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POSITION STATEMENT

Atopic dermatitis: A global health perspective

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Abstract

The International Society of AD (ISAD) organized a roundtable on global aspects of AD at the WCD 2023 in Singapore. According to the Global Burden of Disease (GBD) consortium, at least 171 million individuals were affected with AD in 2019, corresponding to 2.23% of the world population, with age-standardized prevalence and incidence rates that were relatively stable from 1990 to 2019. Based on the panel experience, most AD cases are mild-to-moderate. Without parallel data on disease prevalence and severity, the GBD data are difficult to interpret in many regions. This gap is particularly important in countries with limited medical infrastructure, but indirect evidence suggests a significant burden of AD in low-and-medium resource settings, especially urban areas. The Singapore roundtable was an opportunity to compare experiences in World Bank category 1 (Madagascar and Mali), 3 (Brazil, China) and 4 (Australia, Germany, Qatar, USA, Singapore, Japan) countries. The panel concluded that current AD guidelines are not adapted for low resource settings and a more pragmatic approach, as developed by WHO for skin NTDs, would be advisable for minimal access to moisturizers and topical corticosteroids. The panel also recommended prioritizing prevention studies, regardless of the level of existing resources. For disease long-term control in World Bank category 3 and most category 4 countries, the main problem is not access to drugs for most mild-to-moderate cases, but rather poor compliance due to insufficient time at visits. Collaboration with WHO, patient advocacy groups and industry may promote global change, improve capacity training and fight current inequalities. Finally, optimizing management of AD and its comorbidities needs more action at the primary care level, because reaching specialist care is merely aspirational in most settings. Primary care empowerment with store and forward telemedicine and algorithms based on augmented intelligence is a future goal.

Since the first World Congress of Dermatology (WCD), held in 1889 in Paris during the World Exhibition with the grand opening of the Eiffel tower, the WCD has been a quinquennial—and now quadrennial—forum, in which debates reflect current major specialty issues. In 1889, one of the six main topics of the meeting was around the nosology of 'the lichen group'. This group encompassed several entities, including what we today call atopic dermatitis (AD) because of the long-lasting uncertain classification of chronic prurigo with prominent lichenification.[1,2]

Although the nosology and classification of chronic prurigo versus AD is still somewhat controversial, the epidemiology

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has evolved during the past three decades. Until the beginning of this millennium, AD was primarily perceived as a benign disease of children in high-income countries, correlating with increased hygiene and industrialization.[3] However, this misconception resulted, at least in part, from limited access to skin specialists in low-income settings, for example only one dermatologist for 1 or 2 million inhabitants in Sub-Saharan Africa[4]; a major hurdle for epidemiologic research of AD and related allergic diseases in those settings.[5] AD and asthma are now recognized to be as common in urban settings of low-income countries as in developed nations, with a high burden, regardless of patient age.[6–8]

Atopic dermatitis was again centre stage at the 25th WCD in Singapore. New drugs have become available in clinical practice since the last WCD (Milan 2019), with a large pipeline of new products in development.[9] Many studies, mostly sponsored by industry, have tried to delineate the burden of AD and associated allergic diseases, giving rise to public health concerns. Since 2017 alone, 536 studies have been published on the burden of AD (based on a PubMed search). In addition, climate changes are prone to change our exposome to allergens and pollutants, increasing the risk of allergies, and AD is considered as the main gateway to allergy.[10,11] Of note, in a global perspective, the new framework programme of the World Health Organization (WHO), which focuses its action on low resource settings, now considers prevalent non-communicable skin diseases, such as AD, as part of its strategy for skin health at the primary care level.[12] Paradoxically, AD is now paradigmatic for health inequalities in dermatology worldwide, with the introduction of high-cost biologics and innovative small molecules prioritized in high-income settings but with limited to no access elsewhere.

Within this context, the International Society of AD (ISAD) organized a roundtable on global aspects of AD, which was held at the WCD in Singapore. This report describes the major conclusions of that conference.

