

# Improving Psychological Health Outcomes in Children with Atopic Dermatitis

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**Introduction:** Atopic dermatitis (AD) is a chronic inflammatory skin disease that usually develops in early childhood. AD has a significant impact on quality of life and psychological health outcomes in both adults and children. There are increased reported rates of psychiatric comorbidities including anxiety, depression, ADHD and suicidal ideation compared to the general population. Primary caregivers of children with pediatric eczema and their families may also have derangements in psychological health and quality of life. A number of interventions exist for AD and address wellbeing outcomes as an important aspect of effective treatment.

**Methods:** A comprehensive literature search was conducted using PubMed/Medline, Embase, the Cochrane Central Register of Controlled Trials in February 2023. Published studies up to April 2023 were included related to interventions for childhood AD that included psychological health or quality of life outcomes. These interventions were stratified according to type and evidence quality.

**Results:** Search strategy revealed a wide variety of interventions with demonstrated improvements in quality of life or wellbeing of patients with pediatric AD or their families. Both pharmacological and non-pharmacological interventions demonstrated effectiveness in improving disease outcomes.

**Conclusion:** A variety of both pharmacological and non-pharmacological interventions may be employed to improve psychological health outcomes in children with AD.

**Keywords:** eczema, atopic dermatitis, psychology, wellbeing, children, pediatric

## Introduction

Atopic dermatitis (AD) is a chronic inflammatory skin disease that usually develops in early childhood. The disease is characterised by the presence of pruritic, scaly and erythematous lesions that are relapsing and remitting.<sup>1</sup> The worldwide prevalence of AD in children is estimated to be as high as 15%.<sup>2</sup> These rates of prevalence are growing worldwide, and vary based on geographical location.<sup>3</sup>

AD has a significant impact on quality of life and psychological health outcomes in both adults and children. Symptoms of AD, specifically pruritus, are associated with a lower health-related quality of life.<sup>4</sup> AD also has a serious impact on the mental health of both adults and children, with increased reported rates of psychiatric comorbidities including anxiety, depression, ADHD and suicidal ideation compared to the general population.<sup>5,6</sup> Primary caregivers of children with chronic illness may also be adversely affected.<sup>7</sup> Previous reports of parents of children with AD have been demonstrated to have increased rates of stress, anxiety, depression and suicidal ideation than those without.<sup>8,9</sup> These effects on quality of life extend beyond parents and can affect families of children with AD across various domains including sleep, relationships and finances.<sup>10</sup>

Across the literature, a wide variety of interventions have been investigated for AD, ranging from medical therapies to therapeutic adjuncts such as educational programs.<sup>11,12</sup> Given the significant burden of AD on psychological health and quality of life (QoL), improvements in these domains have become an important indicator for effectiveness when investigating interventions. Various outcome measures exist to quantify changes in mental health status, which directly address related symptoms of mental health derangement.<sup>13</sup> However, an increasingly used measure related to wellbeing

and psychological health are health-related quality of life (HRQoL) outcome measures, such as the dermatology life quality index (DLQI) and the children's dermatology life quality index (CDLQI).<sup>14,15</sup> These measures, including the DLQI, have previously demonstrated correlation with psychiatric outcome measures.<sup>16</sup> In paediatric eczema, a number of studies have utilised HRQoL measures as a marker for holistic health and improvements in wellbeing. However, there is limited literature summarising the interventions that may improve HRQoL and psychological outcomes in childhood AD.

In order to address this knowledge gap, this review article aims to identify and stratify strategies to improve psychological health outcomes in children with atopic dermatitis.

## Methods

A comprehensive literature search was conducted using PubMed/Medline, Embase, the Cochrane Central Register of Controlled Trials in February 2023. Variations of the search terms “atopic dermatitis” and “children” and “quality of life” or “psychology” were combined either as text words or MESH headings. Published studies up to April 2023 were included. Any study investigating a form of intervention for children or caregivers of children with AD in atopic dermatitis was included if they reported any quality of life outcome or anecdotal mention of psychological health or quality of life improvement. The highest level of evidence and grade of recommendation was noted for each intervention, using a modified version of the Oxford Centre for Evidence-based Medicine levels of evidence table (Table 1).<sup>17</sup>

## Results

### Pharmacological Interventions

The psychological health and HRQoL outcomes in children with AD are directly related to objective disease severity and improvements in disease severity correlate with improvements in psychological wellbeing.<sup>18</sup> Medical management of AD is an effective method in improving disease severity. A number of evidence-based clinical guidelines recommend a stepwise approach to treating childhood AD based on the degree of eczema severity.<sup>19</sup> Current recommended therapeutic options include emollients, topical treatments and systemic therapies.

