Atopic Eczema Patient Burden Landscape Analysis

A Landscape Analysis for GlobalSkin Prepared by High Lantern Group

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The purpose of this document is to provide GlobalSkin with a landscape of atopic eczema. The document summarizes extensive desk research across areas of most interest in considering GlobalSkin's current and future position within the atopic eczema public policy landscape. The document represents research conducted between May – July 2020.

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Introduction

The World Health Organization (WHO) Global Burden of Diseases initiative estimates more than 230 million people globally have atopic eczema. While this is approximately 3 percent of the global population (compared to the 1.3 percent of people globally with cancer) and can have a significant impact on health and society, atopic eczema receives little attention on the global policy and advocacy stage. Because of this lack of attention, research is undervalued, healthcare professionals are underinformed, and patients go unheard.

Since its inception, GlobalSkin has actively with dermatological patient organizations to improve the lives of dermatology patients worldwide to diminish stigma, shame, and the psychosocial challenges they face every day. The implications of this study are immense. Atopic eczema is the greatest cause of economic and health burden among skin diseases globally. ⁱⁱⁱ Both patients and caregivers face mounting obstacles in diagnosis, treatment, and social navigation as stigma is prevalent. Additionally, as atopic eczema is often treated solely as a skin disorder and not a systemic disease that affects many part of the body, patients also do not receive the full extent of research, funding, and treatment to support their condition. This situation has further been exacerbated due to the global COVID-19 pandemic, causing many patients to not receive the treatment they need due to limited access to healthcare.

In order to promote broader understanding of the disease and bring to light necessary insights that may elevate atopic eczema to global public and policy attention, GlobalSkin has developed the following landscape to explore the current state of atopic eczema, to review promising strategy and activity recommendations for GlobalSkin and other patient organizations, and to consider new opportunities to engage with partners whose interests align with atopic eczema.

Firstly, the landscape will thoroughly investigate the current atopic eczema disease state including its prevalence, risk factors, comorbidities, patient costs, and specifically how atopic eczema is addressed in Asia, the Middle East, Africa, and South America. It will also look into how atopic eczema is currently being addressed at the public-policy level and if anyone is doing enough to address these important issues.

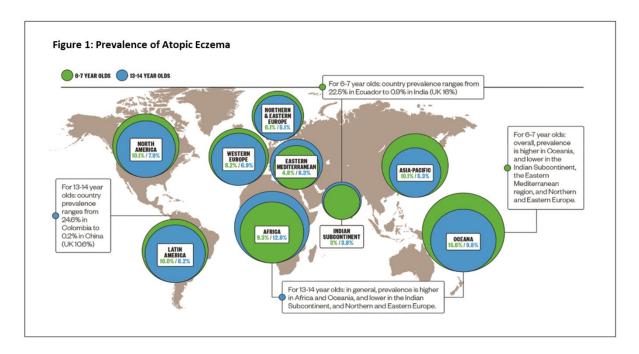
Secondly, the landscape will offer a series of promising strategy and activity recommendations based on the insights discovered in the landscape and aligned with GlobalSkin's three-year strategy. From these recommendations, the GlobalSkin Atopic Eczema Community can decide the best direction to go to achieve their long-term goals for their organization and their patient leader organizations.

Thirdly, the landscape offers recommendations of promising stakeholders to engage with. These stakeholders include societies and organizations both from within the dermatological community and adjacent organizations, whose goals might align with those of GlobalSkin's.

Part I: Landscape Overview

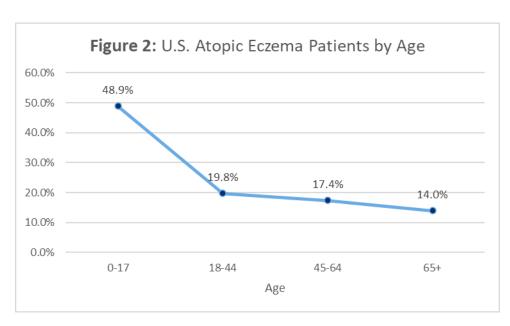
Prevalence

The traditional understanding of atopic eczema is that the condition usually occurs during childhood and resolves before adulthood; however, current research indicates that atopic eczema may persist into adulthood more often than previously thought. This runs parallel to epidemiological data demonstrating the steady rise in autoimmune diseases worldwide, whose incidence and prevalence have increased significantly over the last 30 years.



Studies on atopic eczema prevalence are mixed. While numbers in Western countries suggest that atopic eczema affects up to 20 percent of children and 3 percent of adults, a recent 2018 global survey, that included China, South Korea, Brazil, Mexico, and Israel, suggests it affects fewer children than historically thought (4-8 percent) and more adults (10 percent). Recent data show that its prevalence is still increasing, especially in low-income countries. Figure 1 illustrates the wide variation in the global prevalence of atopic eczema, common in both developed and developing countries in children with age ranges from 6 to 14 years old. An estimated 10 percent of all people worldwide are affected by atopic eczema at some point in their life. Another study indicated that atopic eczema affects 1-3 percent of the elderly in industrialized countries.

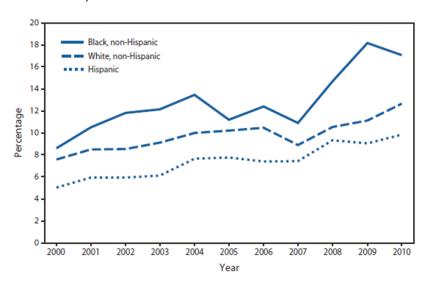
Figure 2 illustrates the percentage of atopic eczema (also referred to as atopic dermatitis) patients seen by a physician per age group. While there is a decrease in prevalence overtime, the disease endures over lifespans.x As such. the development of atopic eczema in infancy and the subsequent



appearance of allergic rhinitis and asthma in later childhood is known as the "atopic march." This temporal pattern described in the atopic march is confirmed when examining data on the prevalence of each atopic disease across the lifespan. Classically, the clinical signs of atopic eczema precede the development of food allergy, allergic rhinitis and asthma, suggesting that atopic eczema marks the commencement of the atopic march. While some studies debate the prevalence of the atopic march amongst atopic eczema patients (some studies suggest as low as 3 percent of children follow the march), the progressive nature of the march is important, as it provides identifiable characteristics that could allow for risk stratification and early intervention or prevention, if available. The link between atopic eczema and the development of other disease areas is type-2 inflammation – atopic diseases ignite the type-2 inflammatory pathway because of increased water loss in the skin (See 'The Inflammation Connection' for further details).

Children & Atopic Eczema: As stated, atopic eczema usually starts in infancy or early

Figure 3: Percentage of Children Aged ≤17 Years with Eczema or Any Kind of Skin Allergy, by Selected Ethnicities - National Health Interview Survey, United States, 2000--2010



childhood. Children with family history of atopic eczema or asthma are more likely to develop atopic eczema. About 75 percent of children with moderate to severe atopic eczema develop allergic rhinitis or hay fever. Food allergies are also common and the likelihood of having one atopic condition increases the risk of developing another as they are inextricably linked.xv From 2000 to 2010 there has been an

increased prevalence of atopic eczema in the U.S. from 9 percent to 17 percent in black children, 5 percent to 10 percent in Hispanic children, and 8 percent to 13 percent in white children, as portrayed in **Figure 3**.xvi The difficulties associated with itching, scratching, and emotional distress are typically among the first to be mentioned by parents when asked about the effects of their child's disease, followed closely by comments on sleep disturbance. Because of the cluster effects of these difficulties, the more severe the disease, the poorer quality of life for the child.xviii Atopic eczema's increase in prevalence is consistent with trends in allergies, whose rates are also increasing among US children. It is suspected that these increases arise from environmental factors though the disease's expression is not fully understood.

Higher Frequency in Biological Females: Evidence shows that atopic eczema is more frequent in females in their thirties, although it's more prominent in elderly male patients (>65 years old). Clinical features of atopic eczema differ characteristically according to the age of patients; in adults and older patients, atopic eczema often presents with clinical manifestations that differ from children and younger adults, which sometimes make diagnosis very difficult.*

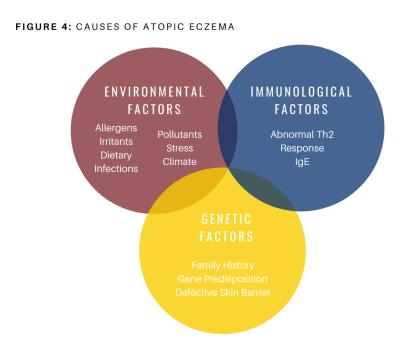
Older Adults as a New Subgroup: Atopic eczema in older adults represents a newly defined subgroup; while the actual cause of elderly atopic eczema is unknown, research suggests it might be associated with immunosenescence, age-related changes to hormones, and age-related barrier dysfunctions in the skin and gut.xix These changes make the elderly more susceptible to the entry of irritants and allergens through the skin, leading to inflammation and pruritus. In an analysis of hospital-based patient registry records, 11.5 percent of hospital admissions in elderly patients were attributed primarily to pruritus.xx Sensitivity to aeroallergens, especially dust mites, is demonstrated in the majority of adult atopic eczema patients, including elderly adults, by patch tests.xxi There is also a relationship between the severity of atopic eczema and IgE-mediated food allergy reaction: the higher the time to food reaction, the more severe atopic eczema.xxii The male predominance in elderly atopic eczema may be a characteristic feature that differs from adult atopic eczema, as well as reveals particular patterns of onset and offset courses.xxiii Unfortunately, most elderly patients with atopic eczema reach the end of life without any cure to this disease.