WHAT IS THE GLOBAL PREVALENCE AND BURDEN OF AD?

The Global Burden of Disease (GBD) consortium[13] accesses big data through representative population surveys, published prevalence investigations, health service visits, surveillance data, survey data and medical claims information for case detection. It estimates burden as disability-adjusted life years (DALYs) and crosses data with the development status of each country graded based on a socio-demographic index (SDI), a composite score based on the total fertility under age 25 years, average education in those over age 15 years and lag-distributed income per person. As recognized by the authors, this methodology is adapted for high-mid income countries but risks under-reporting disease burden in low-income settings with poor medical infrastructure. Despite this fact, this study shows that at least 171 million individuals were affected with AD in 2019, corresponding to 2.23% of the world population, with age-standardized prevalence and incidence rates that were relatively stable from 1990 to 2019. Both age-specific prevalence rates and total number of prevalence cases were higher for females in all age groups, with the difference being almost two-fold in young adulthood (ages 25–45 years). Contrary to asthma, the prevalence and DALYs rates of AD did not vary as drastically among countries and regions. DALYs were stable from 1990 to 2019 and the relationship between DALYs and SDI in AD was reversed, as compared to asthma. Specifically, higher SDI levels had higher DALY rates of AD in 1990–2019. Without good parallel data on disease severity, these data are difficult to interpret and may suggest instead that DALY rates are a proxy with limited value for burden assessment of AD in many countries. Several parts of the world are lacking studies that simultaneously assess point prevalence and overall severity. This gap is particularly important in countries with limited medical infrastructure, but data from tertiary care centres focusing on hospitalized severe cases highlight the significant burden of AD in low-and-medium resource settings, as well as the indirect evidence of increasing numbers of AD cases in urban areas.[4]

Those GBD prevalence data fit with the earlier global AD prevalence data based on the international study of asthma and allergies in childhood (ISAAC)[14,15] (Figure 1) showing a tendency to increasing AD prevalence in low-and-middle income countries over time, whereas AD seemed to be levelling or decreasing in some countries with previously high prevalence rates, suggesting a ceiling effect reached when adverse environmental conditions, probably related to industrialization and a Western lifestyle, lead to disease manifestation in predisposed individuals.[16] Confirmatory data were shown at the meeting concerning trends in prevalence according to region. For example, based on data from some countries from Africa and the Middle East, prevalence of AD doubled over a 7-year period.[17–20] In the GBD study, AD peaked as expected at younger ages, typically ages 5–9 years but age-standardized rates increased throughout adulthood.[13]

The population data presented at the ISAD Singapore meeting from China,[21] Singapore,[22] Japan,[23] Australia[24,25] and the United States[26] confirm the peak prevalence during childhood and show clearly that worldwide most AD cases are mild to moderate in severity, regardless of age group (Figure 2). Concerning prevalence geographic variations occur across some large countries where studies were conducted, for example in China inland—higher—versus north and east of China -lower-.[21] One of the major gaps in AD epidemiology is the limited data on morbidity and mortality for bacterial/viral superinfection. As an example, mortality due to AD in sub-Saharan Africa is unknown, suggesting underdiagnosis of severe bacterial superinfection.[27] Streptococcal glomerulonephritis was highlighted as a public health problem in a WHO report on pyoderma without data on underlying AD.[28] Eczema herpeticum was a cause of death in Western countries before the introduction of acyclovir[29] but there is surprisingly no report from low resource settings where the diagnosis the diagnosis is probably missed. This applies probably also for severe bacterial superinfection of AD.

