Research Prioritization Topic Brief

Topic 9: “Eczema”

Comparative effectiveness of treatment options for topical or systemic eczema in children and adults.

PCORI Scientific Program Area: Assessment of Prevention, Diagnosis and Treatment Options

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<table>
<thead>
<tr>
<th>Criteria</th>
<th>Brief Description</th>
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| **Introduction** | DESCRIPTION OF CONDITION<sup>1,2</sup>  
- Eczema (also known as atopic dermatitis) is a chronic inflammatory skin condition.  
- It is often the first manifestation of other allergic diseases (allergic rhinitis or hay fever, asthma, food allergy).  
- It typically presents in early childhood but can develop in adulthood.  
- It is characterized by defects in the skin’s protective outer layer. These defects can either develop over time (acquired) or be something a patient is born with (genetic).  
- An inadequate immune response may increase one’s susceptibility to infections. |
| Relevance to patient-centered outcomes | SYMPTOMS<sup>1,2</sup>  
- Three recurring phases of itchy skin lesions:  
  - Acute—weeping, crusted skin lesions  
  - Subacute—dry, scaly, red skin lesions  
  - Chronic—thickened skin lesions from scratching  
- Can be exacerbated by temperature, humidity, irritants, infections, food, allergens and emotional stress.  
DIAGNOSIS  
- No objective diagnostic test  
- Diagnosis based on clinical features  
COMPLICATIONS  
- Sleep disturbance  
- Chronic skin changes  
- Scarring from picking and scratching  
- Secondary skin infections (bacterial and viral) |
| **Burden on Society** | PREVALENCE<sup>2,3</sup>  
- 17.8 million people in the United States are living with eczema  
- 10-20% of US children  
- Prevalence is increasing  
- Study of US children 17 years of age or younger:  
  - Prevalence ranged from 8.7% to 18.1% from state to state  
  - Higher disease prevalence associated with metropolitan living, African American population, and educational levels in the household greater than high school  
QUALITY OF LIFE<sup>1,4</sup>  
- Significant impact on patients (and difficult for caregivers to manage in children)  
- Sleep disruption (from itching)  
- Inhibited bonding and touching between parent and affected infant  
- Parental feelings of inadequacy about caring for their affected child  
- Embarrassment and avoidance of daily activities  
- Emotional distress and at risk for behavioral problems, anxiety, and depression  
- Financial costs, time demands, and lifestyle changes associated with disease management  
PRODUCTIVITY<sup>4</sup> |
- Missed school or work days
- Lost work days for medical appointments and when children miss school

**USE OF HEALTH CARE SERVICES**
- Moderate disease—13 physician visits per year and annual cost of $1700 for family
- Severe disease—23 physician visits per year and annual cost of $2500 or more

**How strongly does this overall societal burden suggest that CER on alternative approaches to this problem should be given high priority?**

US costs are estimated between $364 million and $3.8 billion annually.\(^5\)

### Options for Addressing the Issue

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<th>Based on recent systematic reviews, what is known about the relative benefits and harms of the available management options?</th>
<th>MANAGEMENT OPTIONS</th>
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<td>Standard therapy for eczema includes skin hydration, topical corticosteroids, and antihistamines. Studies comparing topical corticosteroids with calcineurin inhibitors have shown that calcineurin inhibitors are more effective at reducing skin inflammation than low-potency topical corticosteroids; but have similar efficacy to mid-potency topical corticosteroids.</td>
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<td>Other therapies are introduced if the eczema does not respond to standard therapy. Costs and side effects influence the choice of therapy. For example, calcineurin inhibitors are expensive, and the side effect profile includes immunosuppression and increased risk of skin cancer. Brief descriptions of the benefits and harms of routine therapies follow.(^1,2)</td>
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**Skin hydration:** Warm, soaking baths and application of a moisturizer:
- Potential benefits are improvement of skin-barrier function, decreased itching, maintenance of skin texture, decreased need to use corticosteroids.
- Potential harms are skin irritation or drying (if lotion or cream) and interfering with sweat ducts (if occlusive ointment).