### Emollients

Emollients are routinely used in pediatric eczema and are effective in improving the skin barrier and reducing flares in AD by increasing skin hydration. Multiple national treatment guidelines recommend the use of regular emollients in the management of eczema for all severities of disease.<sup>20</sup> Previous evidence has demonstrated improvements in both

**Table 1** Levels of Evidence and Associated Grade of Recommendation. Modified from the Oxford Centre for Evidence-Based Medicine Levels of Evidence

Grade of Recommendation	Level of Evidence	Description
A	1a	Systematic review of RCT (Randomized controlled trial)
	1b	Individual RCT with narrow confidence interval
	1c	All or none
B	2a	Systematic review of cohort studies
	2b	Individual cohort study (including low quality RCT, eg, <80% follow up)
	3a	Systematic review of case-control studies
	3b	Individual case-control study
C	4	Case series and poor-quality cohort and case-control studies
D	5	Expert opinion without explicit critical appraisal, or based on physiology, bench research or first principles

disease severity and quality of life through routine use of emollients.<sup>21</sup> However, there is limited difference in effectiveness between the different major types of emollients including lotions, creams, gels and ointments. Instead, the type of emollient should be selected based on individual patient needs and the type that will be used most consistently.<sup>22</sup> Prophylactic use of emollients may also reduce the risk of developing eczema in some infants by improving the skin barrier from birth.<sup>23</sup>

Grade of recommendation: A (Level 1a evidence)

## Topical Therapy

In mild-to-moderate AD, topical therapeutic options such as topical corticosteroids and topical calcineurin inhibitors are the current gold standard as first-line treatment and recommended for use in most clinical guidelines.<sup>20</sup> There is extensive documented evidence supporting the use of both of therapies in terms of safety, improving disease severity and patient quality of life.<sup>24</sup> However, effective treatment use is marred by a number of barriers. Examples of treatment barriers include poor treatment adherence, user dependency and topical corticosteroid phobia.<sup>25</sup> Overall, topical therapy remains an optimal treatment approach in the management of pediatric eczema and improving related psychological health outcomes.

Grade of recommendation: A (Level 1a evidence)

## Systemic Treatment

In severe or treatment-resistant childhood AD, systemic treatment may be considered as a therapeutic option. Cyclosporine is the recommended first-line systemic treatment for short-term use due to its efficacy, safety and tolerability.<sup>26–28</sup> Cyclosporine may also improve the HRQoL of mothers of children with paediatric eczema.<sup>29</sup> However, there is a lack of consensus for long-term treatment options in pediatric AD.<sup>26</sup> Methotrexate and mycophenolate mofetil are both possible treatment options that have demonstrated efficacy and improvements in HRQoL.<sup>30–32</sup> Similarly, azathioprine is an effective alternative in pediatric eczema, however usage of these treatments is cautioned due to the risk of adverse events.<sup>33–35</sup>

In recent years, biological therapy has found increasing use in dermatology. Dupilumab is the only FDA approved treatment for children older than 6 months with demonstrated improvements in disease severity and HRQoL.<sup>36</sup> Additional promising monoclonal agents including lebrikizumab, tralokinumab and nemolizumab which have demonstrated efficacy in adult populations are presently undergoing pediatric trials.<sup>37</sup> Janus kinase inhibitors (JAK) are another new class of oral and topical medications that have emerged in the treatment of pediatric eczema. Topical ruxolitinib and oral upadacitinib are both medications that have been FDA approved for adolescent cohorts, with demonstrated improvements in disease severity and quality of life.<sup>38,39</sup> While there are numerous systemic therapies available with demonstrated efficacy in pediatric, cohorts, their safety profile needs to be considered in conjunction to their indication for use.

Grade of recommendation: A (Level 1a evidence)

## Non-Pharmacological Interventions

While medical interventions are the mainstay of treatment for childhood AD, given the chronic nature of the disease and lack of an established cure, there is a significant role in non-medical interventions as treatment adjuncts. These interventions can improve the use of medical interventions or address wellbeing related comorbidity and overall, help to improve disease severity, QoL and psychological outcomes.

## Phototherapy

Phototherapy is a recommended treatment in both adult and pediatric AD as an alternative treatment in disease recalcitrant to topical therapies.<sup>40</sup> While there is previously documented evidence favouring ultraviolet A and ultraviolet B phototherapy as both safe and effective in children, there is limited efficacy on psychological health and HRQoL.<sup>41–44</sup> Further, there is also no long-term safety and efficacy data on phototherapy use in children.<sup>45</sup> Phototherapy may improve

psychological health outcomes, by improving disease severity, however further research in this domain is required to support continued use.