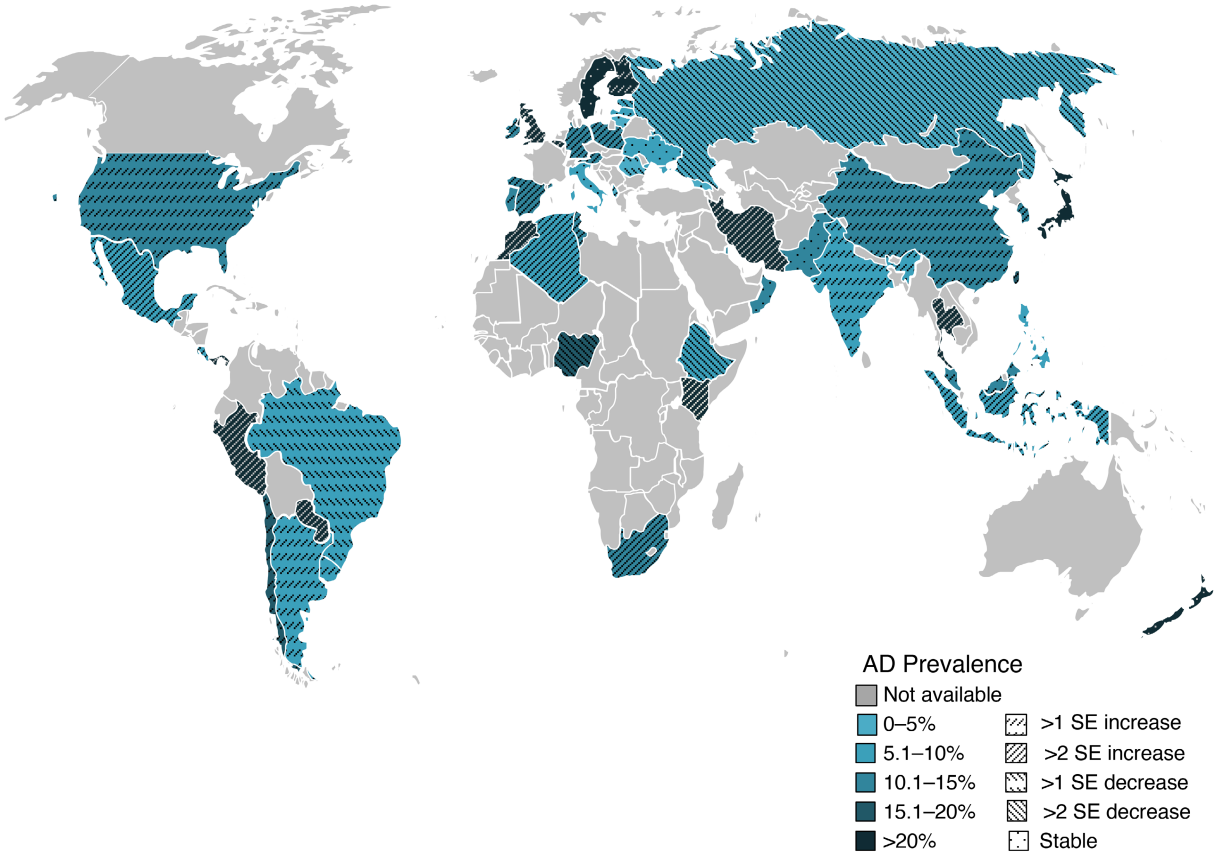

FIGURE 1 Lifetime prevalence of atopic dermatitis in children 13–14 years of age based on data from the International Study of Asthma and Allergies in Childhood (ISAAC) phase III (Ref. [15]), modified by Weidinger et al. (Ref. [16]), reproduced with permission. The ISAAC assessed the prevalence of AD symptoms at two time points; the first was based on reports collected between 1992 and 1998, and the second was based on reports dated between 1999 and 2004. The direction of change in the prevalence between the two time points is expressed as a multiple of the standard error (SE) of the average value at the first time point.