Risk Factors

Risk factors are complex and not thoroughly understood. There are 195 ongoing studies^{xxiv} in the United States alone that are investigating a broad spectrum of atopic eczema-related factors such as those to better understand its environmental and immunological links, behavioral interventions, and evaluations of medications.^{xxv}

Genetic & Environmental

Factors: Atopic eczema arises in patients through complex interaction between genetic and environmental factors.xxvi Dry skin, irritants, stress, temperature, sweating, infections, allergens, and hormones can all serve as triggers for flare-ups. Those with atopic eczema often have allergies and are at risk for allergic asthma and allergic rhinitis,



though the exact relationships among these three diseases is unknown.xxvii **Figure 4** summarizes the common causes of atopic eczema which include environmental, genetic, and immunologic factors.xxviii By reviewing both hereditary and atopic eczema characteristics at diagnosis, doctors can create a personalized map for the disease course.xxix

Comorbidities: As previously noted, atopic eczema is linked to increased susceptibility to infections. Hospitalization due to atopic eczema flare-ups and associated infections and/or viruses is associated with an 8-year reduction in lifespan.** Aside from infections, atopic eczema is also associated with a number of multi-organ and systemic disorders. The origin of these comorbid conditions is multifactorial, with combined effects of skin-barrier disruption and immune dysregulation. Some of these comorbid conditions appear to be related to the underlying severity of atopic eczema and inadequate disease control. Others, like increased smoking and alcohol use are as a result of atopic eczema can increases risk for cardiovascular issues. **Figure 5** lists these comorbidities.**

Figure 5: Comorbid events & risk factors associated with atopic eczema

Cutaneous and Extra-cutaneous Infections	Mental Health	Sleep Disturbances	Cardiovascular Risk Factors		Additional Comorbid Links
Impetigo Cellulitis Viral Fungal Staphylococcus aureus Sepsis	Depression Anxiety Stress Emotional instability Social Functioning Suicide ideation	Difficulty falling asleep and staying asleep Poor sleep efficiency Poor quality of life	Obesity Hypertension High cholesterol Type 2 diabetes Smoking Alcohol consumption Sedentary activity	Coronary artery disease Angina Heart attacks Congestive heart failure Strokes	Recurrent ear infections Sinus infections Head and chest colds Strep throat Gastroenteritis Chickenpox

Comorbid links: Several studies have found these comorbid links indicating that children with atopic eczema had higher rates of recurrent ear infections^{xxxiii} and significantly higher odds of sinus infections, head or chest colds, and strep throat.^{xxxiii} Adult studies also found significantly higher odds of strep throat, head or chest cold, sinus infection, gastroenteritis, and chickenpox.^{xxxiiv} Both population-based studies demonstrated consistently increased risk of extra-cutaneous infections.

Bacteria Staphylococcus: The bacteria *Staphylococcus aureus* is found on the skin of 50-90 percent of patients with atopic eczema and much less commonly on people with healthy skin.xxxx Additionally, the prevalence of staphylococcal colonization in children with atopic eczema is comparable to that in younger adults, though both see a higher prevalence than older adults.xxxviThe bacteria can colonize, causing infections, and certain strains of the bacteria are resistant to antibiotics, making them considerably more difficult to treat. Atopic eczema patients are more susceptible to *Staphylococcus aureus* infection because: 1) they have a leaky skin barrier that allows bacteria to cling to the skin; 2) they produce fewer natural molecules to fight bacteria on the skin; and, 3) *Staphylococcus aureus* produces molecules that aggravate and inflame atopic eczema skin, which makes the skin barrier even weaker.xxxvii

Impaired Sleep: Impaired sleep has also been shown to be a significant burden of atopic eczema in both children and adults with reduced sleep overall, more regular and protracted awakening, overall decreased sleep efficiency, and increased daytime dysfunction. **xxviii* Poor sleep in combination with atopic eczema were associated with a greater chance of negative outcomes than either sleep symptoms or atopic eczema alone. Because of the correlation between severity of atopic eczema and worse sleep outcomes, pruritus and scratching appear to be large contributors to sleep disturbances. **xxxix* Sleep disturbances may be a major driver for developing other comorbid health conditions, including increased risk for cardiovascular events.

Obesity: Overweight and/or obese children and adults have higher odds of atopic eczema than normal-weight patients. Those with moderate-to-severe atopic eczema were also associated with higher systolic and diastolic blood pressure for age, sex, and height percentiles. Any children that exhibit a deviation from their age and sex's body mass index (BMI), and are less physically active are likely to see symptoms of both atopic eczema and asthma. Aggregate results all point toward atopic eczema being associated with increased cardiovascular risk. This relationship is interpreted in two ways by the medical community, though none of have reached a determination if one affects ore than the other: either, obesity causes atopic eczema by igniting a long-term inflammatory status and this status induces immune dysfunction and hypersensitivity, leading to AD; or alternatively, a sedentary life-style induce both AD and obesity.

Mental Health & Well-Being

Common grievances include, lack of sleep, food allergies, asthma and hay fever, and skin infections due to repeated scratching that breaks the skin. **Iiv** Aside from irritation and other physical disease symptoms, atopic eczema can have serious psychosocial and quality-of-life impacts on patients and their caretakers. One study showed that atopic eczema is more detrimental to patients' mental health and quality of life than heart disease, diabetes, and high blood pressure.**Iv** Another reveals that atopic eczema patients are likelier to develop depression and anxiety, regardless of atopic eczema severity.**Iv** Further, atopic eczema patients suffer more intensely in terms of decreased emotional stability, social functioning, mental health, and vitality when compared to patients with other skin disorders including psoriasis, alopecia, acne, and localized eczema.**Iviii Additionally, in a recent study, patients with atopic eczema were 44 percent more likely to exhibit suicidal ideation and 36 percent more likely to attempt suicide compared with patients without atopic eczema.**Iviii

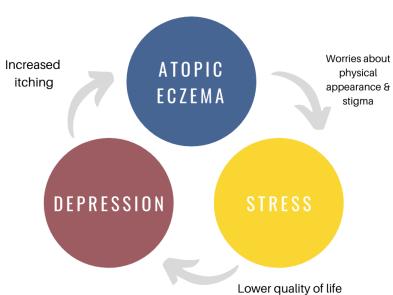
Parent wellbeing: Insights into a cohort of parents demonstrated that 71 percent of them with affected children reported feeling guilty, exhausted, frustrated, and helpless as related to their child's atopic eczema. Another 60 percent reported that their children had been bullied at school and had poor attendance with 5 percent stating that their children were irritable and angry. In another study, among bullied kids, 77 percent of parents said their child had lower self-esteem since being bullied, 54 percent reported their child wasn't as happy since they were bullied for their eczema, and 40 percent said the child had no interest in managing their atopic eczema.

Atopic eczema leads to stress later in life:

Psychological stress in early life may also lead increasing vulnerability to stress later in life. Though the mechanism underlying the association of atopic eczema with psychological stress has not been fully elucidated, the field of psychoneuroimmunology has provided many new insights for understanding the role of stress in atopic eczema, as seen in Figure 6. Recently, it has been further established

Figure 6. Recently, it has been further established via clinical and physiological means that

FIGURE 6: THE ATOPIC ECZEMA STIGMA CYCLE



psychological stress is a significant contributor to atopic eczema disease course through its direct and indirect effects on immune response and skin barrier function. Additional studies suggest that pro-inflammatory causes associated with skin diseases are casually connected to depression.

Problems between child patients & families: Because atopic eczema is more commonly identified in children, the disease often affects the interaction between patients and their families. Children with atopic eczema are more likely to develop behavioral problems such as clinginess, dependency, and fearfulness as compared to children of the same age. Furthermore, children with atopic eczema have been noted to have a less secure attachment to their mothers than children without atopic eczema, which could be the result of the increased stress of having to care for children with atopic eczema.^{IIII}

The problem of stigma: Many of these mental health issues can be attributed to stigma. Because of chronic and often visible lesions, atopic eczema may lead to stigmatization and problems with self-perception. As described above, the type of stigma can vary with the patients' age: in early infancy the problems revolve around mother-child attachment, later on atopic eczema can cause parental distress and exhaustion that in turn leads to exacerbation of atopic eczema and psychosocial problems in children, and in adulthood low self-esteem is a main concern. The emotional toll of atopic eczema may lead to mood disorders such as anxiety and depression; both children and adults with atopic eczema have higher levels of behavioral problems compared to their healthy peers. The condition can be seen as a difficult cycle to break as stress causes negative effects on the immune system, impairs healthy skin barrier function, and creates more inflammation, which can potentially aggravate symptoms such as itching. Additional itching, often in non-affected areas, is thought to be a result of social stress, rather than pruritus.

The Inflammation Connection

A 2014 study demonstrated that participants with eczema who were treated with a drug that targeted specific immune signaling proteins experienced significant symptom improvements. This study opened the door to immune-specific treatments for atopic eczema reiterating that atopic eczema is autoimmune in nature. For example, researchers in 2018 have discovered that an immune system skewed towards allergy alters the skin so that it is dry, inflamed and itchy. However, the broader advocacy and policy community has been slow to adopt this emerging designation. While many publications point to the links between atopic eczema and other autoimmune conditions, literature clearly stating that atopic eczema is itself an autoimmune disease is fewer and farther between. For example, one of the leading advocacy groups for autoimmune diseases, the American Autoimmune & Related Disease Association (AARDA), does not include atopic eczema on its public autoimmune disease list.

Prevalence of autoimmune diseases in those with atopic eczema: Prevalence of autoimmune diseases are higher in adults and children with atopic eczema when compared to those without atopic eczema – in particular, atopic eczema was associated with 18 of 32 autoimmune disorders examined in adults and 12 of 24 examined in children, including disorders of the skin, endocrine, gastrointestinal, hematologic and musculoskeletal systems. ki The four of the most commonly associated autoimmune disease with atopic eczema are celiac disease, rheumatoid arthritis, inflammatory bowel disease, and lupus. |XIII Additionally, approximately 25 percent of people with autoimmune diseases have a tendency to develop additional autoimmune diseases. |Xiiii Biological females are strikingly more susceptible to autoimmune diseases, carrying approximately 78 percent of the burden, when compared to biological males. Ixiv This is due in part to immune regulatory genes located on the X chromosome, of which females have two. Ixv Though exact prevalence varies by age, females shoulder the larger part of the burden. Parallel comparisons can be made with atopic eczema, as it usually affects more women than men in cohorts of patients under the age of 65. IXVI Though progress may be gradual, the scientific community continues to reveal associations between atopic eczema, autoimmune diseases, and other comorbidities. These continual discoveries will place more emphasis on the understanding and discovery of the mechanisms behind this web of diseases.