**Topical corticosteroids:** Seven levels of medication strength, which should be tailored to disease severity:
- Potential benefits include effective treatment (low potency used for maintenance, high potency for treatment of exacerbations over short periods).
- Potential harms are systemic and local:
  - Systemic (suppression of hypothalamic-pituitary-adrenal axis) harms vary with potency, application site, percent of body covered, and duration of use (and is more likely in small children and infants (who have a higher body surface area ratio than adults).
  - Local harms are thinning of the skin; rash around mouth; bumpy, acne-like rash on nose; and contact dermatitis.

**Calcineurin inhibitors:** Tacrolimus and pimecrolimus, approved for use in patients older than 2 years of age. These are particularly useful for eczema on the face that is not responsive to
low-potency topical steroids:
- Potential benefits include reduced itchiness, no skin atrophy, and greater therapeutic margin of safety than medium-strength glucocorticoids for facial and eyelid eczema.
- Potential harms are transient local burning and itching in the first week, facial flushing after drinking alcoholic beverages, possible increase in viral skin infections (herpes simplex, molluscum contagiosum), possible immunosuppression, and possible link to lymphoma and skin cancer (but no conclusive evidence for lymphoma and skin cancer).

- **Tar preparations:** No randomized controlled studies demonstrating efficacy; tar preparations can potentially irritate the skin.

- **Antihistamines:** Little objective evidence demonstrating relief of itching for sedating or non-sedating oral antihistamines. Additionally, topical antihistamines can potentially cause skin to become increasingly inflamed and reactive to irritants.

- **Food allergy testing:** Recommended only if patient has persistent eczema despite optimal management, or if there is a reliable history of an immediate allergic reaction after ingestion of food.

- **Extensive elimination diets:** Based on positive skin tests or specific immunoglobulin-E test results, not recommended because of potential development of nutritional deficiencies.

- **Nutritional supplementation and Probiotics:** Fish oil, zinc sulphate, selenium, vitamin E, vitamin D, pyridoxine, buckthorn seed oil, buckthorn pulp oil, hempseed oil, sunflower oil, DHA, and probiotics:¹²,⁶,⁷
  - There is no convincing evidence for benefits of nutritional supplements or existing probiotics.
  - Nutritional studies were small with low numbers of participants and of poor quality.
  - Two trials of fish oil found some slight improvement in terms of itchiness and quality of life; but these were small trials and larger trials are needed before recommendations can be made.
  - There is also ongoing research regarding giving supplemental Vitamin D if the patient has low vitamin D levels confirmed by a blood test.
  - There is no evidence for harms in nutritional supplementation studies except:
    - There is a potential for vitamin D toxicity if taken in high doses.
    - Probiotics can cause infections and digestion problems.

- **Therapies for difficult-to-manage patients:**¹²
  - Systemic immunomodulating agents (medications that help regulate your immunity) include cyclosporine A, mycophenolate mofetil, azathioprine, interferon-gamma, systemic corticosteroids, and methotrexate.
    - All have potential for serious adverse effects.
  - Phototherapy (ultraviolet therapy, made up of mostly UVA rays), the benefit has to be weighed against the potential skin damage caused by these treatments (similar to sun exposure and tanning beds).
**What could new research contribute to achieving better patient-centered outcomes?**

- Itching is the most significant complaint of patients with eczema; therefore improved patient outcomes must include evaluating therapies that can control itching.
- A recent meta-analysis suggests that topical therapies were preferable to systemic therapies at controlling itching.
  - Further, calcineurin inhibitors were the most effective agent at controlling itching.
  - Studies designed to evaluate the safe use of these agents in children and patients younger than two years of age are needed.
- The role of omega-3 fatty acids in the treatment of eczema symptoms has been evaluated only in small studies. Larger studies are needed that assess the potential role of these dietary supplements.