INCOME LEVEL SCALES AND ALLOCATION OF RESOURCES FOR AD MANAGEMENT

Most of the guidelines so far published for AD do not consider the feasibility of access to medicines. The recent update of AD guidelines[30] includes new medications such as abrocitinib or upadacitinib (JAK inhibitor) and tralokinumab (interleukin-13 inhibitor) for moderate-to-severe AD on top of the stepped care plan, drugs with supposed annual cost/effectiveness for high-income countries of around $30,000 (USD) per year.[31] Population data reveal that at least 1 billion persons live with less than 2 USD/day and another 3 billion with less than 8 USD/day. The World Bank Classification has adopted Rosling's categories, which describe the situation better than dichotomized classifications (rich poor/ developed-in development). Countries are classified each year in one of the four categories, low income/lower middle income/upper middle income/high income, based on the estimate of their gross national income (GNI) per capita for the previous calendar year. The EU and US guidelines are mostly written for the billion individuals who are in the fourth category of income (high income), according to Rosling (more than 32 USD/day) or the corresponding World Bank classification and living in countries with a health national insurance system, allowing the reimbursement of expensive drugs. Currently, the only accessible systemic drug on the WHO essential medicine list is methotrexate, listed for rheumatology.[32] Methotrexate is still on the EU guidelines, but with a light green colour, indicating a weak recommendation for use of an intervention (abrocitinib and tralokinumab are in dark green, indicating a strong recommendation). In general, level 1–2 income countries have limited resources for treating chronic diseases.[33]

The Singapore meeting was the occasion to compare the experience of countries in category 1 (Madagascar and Mali) and category 4 (Australia, Germany, Qatar, USA, Singapore, Japan) with also contributions of category 3 (Brazil, China). We will highlight two extreme settings on the income level/ life expectancy diagram.[34]

The example of Madagascar and Mali shows the importance of redistributing the limited resources to improve primary care using store and forward telemedicine[35] and capacity training of nurses and healthcare workers in dispensaries because of the very limited number of specialists