Grade of recommendation: B (Level 2b evidence)

## Patient Education

Patient education is a useful therapeutic adjunct that can provide patients and caregivers with a better understanding of disease and related self-management strategies. A number of recent Eczema guidelines have recommended patient education as a key part of management approaches.<sup>26,40,46</sup> Systematic reviews of educational interventions have demonstrated improvements in disease severity but did not appear to provide significant improvements in HRQoL.<sup>12,47,48</sup> However, the results are difficult to interpret and generalise due to the variety of different educational approaches. Major differences include scope, frequency, and modality of education as well as study sample size and end points. Study quality is an important factor for consideration as factors such as longer education sessions, multi-disciplinary approaches and nursing led session were effective as forms of education.<sup>12,49,50</sup> Conventional education programs may be limited by lack of attendance, strengthening the role of newer modalities including online interventions, such as the “Eczema Care Online program” as a self-management strategy.<sup>51</sup> Regardless, there is still a lack of consensus in treatment guidelines for optimal educational approaches. However, a structured interdisciplinary program suited to the patient’s educational and cultural needs is recommended in all severities of AD.

Grade of recommendation: A (level 1b evidence)

## Eczema Action Plans

Eczema action plans are a potential treatment guideline that can be used alongside verbal instructions. Two previous studies including a randomised controlled trial and a quality improvement project have demonstrated improved outcomes of adding an eczema action plan to verbally instructed treatment regimens.<sup>52,53</sup> Documented benefits include increased parental understanding surrounding eczema management, decreased disease severity and improved quality of life in parents and children with eczema.

Grade of recommendation: B (level 2b evidence)

## Bleach Baths

Bathing in dilute bleach is a commonly used adjunctive treatment for AD. The antiseptic properties of bleach are believed to improve AD severity due to its antiseptic staphylococcal and anti-inflammatory effects. A recent systematic review of RCTs of mostly pediatric studies (9/10 of included RCTs) demonstrated that bleach baths provided some improvement in disease severity.<sup>54</sup> However, CLDLQI scores were investigated by only one study and revealed no significant difference compared to usual water baths.<sup>55</sup> Given the improvements in disease severity, the use of bleach baths may provide some indirect improvements in psychological health as a treatment adjunct.

Grade of recommendation: A (level 1a evidence)

## Psychological Interventions

The adverse psychological effects of AD may be worsened by behaviours related to symptoms of disease including the itch-scratch cycle. Negative emotions such as anxiety and stress can also be a trigger for itch. Psychological interventions addressing these behaviours and associated mental health comorbidities may lead to improvements in these outcomes as well as disease severity. However, there is limited and heterogeneous evidence of effective psychological interventions in a paediatric population. An early study examining the effect of hypnotherapy and biofeedback strategies has demonstrated some improvements in disease severity.<sup>56</sup> Anecdotal evidence may also support the implantation of psycho-dermatology clinics involving both dermatologists and clinical psychologists in the management of childhood eczema and improving HRQoL for families.<sup>57</sup> In this style of clinic, patients and their caregivers can see both a consultant dermatologist, for medical treatment and a clinical psychologist who manages psychological concerns through strategies such as habit reversal for itch. Mindfulness therapy for parents has also been shown to improve both disease severity and

QoL in a very small case series parameters in small case series.<sup>58</sup> Psychological interventions may have an important role in the management of childhood AD, however further evidence is required to support their benefit.

Grade of recommendation: C (level 4 evidence)

## Allergen Immunotherapy

Allergens may play a role in the pathogenesis of AD by driving innate and adaptive inflammatory responses.<sup>59</sup> Allergen immunotherapy improves disease severity in other atopic diseases such as asthma and rhinitis. In adult populations, allergen immunotherapy for AD improves disease severity and QoL.<sup>60</sup> The evidence in paediatric cohorts is less robust, however may support the use of sublingual allergen immunotherapy for AD.<sup>61,62</sup>

Grade of recommendation: A (level 1b evidence)

## Infant Massage

Infant massage is a traditional practice used across the world, with demonstrated benefits in improving child sleep and increasing interaction with parents and caregivers.<sup>63</sup> One randomized trial has investigated the effect of mother performed infant massage on infantile eczema and maternal state. Their study demonstrated significant improvement in eczema severity, infant quality of life as well as maternal anxiety and depression scores. Infantile massage performed in children with eczema may be mutually beneficial for the psyche of both child and caregiver.<sup>64</sup>

Grade of evidence: B (Level 2b evidence)

## Conclusion

AD has a significant psychological burden on children and their families, due to the chronic nature of disease and its associated symptoms. Improving HRQoL and psychological outcomes is an important factor when considering management approaches. A range of pharmacological and non-pharmacological outcomes may provide benefit in this domain and should be utilised based on patient needs, in order to achieve optimal treatment outcomes. Emerging evidence will strengthen guidance and recommendations on addressing these psychological outcomes in the clinical setting, in order to improve disease outcomes and HRQoL of patients and caregivers.

## Disclosure

Niyaz Mostafa reports no conflicts of interest in this work. Saxon Smith is a principal investigator for ABBVIE and Sanofi Genzyme; on the advisory board for ABBVIE, Sanofi Genzyme, Pfizer and Eli Lilly; received education speaker fees from ABBVIE; received consultancy and education speaker fees from Sanofi Genzyme, Pfizer and Eli Lilly; outside the submitted work.

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