**Have recent innovations made research on this topic especially compelling?**

- The most recent innovation has been the approval of calcineurin inhibitors.
- However, the black-box warning for these topical agents (lack of long-term safety data and the potential risk of the development of skin cancer) has likely limited their use, particularly in children.
- Attempting to better define the role of calcineurin inhibitors in treating childhood eczema is compelling.

**How widely does care now vary?**

- Care varies widely:
  - Eczema is a common condition for which patients seek care from health care providers representing a wide variety of different specialties.
  - Many patients self-treat with over-the-counter creams without consultation from health care professionals.

**What is the pace of other research on this topic (as indicated by recent publications and ongoing trials)?**

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<tr>
<th>Clinicaltrials.gov:</th>
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<tr>
<td>Search: Eczema</td>
<td>Search: Dermatitis</td>
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<tr>
<td>Total ongoing trials: 75</td>
<td>Total ongoing trials: 139</td>
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<tr>
<td>Completed trials: 122</td>
<td>Completed trials: 339</td>
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**How likely is it that new CER on this topic would provide better information to guide clinical decision making?**

- New comparative-effectiveness research (CER) that provides compelling information about treatment or prevention approaches that can be easily understood and implemented by patients or caregivers is likely to guide patient-driven clinical decisions.
- There is a need for better, faster ways to identify the allergen causing the eczema to reduce a patient’s exposure to the allergen or to identify a medication that will treat the reaction. Until we have better diagnostic methods, clinical treatments are chosen by trial and error (that is, “Let’s see if this works, and if not, we’ll try something else”).

**Potential for New Information to Improve Care and Patient-Centered Outcomes**

**FACILITATORS**

- Desire by stakeholders to improve care
- Generally well-informed patients who may be able to access new findings via the Internet

**BARRIERS**

- Diversity of health care providers (dermatologists, general internists, family physicians, gynecologists, alternative medicine practitioners, and the like) who treat eczema
- Large amount of currently available information on the Internet
- Wide variation of beliefs about what causes eczema and what are plausibly effective
How likely is it that the results of new research on this topic would be implemented in practice right away?

- Results of new research on this topic would need to be disseminated to a diverse group of stakeholders.
- However, with targeted efforts towards dermatologists and allergists (who see a large volume of eczema in their practices), this information would be helpful for discussing the risks and benefits of treatment options with those who suffer with eczema.

Would new information from CER remain current, or would it be rendered obsolete quickly by subsequent studies?

- Eczema seems to be a relatively active topic in ongoing research.
- Many different claims of efficacy and harms associated with a variety of different treatment approaches are readily available on the Internet.
- In order for new CER information on this topic to remain current, it would have to be perceived by stakeholders as compelling in order to compete with existing and future information (substantiated by evidence or not).

REFERENCES


APPENDIX: Topic Question

Nominated over the Web

1) What safe therapies are there to stop the itch associated with eczema, either topical or systemic? Topical corticosteroids do not work for everyone, and they are not appropriate for the face. For infants, it is not always a great option to cover the entire body and does not stop the itching.
**Population**: All ages and ethnic groups.
**Importance**: Because there are so many people still suffering with eczema.

2) I would like to see more research on eczema, what causes it, and most importantly nonmedication treatment options. I am particularly interested in the link between nutrition, omega-3 fatty acids and eczema. Thank you!

**Population**: Adults and children
**Importance**: Both my daughter and I suffer from eczema and have spent countless hours researching this very common condition. We accidentally discovered a link between fats and eczema, and use a self-prescribed treatment, consisting of bumping up fatty acids in our diet. I would like to see a more scientific study on this topic. It seems, at least based on our experiences, and those of the many people posting in Internet forums, that the omega-3 could be a cure for eczema! Much simpler and probably safer than the many medications (creams) that we have been prescribed, unsuccessfully, over the years.