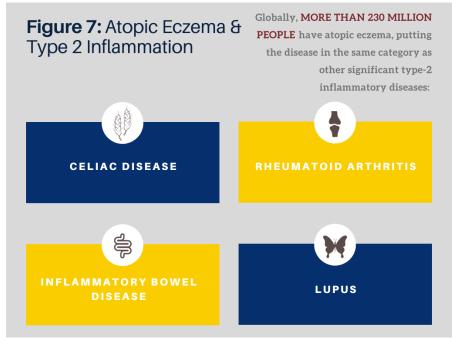
Atopic eczema and the type-2 inflammatory pathway: As revealed in the atopic march, atopic eczema is not a disease in isolation, but a systemic process. The type-2 inflammatory pathway occurs in response to atopic diseases. Atopic eczema often precedes the onset type-2 inflammatory conditions, such as food allergy, asthma, and allergic rhinitis. Ixvii One hallmark of atopic eczema is skin barrier dysfunction, which leads to increased water loss in the skin and allows for the penetration of noxious environmental stimulants, triggering this immune response pathway. Ixviii Barrier dysfunction in atopic eczema-affected skin can be attributed to a deficiency of filaggrin, associated with poor skin hydration and enhanced penetration of allergens through the skin. Ixix

The immune response has been confirmed by findings which show that patients with severe atopic eczema experience significant improvement when treated with dupilumab, the first of many new treatments for atopic eczema in nearly 25 years. Dupilumab, and others like it, limits

the overreaction of the immune system (specifically IL-23) which tones down the inflammatory response and subsequently lessens the symptoms of atopic eczema. These early case reports suggest that inhibiting IL-23 can lead to improvement of severe atopic eczema.

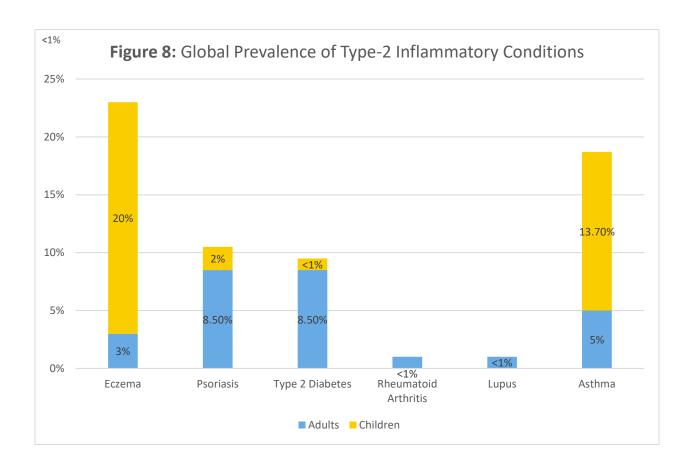
By classifying atopic eczema as a type-2 inflammatory disease, it puts atopic eczema in a broader group of diseases, such as those listed in **Figure 7.**

Environment & the immune system: Over the past ten years, research has shown that the environment influences the immune system response. Research suggests that atopic eczema-associated microbiomes in the environment can increase the risk to



develop atopic eczema flares by both influencing the microenvironment of the skin surface and also through interacting with the host immune system. Environmental factors interacting with the immune system that may contribute to the severity of atopic eczema flare-ups include heightened humidity, inhabiting in a city, air pollution, tobacco smoke, and frequent hygienic processes (frequent handwashing, clothes washing, baths, etc). Environmental factors that reduced atopic eczema flares include living in the countryside, consumption of fruits and vegetables, and spending time around dogs (not cats) at a young age. Ixxiv

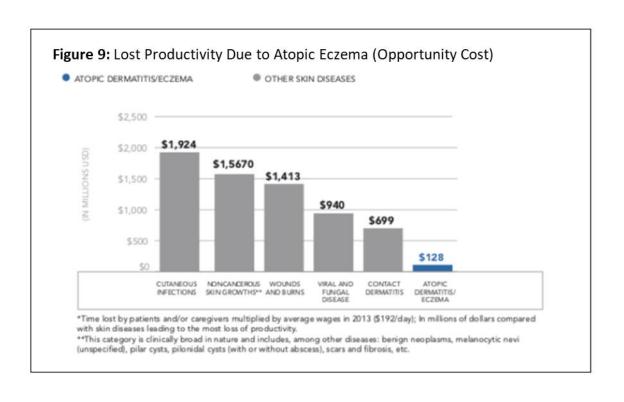
Classifying atopic eczema as autoimmune: If atopic eczema were to be successfully recategorized as an autoimmune disease, it would be one of the most prevalent autoimmune diseases in the world—dwarfing better-known autoimmune conditions such as Type 1 Diabetes and Rheumatoid Arthritis. Data available indicate that the age-sex standardized lifetime prevalence rate for eczema per 100,000 would be 11,526|xxvi| compared to 2,619 for autoimmune thyroiditis, 939 for psoriasis, and 552 for rheumatoid arthritis.|xxvii| Type 1 diabetes, a widely recognized disease that enjoys significant political commitments, has a prevalence of 670 per 100,000—the prevalence rates for eczema are a full 17 times higher.|xxviii| Find an illustration of the prevalence of atopic eczema, as compared to other common inflammatory diseases in Figure 8, below.



Patient Costs

Out-of-pocket cost estimates fluctuate substantially and are partially varied due to the severity of a patient's atopic eczema. Approximations of the personal costs (which include medication, healthcare, and prescribed treatments) of patients with atopic eczema are \$3,302 USD greater per year than patients without atopic eczema; those with more advanced therapies have costs \$4,463 USD more a year. Supportive products outside of medication have shown to decrease patient costs by decreasing the number and length of doctors' visits. In one UK study, costs of patients taking emollients were £125.80 versus costs of those who didn't take them were at £128.13. Those taking emollients had fewer doctors' visits per patient (2.44 vs. 2.66) and lower mean per-visit costs (£104.15 vs. £113.25), compared with those not taking emollients.

Lost productivity: Lost productivity is another important cost burden for those afflicted with atopic eczema. Eczema accounts for more healthy life years lost to ill-health, disability, or early death than any other skin disease. Patients and caregivers seeking treatment for their disease lost \$128 million in wages in 2016. Patients of people with eczema say that their disease interferes with their job and household chores and 12.2 percent missed 1 or 2 days of work and 2.3 percent missed 3 or more days. Patients With eczema reported that they turned down a job or an educational opportunity due to their disease. Figure 9 illustrates lost productivity when compared to other skin diseases, ranking atopic eczema in the top six.



Atopic Eczema in Asia

While the majority of research in atopic eczema has been devoted to Western, high-income countries, atopic eczema is also a rising issue in Asian countries. This is likely due to the increase of urbanization, pollution, consumption of a Western diet, and obesity. IXXXV

Prevalence of atopic eczema in Asia: The prevalence of atopic eczema across the Asian Pacific and Indian subcontinent is comparable to the United States and European Union (EU). However, there is a distinct difference in prevalence between older and younger children. According to an older study in 2013, among 13- to 14-year-old adolescents, atopic eczema prevalence for Asian-Pacific countries (including China, Japan, South Korea, etc.) and the Indian subcontinent (including India, Bangladesh, Pakistan, etc.) values fell at 3-6 percent; however, while among 6- to 7-year-old children, atopic eczema prevalence for Asian-Pacific countries was high at approximately 10 percent, whereas values for the Indian subcontinent were lower at 3–5 percent. The prevalence of atopic eczema in adults appears to be greater among some Asian populations (11-13 percent in Singapore and Malaysia, comparable to rates in Sweden) potentially because of higher rates of disease onset in adulthood.

Adherence to treatment in Asian countries: Adherence to dermatological treatments in Asia varied by country. While most patients showed willingness to adhere to physician guidance on treatment, if they consulted a physician at all, in many cases there is evidence of a lack of access to certain medications, particularly topical calcineurin inhibitors (TCIs).

According to physicians in Southeast Asia, adherence to topical treatment of atopic eczema, such as creams and lotions was high compared to systematic treatments. For example, the use of emollients was high (86–100 percent) from the Philippines, Thailand, Malaysia, and Singapore but was significantly less likely from Vietnam or Indonesia. The use of topical anti-inflammatory therapies was also quite high, with 91–100 percent of dermatologists prescribing topical corticosteroids (TCSs). Most patients from Singapore, Thailand, and South Korea used topical calcineurin inhibitors (TCIs); however, only some patients (9–24 percent) from Indonesia, Malaysia, or Vietnam used them, mostly because 55-67 percent of them lacked access to these medications.^{xc}

While oral treatments are not often recommended, the use of oral antihistamines (86–100 percent) and oral corticosteroids (67–100 percent) is quite high. Studies in India and Pakistan showed that most patients are treated with emollients (95 percent) and topical anti-inflammatory therapies (75 percent, nearly all TCSs). Despite guidelines disincentivizing the use of oral treatment, 75 percent of patients there received antihistamines and 25–78 percent received oral corticosteroids, although they were prescribed on a short-term basis.xci

The prevailing use of traditional medicine: Despite physician recommendations about the lack of efficacy in traditional medicines, many people across Asia still use them. In surveys of South Korean patients with atopic eczema, approximately 70 percent reported using complementary alternative medicine (i.e., bath therapy, dietary therapy, health supplements, massage, traditional Chinese medicine, topical applicants) alongside clinically prescribed treatments.^{xcii}

Often this is due to a lack of access to clinical treatment and medications. In fact, 15 percent of patients reported receiving no treatment in one Singapore community-based study. In another

study, only 36 percent of patients in North India with limited resources sought medical care for their dermatologic condition, and 69 percent received inappropriate or ineffective treatment.xciii

Atopic Eczema in the Middle East

While the Middle East encompasses several countries, the majority of data and research on atopic eczema has been done in Saudi Arabia, likely due to abundance of resources and strong connections to the international medical community.