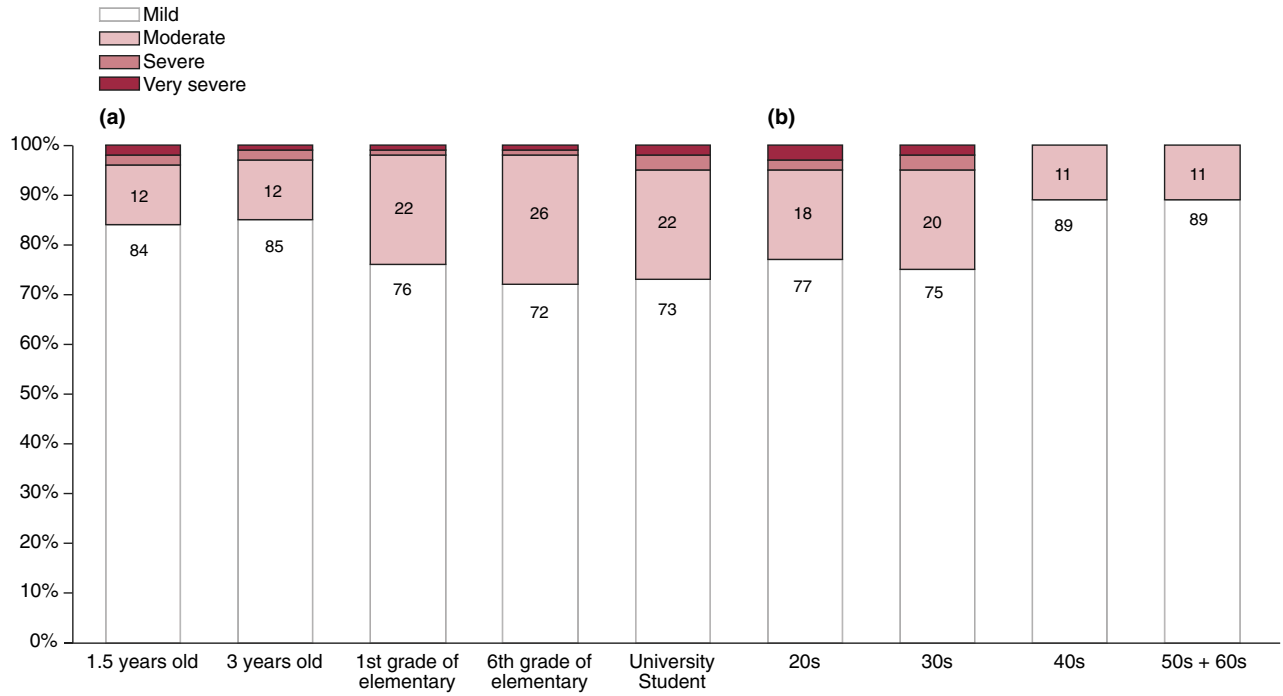

FIGURE 2 Physician-assessed severity of AD across age groups in Japan for survey years (a) 2000–2002 and (b) 2006–2008. *From*: Saeki et al. (Ref. [23]) reproduced with permission.

(Table 1). Out of the pocket expenses for moisturizers and topical corticosteroids to treat AD, the first two steps of the EU guidelines are already out of reach within the category 1, because of very low income and absence of reimbursement.

In contrast, patients in very high-income countries, for example in Qatar, which has a GDP of USD 250 billion per year and an income per person which averages USD 100,000 and where life expectancy exceeds 83 years, patients have access to all approved medications including biologics and systemic therapies. In ward patients are treated for free and the health care is substantially subsidized by the government. A specialized dermatology centre takes care of treatment and prevention for patients of all nationalities. Teledermatology has been established for patients in rural areas with access to drug delivery. Patients are educated about the hazardous potential side effects of some herbal drugs (used in rural areas in the Middle east and Africa to treat atopic eczema) since severe adverse events including erythroderma can be observed induced by herbal drugs.[17,36]

ORGANIZATION OF CARE FOR AD: A VERY HETEROGENEOUS APPROACH, BUT PRIMARY CARE IS CENTRAL AND UNDERTRAINED

The exchanges at the roundtable organized around regional specificities at the global level for AD showed a very large heterogeneity both between and within countries according to the organization of care. Primary/secondary and tertiary care is modulated by the number of specialists (dermatology, paediatrics and allergy) the national and individual insurance system and the weight of traditional or alternative medicines (Table 1).

Australia

Primary care physicians manage most adults and children with AD. They have been found to commonly convey misinformation and unintentional risk messages about AD therapies leading to non-adherence, to rarely use non-TCS topical therapies, but conversely, to use concerning amounts of oral steroid therapy.[25] Dermatologists are the primary specialists consulted, although allergists, paediatricians and dermatology nurse practitioners are also involved in care, depending on AD severity and comorbidities. Over 90% of dermatologists are in the capital cities. Nationally, about 25 dermatology trainees graduate annually.

Brazil

Although there is a universal public healthcare system, many patients resort to private specialists for AD treatment. Most cases are seen by dermatologists, followed by allergists and paediatricians. Most dermatologists are in large cities and in the southern region of the country. An unpublished recent AADA[37] (Brazilian AD Association https://www.aada.org.br/) survey showed that 62% of patients were seen by 3–10 doctors and 29% refer seeing more than 10 doctors to treat their AD.

TABLE 1 Dermatology specialists and insurance systems according to country and World Bank classification.

