayneh A, Tegegne BA, et al. Prevalence of medication non-adherence and associated factors among diabetic patients in a tertiary hospital at Debre Markos, Northwest Ethiopia. *Ethiop J Health Sci.* 2022;32(4):755-764. doi: 10.4314/ejhs.v32i4.12. PMID: 35950057; PMCID: PMC9341031.
- Abegaz TM, Shehab A, Gebreyohannes EA, et al. Nonadherence to antihypertensive drugs: a systematic review and meta-analysis. *Medicine (Baltimore).* 2017;96(4). doi: 10.1097/MD.0000000000005641.
- Efremova E, Shutov A, Suvorova S, et al. Adherence to lifestyle therapy and drug therapy in patients with arterial hypertension and comorbidity. *J Hypertens.* 2019;37. doi: 10.1097/01.hjh.0000573212.41860.01.
- Patel NU, D'Ambra V, Feldman SR. Increasing adherence with topical agents for atopic dermatitis. *Am J Clin Dermatol.* 2017;18(3):323-332.
- Krejci-Manwaring J, et al. Stealth monitoring of adherence to topical medication: adherence is very poor in children with atopic dermatitis. *J Am Acad Dermatol.* 2007;56(2):211-216.
- Storm A, Benfeldt E, Andersen SE, et al. A prospective study of patient adherence to topical treatments: 95% of patients underdose. *J Am Acad Dermatol.* 2008;59:975-980.
- Bowie AC, Tadrous M, Thiruchelvan D, et al. A comparison of family physician and dermatologist topical corticosteroid prescriptions: a population-based cross-sectional study. *J Am Acad Dermatol.* 2023;88(6):1291-1299. doi: 10.1016/j.jaad.2023.01.036. Epub 2023 Mar 11. PMID: 36914480.
- Xu S, Kwa M, Lohman ME, et al. Consumer preferences, product characteristics, and potentially allergenic ingredients in best-selling moisturizers. *JAMA Dermatol.* 2017;153(11):1099-1105. doi: 10.1001/jamadermatol.2017.3046.
- Lavrador M, Cabral AC, Castel-Branco M, et al. Polypharmacy and medication adherence. In: Oliveira PJ, Malva JO, eds. *Aging.* Academic Press; 2023:435-453.
- Wollenberg A, Barbarot S, Bieber T, et al. Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis) in adults and children: part I. *J Eur Acad Dermatol Venereol.* 2018;32(5):657-682. doi: 10.1111/jdv.14891. Published correction appears in: *J Eur Acad Dermatol Venereol.* 2019;33(7):1436.
- Yentzer BA, Ade RA, Fountain JM, et al. Simplifying regimens promotes greater adherence and outcomes with topical acne medications: a randomized controlled trial. *Cutis.* 2010;86:103-108.
- Zouboulis CC, Fischer TC, Wohlrab J, et al. Study of the efficacy, tolerability, and safety of 2 fixed-dose combination gels in the management of acne vulgaris. *Cutis.* 2009;84:223-229.

AUTHOR CORRESPONDENCE

Max Oscherwitz BS

E-mail: moscherw@wakehealth.edu