Prevalence

Looking all across the Middle East, questionnaires have reported atopic eczema prevalence rates in adolescents aged 13–14 years of 3.9 percent in Syria, 10.1 percent in Iran, 11.3 percent in Kuwait, and 14.4 percent in Oman. The highest prevalence of atopic was recorded in a study of Taif, Saudi Arabia, where a whopping 45.4 percent of adolescents and adults experienced the disease. xciv

In these surveys, atopic eczema was the second most prevalent dermatological diagnosis with acne vulgaris (29.5 percent) in the lead, then atopic eczema (22.3 percent), vitiligo (20.7 percent), and finally psoriasis (6.4 percent).xcv

Comorbidities

Amongst young adults in Saudi Arabia, there has also been studies of comorbidities with atopy present in 40.5 percent of tested young adults with bronchial asthma, atopic eczema, and allergic rhinitis and those with an atopic disease were likelier to have any of these diagnoses. Atopy and polysensitization was more frequent among male than female students. SPT results were positive in 20.8 percent of participants for Bermuda grass, 18.9 percent for cat fur, and 12.7 percent for Dermatophagoides pteronyssinus.xcvi

There has also been significant study on psychiatric conditions adjacent with atopic eczema. One study in Saudi reported that among those with dermatological diseases, overall prevalence rates for depression, anxiety, and stress of 12.6 percent, 22.1 percent, and 7.5 percent, respectively. These reflected similar rates for those specifically with atopic eczema: 10.7 percent (depression), 21.4 percent (anxiety), and 7.1 percent (stress). Dermatology patients with poor qualities of life were over three times likelier to report depression, anxiety, or stress.

Quality of Life

Saudi patients with atopic eczema had the third highest mean Dermatology Life Quality Index (DLQI) score of eight skin diseases, with only patients who have papulosquamous disorders and connective tissue/immunological disorders showing poorer QoL.xcviii In short, atopic eczema patients have one of the worst quality of life amongst all skin diseases in Saudi.

Atopic eczema patients reportedly suffer more than other disease areas. A study of Saudi Arabian adult and teenaged dermatology outpatients found that most patients with dermatologic disease (79 percent) experienced low QoL, as measured by the DLQI.xeix

This is not limited to Saudi. A study conducted in the Sanandaj, Kurdistan province of Iran found that 1- to 6-year-old children with severe atopic eczema had significantly lower QoL than the same-age children with moderate atopic eczema.^c The authors reported itching/scratching and sleep problems as the greatest contributors to poor QoL in patients with severe atopic eczema.

In the study measuring QoL of Saudi Arabian patients with skin diseases, one study found that 31.4 percent of patients had comorbidities, the most common being diabetes (43.8 percent) and hypertension (47.2 percent).^{ci} About 20 percent of patients reported a comorbid psychiatric condition.

Those who appear to have the worst QoL are women: In Saudi, women with atopic eczema were nearly three times more likely to report at least one negative emotional condition than men. Another study estimated high overall prevalence of anxiety (29%) and depression (14%).^{cii}

Access to Treatment

There is little information about access to medications in the Middle East. In the minimal amount of research found, in Saudi Arabia, it seems as if treatment is plentiful, as long as one is diagnosed. According to one study, numerous AD medications are available over the counter, and medical consultation and treatment are free for citizens at government hospitals.^{ciii}

Advocacy

Currently, advocacy and study of dermatological disorders is minimal across the Middle East. Unsurprisingly, of all Middle Eastern countries, Saudi Arabia is most advanced in their advocacy of dermatological disorders. This aligns with a national objective for advancement and modernization, called Saudi Vision 2030. civ Part of Vision 2030 is improvement of healthcare systems, where there have been significant advancements. While dermatology is not mentioned in particular, this focus on health improvement has likely trickled down into specialist sectors like dermatology, allowing for a flourishment in this field. cv

Atopic Eczema in Africa

When reviewing atopic eczema across Africa, it's best to note that Africa does not exist as a single entity and rates vary widely across the continent. High income countries like Nigeria and South Africa have better access to diagnosis and treatment than countries in sub-Saharan Africa. Approaches to treatment also different depending on the region and access to certain medical tools.

Prevalence

When compared in a worldwide survey of 6- to 7-year-old children, children from Africa suffered the most from atopic eczema with a high prevalence of 23.3 percent (compared to the low rates in the eastern Mediterranean, where only 7.2 percent of children had the disease.^{cvi}

According to a 2012 systematic review, the prevalence of atopic in Africa has increased over time. The lifetime prevalence of atopic eczema symptoms in 13- to 14-year-old children approximately doubled in Morocco, South Africa, and Kenya over an approximate 7-year period. In contrast, the prevalence of atopic eczema symptoms in 13- to 14-year-old Nigerian children decreased during this period, although this trend may have been impacted by extremely high baseline prevalence.

Some studies found particularly high prevalence in 13- to 14-year-old children in Kenya and Algeria. Of nine African regions/countries surveyed, seven had higher lifetime prevalence in more recent years among 13–14 year olds. CVIIII

This high prevalence across African countries, in comparison with many other regions, has led researchers to hypothesize why atopic eczema might be more abundant in these areas. Most have come to the conclusion that hygiene is the primary factor.

Findings in Africa support the "hygiene hypothesis," which argues that increased prevalence of atopic eczema stems, at least in part, from decreased exposure to infection and microorganisms in early childhood.^{cix} In rural Ethiopia, higher rates of atopic eczema have been reported in children with access to piped drinking water than in children who drink river water, an effect attributed to reduced exposure to enteric infections.^{cx} Helminth (parasitic) infections, which are highly prevalent in Africa, have been shown to promote protection from atopic illness.^{cxi} Results of an analysis of more than 2000 children in Uganda showed that maternal hookworm infection during pregnancy and early childhood infection with *Trichuris trichiura* or hookworm both were negatively associated with atopic eczema.^{cxii}

Diagnosis and Care

Atopic eczema research and care across Africa might also be affected by underreporting of the disease. This stems from limited access to health care and prioritization of infectious, highly virulent diseases such as malaria and tuberculosis. Furthermore, many diagnostic tests were developed for use in European and North American individuals, and may not be relevant to African local environments.

However, new efforts are being made to create more opportunity for diagnosis and care. In regions with severe shortages of medical care such as sub-Saharan Africa, innovative tools to promote access to atopic eczema care such as the African Teledermatology Project, which connects sub-Saharan medical facilities to dermatologists in the USA, Europe, and Australia, are emerging. CXIV In South Africa, training programs are active at improving the status and number of nurse practitioners (160 nurses have been trained from all over sub-Saharan Africa). These nurses provide primary care services, which have improved referrals patterns at tertiary level and improved patient skin care generally at local level. CXV

Access to Treatment

In sub-Saharan Africa, the use of local long-term treatments for atopic eczema, particularly emollients, varies between patients. In some areas, access to essential drugs is assured but in others it is difficult or impossible, especially if imported products from branded cosmetic houses are used (e.g. one emollient tube represents 15 percent of local minimum monthly salary in Madagascar). In addition, AD care is hampered by the absence of coverage by health insurance in some countries. Possible solutions were discussed such as local emollient production with glycerol, shea butter or coconut oil.cxvi

Advocacy

While African countries often get a great deal of attention when it comes to rare and tropical diseases, there are fewer efforts taking place on atopic eczema. While a few higher-income countries like South Africa and Nigeria have specific dermatological societies, such as the Dermatology Society of South Africa (DSSA), the only broadly collective movement for eczema is by the African Society of Dermatology and Venerology (ASDV). The ASDV includes dermatologists from Kenya, South Africa, Nigeria, Rwanda and Ghana and they work fairly actively to address skin disorders of all kinds, atopic eczema included.cxvii

However, there are some active local organizations as well. For example, the Eczema Association of Zimbabwe Trust has hosted events to promote awareness, bringing together health practitioners and officials from the Ministry of Heath to discuss eczema. Another example from South Africa is from a patient-run eczema advocacy organization, South African

National Eczema Society (SANEA), offering direct patient communication and discussion including simple basic techniques such as how to wash the skin and apply medication. The case for training traditional healers was also discussed as some traditional healers are amenable to training in the essentials of dermatology for working in conjunction with health services.^{cxix}

Outside of these few exceptions, all other significant dermatological work in Africa comes from outside organizations, particularly the WHO. However, their focus is not on atopic eczema but NTDs.

Atopic Eczema in Latin and South America

Unlike the Middle East and Africa, Latin and South American studies on atopic eczema focus less on the general region and more on specific countries. Higher income countries like Brazil and Argentina offer the most data as well as the most interest in dermatological diseases.

Prevalence

Overall, Brazil performs moderately well compared with the other countries in South America. According to that epidemiological data, 14 percent of the Brazilian population across the life span will have atopic eczema at some point in their life, a mid-range finding compared with the other countries, (for example, Israel 9 percent, Africa at 23 percent, and Australia 32 percent). Atopic eczema is also among the most common dermatological diseases in Brazilian children. CXXI

The mean prevalence of mild to moderate atopic eczema in schoolchildren was 11.3 percent, ranging from 3.2 percent in Ciudad Victoria (Mexico) to 25.0 percent in Barranquilla (Colombia). For adolescents, the prevalence varied from 3.4 percent in Santo André (Brazil) to 30.2 percent in Barranquilla (mean prevalence, 10.6 percent).

The amount of severe atopic eczema cases was comparatively high to other countries, at a mean of 1.5 percent, ranging from 0.3 percent in Ciudad Victoria, Toluca, and Cuernavaca (Mexico) to 4.9 percent in La Habana (Cuba). For adolescents, the mean prevalence was 1.4 percent, ranging from 0.1 percent in Mexicali Valley (Mexico) to 4.2 percent in Santa Cruz (Bolivia). In general, the prevalence of current symptoms of eczema was higher among the Spanish-speaking centers for both schoolchildren and adolescents. CXXIII

Across Argentina, most patients who had eczema were quite young. 46 percent under 5 years old, 24 percent between 5 and 16 years old and 29 percent older than 17. As a result, the quality of life was extremely affected in 9.76 percent of the cases, severely affected in 29.27 percent, moderately affectated in 34.15 percent, and only a minority did not have their quality of life affected. Quality of life was most acute for children under 5, either in a severe way or in a small way, unlike the age groups over 6 years old, where their quality of life was moderately affected. CXXIII

Diagnosis and Care

In an unfortunate survey of care, Brazil is severely understaffed in terms of dermatology professionals. In a recent survey, Brazil was noted o have only 6,718 dermatologists for a population of 208 million, totaling nearly 3 dermatologists per 100,000 people. The despite this tragically low number, among the studied countries, this is on the higher end on a per-head basis. Around 59 percent of these dermatologists in Brazil are located in the south-east of the country, skewing the balance of regional access to treatment.