Country	World Bank category	Dermatologists (total number *n* by country)	Country population *N* (Millions) (ratio *n*/*N*)	National insurance system	Remarks
Australia	4	600	26.4 (22.7)	Yes	Restricted cover for new therapies
Brazil	3	9600	214 (44.8)	Yes	Private care more common for AD
China	3	Around 70,000	1300 (53.8)	Public insurance + private insurance, out of pocket at least 20%	
Germany	4	7000	83 (84.3)	Yes	
Japan	4	10,000	123 (81.3)	Yes	Government cover at least 70% of total costs
Madagascar	1	15	29 (0.5)	None, only for public and private workers	Private health insurance available
Mali	1	47	22 (2.1)	Yes	Private health insurance very limited
Qatar	4	262	2.8 (93.6)	Government (100% for GCC nationals, 80–90% for non-nationals); Insurance; Co-payments socially affordable Charities	Different sources; all in-patients treated without co-payment; out-patients no costs to 20% co-payment, if no coverage (e.g. tourists) treated at no costs.
Singapore	4	163	6 (27.2)	No	Mainly out of pocket expenses supplemented partially by personal private insurance or national medical savings scheme
United States	4	11,000	334 (33.0)	None other than publicly supported Medicaid for low-income families and Medicare ≥65 years old	Many restrictions to publicly funded programs; many with Medicare have supplemental private insurance

Note: World bank categories 1: low income, 2 lower middle income, 3 upper middle income, 4 high income.

China

Dermatologists oversee most AD patients, and in addition paediatric dermatologists in major cities. Other possibilities for managing paediatric AD include paediatricians, GPs and allergists. The huge patient population, limited time at clinical visits combined with topical steroid phobia contribute to impaired patient compliance, which significantly challenges physicians.

Germany

Adult AD patients are seen mainly by dermatologists, children by paediatricians and dermatologists, and refills of medication are frequently done by primary care doctors. The innovative drugs are mostly prescribed by dermatologists. While all licensed drugs for AD are reimbursed even if they are expensive, a dermatologist's honorarium for speaking with a patient is very low. There is minimal time for therapeutic patient education in a practice setting. Emollients are reimbursed only for children below 12 years of age, and innovative topical drugs have not been introduced successfully yet.[38]

Japan

In the first year, AD patients (about 10% of children) are mainly seen by paediatricians. Some young patients are also seen by paediatricians (for mild-to-moderate severity patients), but most AD patients (about 10% of adolescents, 5% of adults) are seen by primary care dermatologists, and moderate-to-severe cases in the academic tertiary Dermatology Departments. Primary care doctors are not usually involved for the care of AD. There are 10,000 dermatologists (about 3% of all physicians)/123 million Japanese population, and 350 new residents/year enter dermatology training.

Madagascar

The prevalence of Ad continues to increase both in children and in adults in Madagascar.[39] Most AD patients are seen by general practitioners or by paediatricians before visiting dermatologists. So, most of cases seen by dermatologists are moderate to severe. A clinical trial of methotrexate is ongoing. There are only 15 dermatologists and 8 residents for 28.9 million inhabitants.

Mali

Access to care and medications for AD in Mali is severely limited. Patients are primarily treated by dermatologists rather than paediatricians. At Bamako Hospital for Dermatology, a key referral centre, AD accounts for 3.6% of visits in their 2022 annual reports. Three out of four patients have moderate-to-severe cases. Systemic and topical steroids are widely available even at most peripheral level, but essential medications like cyclosporine and JAK inhibitors are notably absent, hindering treatment options for severe AD cases.

Qatar

In first year, AD patients (prevalence about 15% children) are mainly seen by paediatricians. Later (prevalence about 10% adolescents, 5% adults), mild cases seen by primary care dermatologists, moderate-to-severe cases in academic tertiary Dermatology Department. Cases with predominant comorbid allergic diseases (e.g. asthma) are also treated with Allergy Department or Psychiatry, for example. AD is second highest diagnosis of non-communicable diseases in primary and tertiary centre. All patients can be seen by specialist. The Dermatology Department runs a centre-of-excellence for AD and includes an American (ACGMEi)-accredited residency programme.