Quality of Life

Even among those who are treated, 76 percent of people are noncompliant and do not take their prescribed treatment. Of those who adhered to the treatment (24 percent), a 75 percent has had a great impact on their quality of life (p: 0.05).

Across Brazil, a majority of patients was affected from a moderate to a great manner and that 9.76 percent was extremely affected. It is inferred that when atopic is more severe, patients are more likely to have a greater adherence to the treatments, so strategies should be planned to improve adherence in those patients with moderate symptoms, which represent more than 4 percent of the total. CXXVI

Advocacy

Across Latin and South America, several organizations are quite active in dermatological research and advocacy. Across countries, the most prominent organization is Colegio Ibero Latino-Americano De Dermatologia (CILAD), or the Ibero Latin American College of Dermatology. Representing 23 Latin American countries, they host broad professional and patient education, including an annual congress. As its in-person congress, CILAD 2020, was delayed due to COVID, CILAD hosted its first virtual congress in November, reaching even a broader coalition on professionals and advocates.

Most of the larger countries in Latin and South America have their own active organizations surrounding dermatological issues. While atopic eczema never seems to be a focus of their events and campaigns, some have proven to develop effective awareness campaigns. For example, the Sociedade Brasilera de Dermatologia (SBD), Brazilian Society of Dermatology, officially opened a National Psoriasis Awareness Campaign in October 2020, providing detailed information for the broader public on this prevalent issue. CXXVIIII

Atopic Eczema & the Public Policy Environment

On the whole, there is limited engagement by the public policy community on the issue of atopic eczema. In The Lancet's Global Burden of Disease study, they highlighted eczema as having the highest disease burden of all skin diseases, measured in disability-adjusted-life-years (DALYS) – with skin conditions contributing to 1.79 percent of the global disease burden, eczema accounted for nearly a quarter of skin disease burden, followed by acne and psoriasis. CXXIX

Despite eczema being the greatest burden of skin diseases, the global community has said and done little. The World Health Organization (WHO) offers no dedicated resources on the topic, and its work on dermatological issues has historically been less comprehensive than its work on other diseases. Public awareness of the condition is limited, and research funding is lacking, with gaps in funding for evaluations and comparative effectiveness of treatments. However, recent movements within the WHO, such as the publication of a new set of guidelines to assist in screenings for skin diseases, suggest that the time is right for pushing for further conversations on atopic eczema at the global level.

World Health Organization: It can be argued that the World Health Organization (WHO) first began to seriously confront dermatological health conditions in the early 2000s, despite having provided prescribing information and essential drug recommendations on the subject for decades. In 2004, the International Foundation for Dermatology organized a workshop to discuss strategies for strengthening community dermatology programs in developing countries. Delegates called for simple diagnostic schemes to allow health-care staff to recognize people who were potentially infected with HIV from changes in their skin, better training for health-care staff on treatment of common skin conditions, and the promotion of existing examples of best practices to be scaled across other communities. cxxx Notably, the lack of a dedicated dermatology vertical within WHO resulted in a Medical Officer from WHO's Stop TB Department, Dr. Jose Figueroa-Munoz, to serve as the official WHO spokesperson and champion for the workshop and associated initiatives. cxxxi Professor Roderick J. Hay, a dermatologist and professor at the Queen's University Belfast in the United Kingdom, led the workshop and appears to continue to play an advocacy role in pushing for the advancement of dermatological issues within WHO. He also sits on the WHO's Committee on the Selection and Use of Essential Medicines, and has for many years.

Later, in 2005, the WHO published its guide to "Epidemiology and Management of Common Skin Diseases in Children in Developing Countries," which provided guidance for the treatment of atopic eczema and other types of eczema, along with information on the prevalence of those conditions within several clinic sites across low- and middle-income countries (LMICs). It would appear that this publication was developed in direct response to the work of the International Foundation for Dermatology workshop.

WHO-level conversations on dermatological issues in the pursuing years focused primarily on HIV-associated skin conditions. Broadly speaking, there have been two recent victories for the field of dermatology at the WHO-level: 1) the addition of scabies to the list of neglected tropical diseases and 2) the endorsement by the 67th World Health Assembly of psoriasis as a research and health-care quality-improvement priority. CXXXXIII

Recently, the WHO-level conversation on dermatological conditions has shifted away from HIV-associated skin conditions and towards the links between skin diseases and neglected tropical diseases. In 2017, the WHO announced its plans to promote an integrated strategy for skin-

related neglected tropical diseases; cxxxiii the pictorial training guide was published in June 2018. The guide aims to make it easier for health workers to identify the signs and symptoms of neglected tropical diseases of the skin and other common skin conditions, and includes guidance specific to atopic eczema and other types of eczema. It also includes persuasive data and a compelling call-to-action for scaling simple skin disease screenings, noting that skin diseases are among the most common of all human health afflictions and affect almost 900 million people in the world at any time. The WHO's Department of Control of Neglected Tropical Diseases is leading and championing the work, with Dr. Kingsley Asiedu, a Medical Officer in the Department, stating:

"This training guide is meant for front-line health workers who do not have thorough knowledge of common skin diseases and supports WHO's efforts to provide health for all and to everyone, everywhere. It is possible to identify the most common skin diseases as their treatment is simple, with many responding to medication that is widely available."

Most recently, in March 2019, the WHO held a meeting in Geneva on enhancing the detection of skin NTDs through integration, highlighting Buruli ulcer and other skin NTDs. The meeting was attended by over 200 participants from 34 countries. In a meeting summary, the WHO confirmed that the integrated approach to skin NTDs was satisfactory; however, "to accelerate integration [of skin NTD treatment], WHO should coordinate the preparation of guidelines to assist countries in standardizing the approach (implementation, data collection, reporting) to achieve comparable results from one country to another" and encourages national programs to collaborate with national dermatologist networks to get the greatest benefit. CXXXXX

While the Department of Control of Neglected Tropical Diseases is taking the most visible leadership role in addressing dermatological conditions within the WHO, the organization does also host a dedicated Topic Advisory Group for Dermatology^{cxxxvi} that consults on various cutaneous issues such as infections, inflammatory dermatoses, pediatric and genetic disorders of the skin, and disorders of cutaneous sensation among others. Current co-chairs are Robert Chalmers from the University of Manchester in the UK and Michael Weichenthal from the University of Keil in Germany.

Just as the WHO offers no dedicated dermatology department, nor does it host a specific body on autoimmune diseases. However, the WHO has published several reports along the topic of autoimmunity^{cxxxxvii} and offers specialized web content on chronic and rheumatic conditions.^{cxxxviii}

Pan America Health Organization (PAHO): Despite its association with the WHO, the Pan America Health Organization (PAHO) has paid minimal attention to the impact of atopic eczema and other types of dermatitis. The only PAHO effort in which skin conditions are a significant factor is in the context of newborn care. During a review of the Technical Advisory Group on ICMI (integrated management of childhood illness) in 2008, PAHO concluded that "Neonatal dermatology is broad and one of the principal pediatric consultations in the first days of life can be associated with severe systemic infections and even death." This includes atopic eczema in addition to other eczemas.

Dermatological problems during childhood may appear as a primary or secondary process in some systemic or genetic diseases. They currently constitute at least 5 percent of all pediatric consultations in outpatient clinics. The objective of the focus was to develop a generic protocol for diagnosis, management and treatment of dermatological problems in infants under two months old, which can help countries in the Americas address the problems at the level of health services and the community. While the Advisory Group mentioned atopic eczema as one

of the most prevalent dermatological issues facing newborns, the focus was distinguishing the different diagnoses and how they manifest, so they might be better identified in these countries.^{cxl}

Atopic eczema is also mentioned as a factor in the Baby Friendly Hospital Initiative, a PAHO and WHO collaboration in Latin America and the Caribbean. At these hospitals, there is reduced incidence of atopic eczema in infants and school-aged children. The benefit was noted in a 2001 trial held in Belarus to assess the effects of breastfeeding promotion on breastfeeding duration and exclusivity on gastrointestinal and respiratory infection and atopic eczema among infants. In this trial, prevalence of atopic eczema was reduced by nearly half for those who received breastfeeding promotion at a BFHI hospital, compared to the control group (3.3 percent vs. 6.3 percent). However, it should be noted that this was one limited study and no further research has been done associated practices at a BFHI hospital and a reduction in atopic eczema.

European Commission (EC): In September 2017, the EC approved dupilumab for use in adults with moderate to severe atopic eczema as the first new treatment for atopic eczema in nearly 25 years. In addition to addressing the symptoms of atopic eczema, including itching, dryness, and skin lesions, dupilumab addresses other kinds of type-2 inflammation, including asthma. The drug was later approved in 2019 for use in adolescents. Because of its wide success in atopic eczema and asthma, many pharma companies are exploring how dupilumab and similar inhibitors can be used in a broad range of type-2 inflammatory diseases. Striiv

In 2018, the EC developed a joint interdisciplinary project to address the treatment of atopic eczema for both adults and children. This project covered a wide array of topics including disease management, patient perspectives, and, perhaps most importantly, regarding atopic eczema as a systematic disease of both dermatological and immunological importance. The project reviewed several different therapy options including antimicrobial, antiviral, systematicanti-inflammatory, biological agents, and other systematic treatments. This study opened the door to multi-system treatments of atopic eczema with new therapies and new medications. CXIV

In 2019, the EC commissioned a study called BIOPMAP on the use of biomarkers to identify atopic eczema and psoriasis. The objective is to provide a taxonomic and predictive systems medicine model of atopic eczema and psoriasis based on clinical and molecular profiling to (i) identify determinants of clinically relevant outcomes (disease manifestation, progression, comorbidity development and treatment response) (ii) improve understanding on shared and distinct disease mechanism(s) and associated signatures, and their relative importance in patient subpopulations and (iii) deliver biomarkers that identify disease trajectories and treatment response for use in drug development and clinical practice. Following the creation of a data resource for researchers, the EC systematically analyzes the data using state-of-the-art methodologies in epidemiology, molecular profiling, skin biology and mathematical modelling to define disease and drug endotypes and how these interact with lifestyle and environmental factors. Though this study will be ongoing through 2024, this is a significant step in the funding for research on atopic eczema and other similar illnesses.