Singapore

Among adults, AD is typically seen at the primary care clinic or Dermatology outpatient clinic while among children, AD could be seen between paediatricians, primary care clinic or dermatology clinic.[40,41]

United States

Most children in the United States with AD are managed by primary care physicians, with only 18% seeing a dermatologist; however, 44% of adults are managed by a dermatologist. If seen by a specialist, the choice of dermatologist versus allergist is largely based on the absence or presence of a comorbid allergic disorder. There is greater utilization of dermatologist and allergist specialists with moderate-to-severe disease.[42] In the United States, the residency is a 3-year programme after internship and there are 500 coming out annually.

The importance of primary care for referring and follow-up was highlighted by the presentations and discussions. In many settings, irrespective of income level, the primary care level is undertrained in dermatology and has difficulties to communicate with the patients/families. A reinforcement of medical school training and continuous medical education would be welcome to address this issue. Training through referral of cases and SAF telemedicine is considered as a good approach for empowerment of GPs and other primary care workers in 1–2 income settings but also in level 3–4 countries.[35]

INEQUALITIES IN ACCESS TO CARE AND DRUGS FOR AD: A VARIED LANDSCAPE

Australia

TCS, TCIs and crisaborole are available although government subsidy is limited to TCS and pimecrolimus. Among newer systemic agents, dupilumab and upadacitinib are approved for AD, subsidized only in those aged over 12 years with severe disease. Baricitinib is approved only for adults, but without subsidy. Access to dermatologists and immunologists, required for these and other treatments (e.g. phototherapy), is very limited for those living in rural and remote regions. First Nations Peoples represent 16% and 45%[43] of inhabitants in remote and very remote areas, where they appear to have comparable AD prevalence[44] to non-Indigenous populations; they are, however, additionally burdened with endemic cutaneous staphylococcal and streptococcal infections in these areas, with infection rates among the highest in the world.[44,45]

Brazil

Accessibility to new systemic medications for AD is very limited. Dupilumab, baricitinib, upadacitinib and abrocitinib are approved by the Brazilian Health Regulatory Agency (Anvisa) but are not available in the Brazilian public health system. A current national survey organized the AADA and supported by national societies of dermatology, paediatrics and allergology, aimed at Identifying and addressing healthcare disparities in AD in Brazil, is underway.

China

Access to care and drugs is overall good. Social medical insurance and urban medical insurance can reimburse patients with different proportions of medical expenses. For topicals, topical corticosteroids (TCS), topical calcineurin inhibitors (TCI) and phosphodiesterase 4 inhibitors are available, but not yet topical JAK inhibitors. For severe or refractory AD, systemic corticosteroids, phototherapy and immunomodulators such cyclosporin and Tripterygium glycosides, based on a Chinese herb, are used. First- or second-generation antihistamines are occasionally used to control itch. MTX and cyclosporin are used in adult patients but rarely in paediatric patients due to safety concerns. In 2023, JAK inhibitors (upadacitinib for AD in

individuals older than12 years, abrocitinib for adults) and dupilumab for people with AD older than 6 months were both approved for the treatment of AD, till the year 2023. For AD in children and adults, traditional Chinese medicine remains popular.

Germany

The accessibility to new systemic medications for AD is excellent—dupilumab, tralokinumab, baricitinib, upadacitinib and abrocitinib are all approved and reimbursed. In contrast, new topical medications may or may not be marketed there because of the regulations for setting the price in the healthcare system.

Japan

Access to care and drugs is overall good (among new drugs, dupilumab, nemolizumab, tralokinumab, upadacitinb, abrocitinib, baricitinib, topical delgocitinib and topical difamilast are available) with a safety net reimbursing totally vulnerable individual. For drugs, monthly and annual caps vary by age and income. As an example, biologics/JAK inhibitors out of the pocket costs are 300 USD/month between 7 and 69 years, 200 USD between 70 and 74 years, 100 USD for more than 75 years. But in some areas, the cost for patients aged less of 15 or 18 years is fully covered.