Asia-Pacific Economic Cooperation (APEC): In both their health and economic initiatives, APEC has not mentioned atopic eczema or any other skin diseases specifically. However, in 2018 the APEC LSIF Rare Disease Network announced the official launch of a Rare Disease Action Plan to provide APEC Economies with a framework for policy action to tackle the challenges of rare disease. CXIVIII While the APEC Action Plan on Rare Disease does not mention any rare diseases specifically, there are a number of rare skin diseases. CXIVIII CX

Policy in Africa, the Middle East, and South America: A few significant exclusions in this review are policies in Africa, the Middle East, and South America. This landscape covered a review of significant African, Middle Eastern, and South American organizations often involved in international policy. These include the African National Congress, African Union, African National Bank, Gulf Cooperation Council, Council of Arab Economic Unity, Arab Cooperation Council, the Development Bank of Latin America, and the G20.

While each of these areas show marked interest in improving healthcare in their respective regions, atopic eczema and other skin disorders are significantly left out. There may be several reasons for this. The first might be that there are deadlier health concerns in these regions including malaria, tuberculosis, and HIV/AIDS.^{cl} Another might be a lack of awareness and data on the subject, therefore lack of movement. There is also minimal advocacy engagement from the atopic eczema and skin disorder communities in these regions; however, there are several scientific societies doing research on the topic. This leads to the probability that if advocacy were connected to these scientific communities, there could be more of a policy movement in atopic eczema and other skin disorders.

Public Dialogue: Dermatology is not yet a subject of major public discussions. While global trade deals and indictments are currently dominating the international news and the public's attention, and drug prices are dominating the pharmaceutical conversation, we should not assume that dermatology will remain out of the public eye in perpetuity.

There has been little research into the comparative effectiveness of eczema treatments, limiting insights into the space. Recent trends in consumer spending point toward a desire for "natural", ecologically sound products, with attention paid toward avoiding what are perceived as harsh or unnecessary chemicals. While this strategy sometimes backfires for businesses, cii we can nevertheless take note of this particular trend and how it may impact dermatology in the near future. One study noted that compliance with pharmacological treatment and medical recommendations was high but patients' satisfaction with these recommendations was lower with respect to pharmacological treatment, indicating a non-compliant attitude and concerns about treatments.

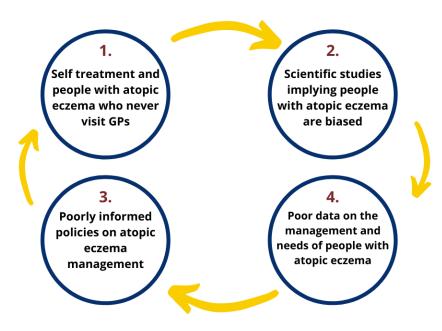
Limited Awareness: There has been increased effort by eczema and other dermatology-focused organizations to boost awareness on atopic eczema. Since the launch of World Atopic Eczema Day by GlobalSkin—held annually on September 14—there has been an increase in global awareness. Through the joint work by dermatology organizations around the world, advocates for skin health have rallied to empower a cross-sector and multinational community focused on improving the lives of people with eczema. Still in its early years, there is promise of growth in World Atopic Eczema Day.

However, despite advocacy efforts, for many organizations, diverse research priorities have taken precedence over funding for atopic eczema.

The National Eczema Association (NEA) considers funding a major issue and encourages members and concerned patients to discuss it with their legislators. Cliv Specifically, the NEA is calling for higher funding to the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS).

For its part, NIAMS lists no federally funded studies of eczema, and its most extensive scientific discussion of the ailment is more a literature overview than anything else, focusing on research done at American universities.clv In Europe, there have been efforts to build European guidelines for treatment of atopic eczema both in children

Figure 10: Consequences of Controversial Terminology



and adults, as shown in a two-part paper "Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis) in adults and children" published in the Journal of European Academy of Dermatology and Venereology in May 2018. Clivii This guideline was developed as a joint interdisciplinary European project, including physicians from all relevant disciplines as well as patients. It is a consensus-based guideline, taking available evidence from other guidelines, systematic reviews, and published studies into account. The paper focuses exclusively on the treatment of atopic eczema and tries to go around the still ongoing controversy about the terminology that is used in the diagnosis of atopic eczema (when is atopic eczema mild, severe, etc.), highlighting that the controversy has negative impacts on how atopic eczema patients are treated, as illustrated in **Figure 10.** It is also interesting to note that the research has received no funding, showing the lack of awareness by public institutions and policy makers.

Across Asia, awareness is far more limited. There are few advocacy organizations across the region to promote skin health, treatment, and research into skin diseases like atopic eczema. One organization of note is the Eczema Awareness Association of Australasia (EAA). In addition to providing support services for those with atopic eczema, they host several events throughout the year to promote eczema awareness at allergy and health-related expos. clviii

However, there are some areas of encouragement. In consultation with a panel of experts from eight countries across Asia (Malaysia, Singapore, Philippines, India, Cambodia, Vietnam, China, and Indonesia), the Asia Pacific Association of Allergy, Asthma, and Clinical Immunology (AAACI) and Asian Academy of Dermatology & Venerology (AADV) compiled a clinicians reference guide for management of atopic eczema in an approach based on disease severity. These guidelines discussed diagnosis, treatment, and education programs to promote awareness of atopic eczema management in conjunction with conventional therapies. In 2013, the Asian Consensus Group for Atopic Dermatitis (comprised of experts from Australia, Singapore, Indonesia, Malaysia, the Philippines, Taiwan, India, and China) also developed a set of consensus guidelines for management of atopic eczema.

Additionally, in the emergence of biologic treatment options, such as dupilumab, many countries across Europe, the U.S., and Asia have adopted these treatments and included them in their care. It has been approved in 60 countries thus far including Japan and China. This opens multiple opportunities for new biologic treatments, new approaches, and new methods to care for those with atopic eczema.

Rarely have individual countries posted guidelines until recently. In April 2020, Japan has just released guidelines for atopic eczema, that looks at atopic eczema from the perspective of evidence-based medicine consisting of three primary measures: (i) the use of topical corticosteroids and tacrolimus ointment as the main treatment for the inflammation; (ii) topical application of emollients to treat the cutaneous barrier dysfunction; and (iii) avoidance of apparent exacerbating factors, psychological counseling, and advice about daily life.clxi lt offers recommendations both for dermatologists and patients on treatment and prevention.

Rise of Autoimmune Awareness: As research into atopic eczema has increased, there has been greater interest and study into atopic eczema's connection with autoimmune and type-2 inflammatory conditions. Founded in 1997, the International Society of Systematic Auto-Inflammatory Diseases (ISSAID) has worked dutifully to promote knowledge, research, and guidelines around auto-inflammatory diseases, like atopic eczema. In their last biannual congress in 2019, dermatology was featured as a special topic, focusing on "The Skin as a Target in Auto-Inflammatory Diseases." clxiii

In Asia, the Asia Pacific Association of Allergy, Asthma, and Clinical Immunology (APAAACI), World Allergy Association, Japanese Society of Allergology (JSA), and the Asia Pacific Academy of Pediatric Allergy Respirology and Immunology (APAPARI) have partnered to create a congress that looks over all areas of systematic autoimmune diseases, with a significant portion of the agenda devoted to skin conditions and dermatitis.clxiii

Impressions and Opportunities: The WHO is not currently active on the topic of atopic eczema, nor does it offer any dedicated resources on the topic, beyond simple prescription guidelines. However, the recent move by the WHO to embrace widespread screenings for common skin diseases as a method of combatting neglected tropical diseases has promising implications and ancillary benefits for identifying and treating more cases of atopic eczema. Further, recent political victories around recognitions for scabies and psoriasis suggest that amplifying an issue such as atopic eczema to the WHO is possible. Based on the landscape of atopic eczema and dermatology issues within the WHO, soliciting the input and support of champions with a history of engagement with the WHO on dermatological issues, such as Dr. Roderick Hay, will likely be critical to any successful policy campaign.

Part II: Recommendations

As part of our efforts in building an effective advocacy roadmap for atopic eczema, we would like to present a series of promising recommendations based on GlobalSkin's current plans and activities and insights found within this landscape. Firstly, we will review a few significant information gaps in current research and study on atopic dermatitis. Secondly, we will provide a series of recommendations that address the current gaps and opportunities offered in this landscape. Our recommendations are threefold: promising strategies to consider, promising activities to activate, and promising stakeholders to engage.

Information Gaps

Focus on Western countries. Most current research on atopic eczema focuses exclusively on Western countries. This comes from the predominant early belief that eczema was a Western disease. However, some country-specific studies prove that atopic eczema may be just as prevalent in Asia, Africa, and South America. However, the studies in these geographic regions are few. Increased funding for non-Western studies is necessary to both understand the global extent of atopic eczema—which may be far greater than current numbers presume—and provide more information on its systemic nature.

Lack of research on related disorders. Despite the fact that atopic eczema has been associated with various other disorders (including respiratory, mental health, immunology, and rheumatology etc.) there has been little investigative research into the disease's relationship with these disorders. Though there has been a noted increase in interest in the past five years, doctors still don't have a comprehensive knowledge of related illnesses.

Lack of accessible information on inflammatory conditions. While research has now acknowledged atopic eczema as an inflammatory, systemic condition, not only as a skin disorder, the information provided to the public and to patient is muddled and highly insular. Information is not made accessible to patients, caregivers, and even primary care physicians in accessible ways. This prevents both awareness and connections to public policy; without properly articulated information around atopic eczema, policymakers cannot make muchneeded policy changes to ensure it is getting the funding and attention it needs.

Global scale studies nearly nonexistent. As far as current research has shown, there has been only one attempt at a global survey of atopic eczema. Clariv All other research has been country or region specific. Without a global count of atopic eczema, it is impossible to accurately estimate prevalence, severity, and related disorders, which means less effective diagnosis and treatment. Global Skin has begun to address this lack of data through the Global Research on Impact of Dermatological Diseases (GRIDD), which is gathering data at country, region, and local levels for a range of dermatological diseases.

Lack of international policy attention. This research revealed that the global health environment is an enormous opportunity to reimagine and redesign conventional assumptions about treatment and care in atopic eczema. There is a notable absence of awareness in the international health arena around this issue, especially regarding its impact in adult populations. This lack of understanding has resulted in a consequent lack of prioritization of the disease in national health plans and at international level. There is very little available on atopic eczema, with the disease mentioned sparingly by WHO. Without a strong narrative, it is difficult to place the disease in the international health landscape.

Promising Strategies

Highlight atopic eczema as systemic disease: While atopic eczema has long been recognized as a serious dermatological disease, it has not thoroughly been acknowledged as a systemic process. By categorizing atopic eczema has a type 2 inflammatory disease or an autoimmune disease, for example, GlobalSkin can highlight the broad impact atopic eczema has on global health, foster new alliances, and ultimately take a crucial first step in elevating atopic eczema's visibility.

Build a broad advocacy community: Because atopic eczema touches on so many health disciplines from immunology to rheumatology to mental health to respiratory, it is essential to start building that network so atopic eczema can be brought to high global attention. Building a broader community and developing a multi-lateral cooperation between specialists and patients can also help improve research, diagnosis, and treatment of the disease.

Investigate and engage the patient perspective: While there is significant research on atopic eczema as a disease state, there is little attention paid on how patients interact with and view the disease. By further developing tactics that engage with the patient community and including their perspective with current research, GlobalSkin can come to a better understanding of priorities to focus on and issues to address and bring to the broader public and policy platform.

Explore links to traditional medicine: Because of dermatology's long history of being ignored by the higher echelons of the medical community, many people with atopic eczema have turned to traditional medicine and self-treatment in order to ease their symptoms. However, traditional remedies have not been thoroughly investigated either in their use exclusive of or alongside prescribed medication. As an important area of treatment, GlobalSkin can explore these links further to encourage further research and better connections with patients.

Promising Activities

As GlobalSkin determines which strategies they would like to pursue, here are a few next steps aligned with GlobalSkin's current goals and planning (including the roadmap agreed in 2019).

Patient and Caregiver Surveys, including the GRIDD: Based on this landscape, we believe that the patient and caregiver surveys that GlobalSkin is currently undergoing is a necessary addition to current research. While the landscape is necessary to understand the current research, political, and stakeholder environment, it is important to capture the patient perspective which is key to building effective campaigns. We advise to support the launch of GRIDD with a thorough campaign in 2021, using this as a basis to support any of the above strategic policy actions.

Patient-Centred Best Practices Report: From the above Patient and Caregiver Surveys, we recommend that GlobalSkin compounds these results to create a report that highlights the unique perspectives of patients and caregivers, which aligns with current GlobalSkin milestones for 2021. Combining this with additional desk research and what we hear from specialists during the roundtable, GlobalSkin can use this report for both advocacy and informational distribution efforts and build that community support. A new report could for instance include care best practices from specific regions / countries that could inform optimal policy guidelines on atopic eczema.

Signature Initiatives - consider conceiving a signature initiative to shed a light on dermatology from a non-traditional stance: While engaging with policymakers at a global and national level is important to gaining international attention, particularly with the WHO in Q1 2022, you could support these efforts by conceiving a signature initiative to shed a spotlight on atopic eczema from a non-traditional standpoint. We believe that a Mayor's Initiative could lead the way as a creative example of fostering understanding and prioritization of atopic eczema. Similar to dementia-friendly cities, "skin-friendly cities" can highlight the opportunities and the challenges related to atopic eczema care services, and the negative effects a city environment can have on atopic eczema including pollution, housing situations, increased stress, and humidity. By having mayors pledge to counter-act these efforts in countries around the world, it can give atopic eczema advocacy greater momentum in international fora. Significant events in this initiative could align with World Atopic Eczema Day in 2021 or 2022 and would align with engagement with the WHO.

In-School Awareness. Should this be an interesting avenue from a patient population point of view, we suggest carrying out awareness raising campaigns in schools, using creative educational reference material for adolescents aimed to increase understanding of atopic eczema and reduce risk factors and stigma related to the condition.

Part III: Promising Stakeholders

The atopic eczema landscape is marked by the engagement of governments, advocates, patients/consumers, researchers, clinicians, and corporations. In order to elevate atopic eczema's position in the national and global policy realm, it is essential to build stakeholder partnerships not only with atopic eczema-focused stakeholders but a broader realm of systemic and complementary stakeholders. This includes engaging with autoimmune and inflammatory advocacy groups, mental health organizations, women's groups, and older adults' advocates. In this, atopic eczema can be brought to a broader platform of advocates, which are useful in partnership and alliance building.

PROFESSIONAL	SOCIETIES		
Organization	Description	Selected Activities and Other Highlights	Organizational Reach
African Society Of Dermatology And Venereology (ASDV)	Their aim is to improve the care of patients with skin and sexually transmitted disease who do not have access to specialist skills.	 Training local healthcare workers to identify and treat dermatological conditions. Carrying out a series of needs assessments and developing as well as evaluating treatment regimens and protocols for more general use in resource poor regions in Africa. Hosts annual congress. 	Africa
American Academy of Dermatology	As the largest professional society for dermatologists in the United States, the AAD serves over 20,000 members, including a growing number of international members.	Numerous resources on AD, including clinical guidelines and educational modules for practitioners, as well as educational resources for people living with the condition.	National, USA
Asia Dermatological Association	Incorporated on the 21th November 1986 in Hong Kong to promote the study of dermatology and promote, foster, develop and assist the dermatologists of all Asian countries, other medical and allied professions in the study of and the acquisition, dissemination and application of knowledge and information concerning dermatology.	Hosts the semi-annual Asia Dermatological Congress (last session held in 2018).	Asia
Colegio Ibero Latino- Americano De Dermatologia (CILAD)	The Ibero Latin American College of Dermatology (CILAD) is a non-profit organization that brings together more than 4,000 dermatologists as active	Hosts the Training Program for Latin American Resident Physicians in Dermatology (Latinaderm Excellence) and Medical and Educational Assistance Program (PRAMED).	Latin & South America

	members, from 23 Latin American countries.	 Hosts the Ibero-Latin American Congress of Dermatology, which is held every 2 years. The official publications of CILAD are: the electronic newsletter, InfoCILAD, which is sent weekly; and the ILA Medicine Cutaneous Journal, whose scientific content is developed by leading dermatologists from Ibero Latin America. 	
Dermatology Nurses Association	Professional society for over 2,000 dermatology nurses and nurse practitioners providing education, advocacy, and networking opportunities.	 Corporate members include Amgen, Lilly, Regeneron, Sanofi, Cutanea, Pfizer, AbbVie, and Celgene. The Association co-sponsored the <i>Understand AD</i> disease state awareness campaign. 	National, USA
European Academy of Dermatology and Venereology	Focuses on supporting the education of its 7,000 members and providing them with support for research opportunities.	 Convenes meetings, offers online courses, and publishes clinical guidelines and academic journals. Has conducted several public awareness campaigns, but none yet on AD. Has an AD task force – though its focus is notably unarticulated. 	Global with a European focus
International Society of Dermatology	Global society of over 2,000 clinicians and researchers interested in understanding and advancing the latest innovations in dermatological sciences.	 Publishes the <i>International Journal of Dermatology</i>, which covers clinical trials, education, pharmacology and more. Convenes an international congress every 5 years; the next one will be held in 2021. Partners with the International League of Dermatological Societies to organize activities around World Skin Health Day. 	Global
International League of Dermatological Societies	League of dermatologists' societies that promotes skin health around the world by fostering cooperation, knowledge sharing among dermatologists.	 Developed the International Foundation for Dermatology to support education, research, and resources need in underserved global populations. Hosts the World Congress of Dermatology. The last event was held in 2019 and the next event will be held in 2023 in Singapore. Hosts the ILDS World Skin Summit to act as a forum for sharing and discussion, enabling leaders in dermatology to consider and develop strategies to improve skin health at local, national, regional and global levels. The next 	Global

		Summit will be held in Lima, Peru in October 2021. In 2014, in partnership with the Global Coalition on Aging (GCOA) and the International Association of Geriatrics and Gerontology (IAGG)in 2014, the International League of Dermatological Societies released a consensus statement for a Life Course of Healthy Skin.	
Pan Arab League of Dermatologists	Society of professional dermatologists shedding light on science of Dermatology and Dermatologic Surgery and its importance for the society.	 Support of scientific research in the area of Dermatology & Dermatologic Surgery. Emphasis on the important role of the conferences held by the Arab Dermatological Societies. 	Middle East
Saudi Society of Dermatology and Dermatologic Surgery (SSDDS)	The Saudi Society of Dermatology and Dermatologic Surgery was Established in 1989, with community service is one of the society's main objectives. Voluntary work is an integral part of every growing community and the society aspires to aid Saudi Arabia's population and patients by offering an educational platform as a reference that will contribute to more awareness in all that's related to Dermatology.	Hosted and organized several national and international conferences. Every two years, an international conference is organized in one of the kingdom's main cities. In it, the latest developments and updates in dermatology and dermatologic surgery are reviewed.	Middle East
PATIENT SUPPO	RT & ADVOCACY ORGANI	ZATIONS	
Organization	Description	Insight	Organizational Reach
Allergy & Asthma Support Network	The mission of Allergy & Asthma Network is to end the needless death and suffering due to asthma, allergies and related conditions through outreach, education, advocacy and research.	 Hosts free monthly webinars for patients and care providers Organizes Allergy Asthma Day on Capitol Hill Offers continuing education programs for professionals 	USA

Coalition of Skin Diseases	Network of patient advocacy organizations that works to support research, foster patient and physician education, raise awareness, and build capacity of its member organizations.	 Has a strong record of engagement with the US government. Works closely with the NIH's National Institute of Arthritis and Musculoskeletal and Skin Diseases to coordinate research efforts. Meets annually with congress members and testifies before appropriations committee. 	National, USA
Eczema Association of Australasia (EAA)	Founded in January 1994, the Eczema Association of Australasia Inc (EAA) is a not-for-profit organisation that supports and educates eczema sufferers and carers, along with the wider community, in all aspects of eczema and its impact	 Quarterly newsletter – offering valuable tips and information about how to best manage and treat eczema, including an update on the newest treatments available. Social register – for people with eczema and their carers to make contact with others for the purpose of peer support. Consumer and Carer Voice Register – members of the EAA available for media interview and promotional testimonial. Health services directory – list of Australasia's leading health professionals including dermatologists and natural therapists. Education – a range of publications made available on the website including a reading list (clinical studies, national and international articles about the management and treatment of eczema). Support Services – access to people experienced in counselling and support of people with eczema and their carers. Promotion – awareness campaigns and events are organised throughout the year including Eczema Awareness Week and attendance at various allergy and health-related shows and expos. 	Asia, Australia
Eczema Society of Canada	ESC aims to improve the lives of Canadians living with eczema, through supporting patients, caregivers, and the medical community.	 Has a Seal of Assessment to verify eczema products that have gone under formal scientific review. Engaged in advocacy efforts to improve access to care. Provides a healthy variety of patient and HCP resources on eczema. 	Canada

European Federation of Allergy and Airways Diseases Patients' Associations	European alliance of over 30 allergy, asthma and chronic obstructive pulmonary disease (COPD) patients' associations representing 30 percent of European citizens currently living with these diseases. Founded in 1991 in Stockholm, Sweden, EFA currently has 43 members in 25 European countries.	 Strong engagement with the EU institutions and EU leaders. Runs the Secretariat of the European Parliament Interest Group on Allergy and Asthma with the European Academy of Allergy and Clinical Immunology (EAACI). Conducts advocacy activities and represents patients in EU-funded projects and represents the unified voice of patients at EU-level. Conducts capacity building projects for associations in its network. 	Global with a European focus
Global Allergies and Airways Patient Platform (GAAPP)	An international group of over 30 local and national asthma and allergy patient groups forming a network linking organizations with a common interest: the support for and improvement of the quality of life of people around the globe who have allergies and asthma.	• Developed the SECURE-AD Patients Registry to help understand how COVID- 19 specifically affects people with atopic dermatitis.	Global
National Eczema Association (NEA) MENTAL HEALT	The National Eczema Association (NEA) is a non- profit organization with a mission to improve the health and quality of life for individuals with eczema through research, support and education. TH GROUPS	 Developed Eczema Wise tracking app to help patients track their disease process. Hosts annual Eczema Expo Creates strong advocacy initiatives to support eczema awareness and access to care 	USA
Organization	Description	Insights	Organizational Reach
Anxiety and Depression Association of America	International nonprofit membership organization dedicated to the prevention, treatment, and cure of anxiety, depression, OCD, PTSD, and co-occurring disorders through education, practice, and research.	 The only multidisciplinary professional organization in mental health that engages the world's leading experts who focus on anxiety, depressive, obsessive-compulsive, and trauma-related disorders. Particularly active in educating the public on mental health issues. 	National, USA

Asia Australia Mental Health	Partners with leading local and international organizations for improved mental health in the Asia Pacific. Supports a growing program of work in China; large programs with partners in India, Japan, and the Pacific; with growing programs in Indonesia and the Sub-Mekong.	 The POST Program offers tailored clinical training fellowships in mental health for individual psychiatrists, nurses and allied health professionals from the Asia-Pacific region. Led by the University of Melbourne's Department of Psychiatry, AAMH works with leading research institutes in the Asian region to build capacity and develop collaborations across biological, applied and translational psychiatric research. 	Asia Pacific
The European Alliance for Mental Health	Informal coalition of European organizations aiming to promote mental health and well-being in the workplace, advocating for equal access to the labor market for all people experiencing mental illnesses and stimulating policy developments at the EU-level in these domains.	 Produces joint publications and research on mental health in the workplace. Collaborates with the European Commission on analytical reports and recommendations. Coordinates projects and calls for proposals at European level. Partners with likeminded organizations to host conferences on the theme of employment and mental health in the workplace. Shares knowledge, expertise and resources on mental health in the workplace. 	Global with a European focus

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		Heavy advocacy and research focus.	
		GAMIAN is part of many EU-funded projects for advocacy and research on mental health.	
Global Alliance of	European patient-group	November 1, 2018 marked the launch of the European Brain Council (EBC)- coordinated EU project The European Brain Research Area (EBRA).	
Mental Illness Advocacy Networks-Europe (GAMIAN)	representing the interests of persons affected by mental illness and advocating for their rights; members of the Alliance can be persons or organizations.	EBRA was designed to respond to the Horizon 2020 entitled "Coordinating European brain research and developing global initiatives", which called for the reduction of fragmentation and duplication of research efforts; GAMIAN is engaged but not formally a partner.	Global
		GAMIAN chairs The European Parliament Interest Group on Mental Health, Wellbeing and Brain Disorders.	
		Annual Convention and AGM taking place on 29th – 31st March 2019 in Bucharest, Romania.	
		Developed Charter 2020 with Parliament with nine principles on improving the mental health system in the country	
		Engages with the Department of Social Services to identify how health professionals can be better supported to assist consumers with psychosocial disability to access the National Disability Insurance Scheme (NDIS)	
Mental Health Australia	Educates the public about mental illness and works in changing the public's perception about people who are mentally ill to reduce	Created Embrace Multicultural Mental Health which provides a national focus on mental health and suicide prevention for people from culturally and linguistically diverse (CALD) backgrounds.	Australia, Global
	negative stereotypes about mental illness.	Engaged with the National Disability Insurance Agency to conduct consultations to inform the design of a tailored National Disability Insurance Scheme (NDIS) pathway to improve the experiences of people with psychosocial disability entering the Scheme.	
		Developed the National Register, a pool of 60 trained mental health consumer and carer representatives from across Australia, who work at the national level	

World Sleep Society	Association of societies and individuals from 76 countries. Its goals are to advance sleep health worldwide, by promoting and encouraging education, research and patient care throughout the world, particularly in those parts of the world where the practice of sleep medicine is less developed.	 to provide a strong consumer and carer voice in the mental health sector. Organizes the World Sleep Congress every year. It runs the Sleep Medicine Journal with the International Pediatric Sleep Association. Established training criteria for education on sleep medicine and guidelines for practitioners. It organizes World Sleep Day every year in March. 	Global
WOMEN'S H	EALTH & EMPOWERMEN	T ORGANIZATIONS	
Organization	Description	Insights	Organizational Reach
Asian Women for Health	Peer-led, community-based network dedicated to advancing Asian women's health and wellbeing through education, advocacy, and support. We are a diverse group of individuals working together across differences in age, ethnicity, language, sexual orientation, socioeconomic and educational levels, to address individual, community-wide and systemic barriers that affect Asian women and their loved ones. Hear our stories and support our journeys to healthier lives.	 Provides communities with critical access to free breast and cervical cancer workshops to deliver culturally and linguistically appropriate health education with an emphasis on preventative care. Connects women on important health issues, and giving voice to their personal journeys to become inspiring agents of change through a monthly AWFH podcast, "From Resilience to Radiance" (launched in January 2019). Builds online community on WeChat, a group for Chinese women living with breast cancer to share information and support, while reducing language barriers and time/space restrictions. Hosts the State of Asian Women's Health Conference, an annual conference that connects experts from different industries to learn about important healthcare challenges and disparities across racial, ethnic, and socioeconomic groups. Hosts Asian American Mental Health Forum that engages health practitioners, policymakers, researchers, and people with lived experience to combat stigmas 	Asia

European Women's Lobby	A Brussels-based European umbrella network of women's associations representing a total of more than 2000 organizations working to influence the	 and concerns related to mental health within Asian communities. Hosts many projects related to beauty standards and body image, though not specifically focused on skin. Undertakes projects in violence against 	Europe
	general public and European Institutions in support of women's human rights and equality between women and men.	women, women leadership, youth, migrants – health is integrated under these topics.	
AUTOIMMUNE I	DISEASE GROUPS		Organizational
Organization	Description	Insights	Reach
Asia Pacific Association of Allergy, Asthma & Clinical Immunology (APAAACI)	Regional Allergy organization of Asia. Its members consist of Asian societies which are representative of its allergy professionals in their respective geographical area.	 Hosts APAAACI Allergy Training School (APATS), targeted towards clinicians and fellows in training in the Asia Pacific region and other neighboring regions to develop their skills and knowledge base/ understanding and practical clinical aspects of allergic diseases. Co-hosts the JSA/WAO Joint Congress 2020 Conjoint APAAACI/APAPARI 2020 Publishes the Asia Pacific Allergy Journal 	Asia
International Society of Systematic Auto- Inflammatory Diseases (ISSAID)	Non-profit whose purpose is to promote knowledge of Systemic Auto-Inflammatory Diseases; stimulate research in these fields; inform the public in these fields through conferences and publications provide guidelines and standards for good clinical practice.	 Provides up to date information on research, working groups, and research collaboratives Offers up to date resources for patients, friends, and families Hosts the annual ISSAID Congress Developed a Summer School for young doctors and trainees to increase their education around auto-inflammatory diseases 	Global
World Allergy Organization	A United States-based international umbrella organization whose members consist of 99 regional and national allergology and clinical immunology societies from around the world.	 Organizes the World Allergy Congress every year and other international scientific conferences. Offers education programs and resources including a White Book on Allergy and online courses. 	Global

Diseases focus includes immunodeficiency, but not AD specifically.	
 Organizes the World Allergy Week – the meeting's 2018 theme was AD. 	

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