Mali

Access to care and drugs for AD is very limited in Mali. Although the number of certified dermatologists has increased during the past decade, they are unequally distributed throughout the country, with almost 90% of them located in the capital city. At the Bamako Hospital for Dermatology a referral centre for skin diseases in Mali, 3.6% of visits are motivated by AD (internal 2022 annual report) and 3 in 4 patients have moderate-to-severe disease. Systemic and topical steroids are widely available, even at the most peripheral level. They are used in combination with antihistamines and moisturizers to control AD in children and young adults. Methotrexate is also available and reimbursed, just like steroids, by the national insurance system. However, the absence of medications like cyclosporine and JAK inhibitors is a significant limitation, as these newer, effective and potentially safer treatments are essential for treating severe cases of AD.

Madagascar

Access to care and drugs is overall poor, current standard of care for AD patients is limited to TCS, TCI and emollients, at the patient's own cost. Use of a local oil (coconut oil) as emollient treatment is common. Methotrexate is used in few severe cases; monitoring of patients treated by methotrexate remains a challenge in countries endemic for tuberculosis like Madagascar. Cyclosporine is very expensive. Crisaborole, topical JAK inhibitors and new systemic medications for AD (biologics and JAK inhibitors) are not available.

Singapore

Average total annual cost per child with AD was conservatively estimated at USD 7943 in a local study.[46] Those costs are substantially higher when compared with estimates from other countries for example the United States (USD 3288) and Italy (USD 1540). Overall costs for childhood AD were attributed to informal caregiving (46% of total costs) and out-of-pocket expenses (37%) rather than actual healthcare costs (17%). Dupilumab, baricitinib, upadacitinib and abrocitinib are approved by the Health Science Authority, Singapore and are available in most dermatology specialist clinics but they cost between USD 400 to USD 1500 per month and are at prohibitive cost for patients. Most of these expenses are bore out of pocket as there is no national insurance scheme in Singapore. There might be limited partial coverage by personal private insurance. There is also a national medical savings scheme (MediSave) that helps individuals set aside part of their monthly income for medical related expenses. However, this covers only hospitalizations, day surgery and certain outpatient expenses. Most expenses for outpatient care for AD are not covered by this scheme.

United States

Structural barriers cause delay or avoidance of care, more in Black/Hispanic versus White patients.[47] Among those barriers: transportation issues, childcare (or adult care) issues, taking time off work, living far from a medical centre, some of which are paradoxically common with level 1–2 countries. There is variable access to more costly medications, including biologics and JAK inhibitors, because of marked restrictions on access depending on insurance type (e.g. Medicaid) resulting in uncertainty at visit whether a patient will be reimbursed or not. Industry-sponsored programmes can be helpful but are challenging for busy practitioners and families with limited health literacy. Those programmes often come with commercial insurance only.

PHENOTYPIC/ENDOTYPIC VARIATIONS ACCORDING TO COUNTRY/REGION

The panel of the roundtable highlighted the difference between genetically homogeneous populations (Japan, China)

and more heterogeneous ones (Australia, Brazil, Qatar, Singapore, US). In general, AD is easy to diagnose based on simple criteria, with possible exceptions in elderly patients, in whom a more comprehensive workup is needed to exclude other conditions, for example cutaneous T-cell lymphoma. AD in the elderly is considered as a special clinical subtype in China.[48] Moreover, with the presence of multiple comorbidities associated with ageing, more attention is necessary for the handling of drugs, as recently highlighted for JAK inhibitors. Another issue is the applicability of criteria established in White populations to other populations with darker skin types, in whom recognizing skin inflammation is more challenging. The flexural distribution of AD, the objective cornerstone of the United Kingdom Working Party criteria,[49] is frequently lacking, reducing the sensitivity of those criteria in many affected individuals.[50,51]

Concerning endotype and phenotype correlation, mixed TH2-TH17 endotypes are prevalent in Japan, with psoriasiform clinical and histopathological phenotypes,[52] but also in Sub-Saharan Africa.[53,54] In the United States, endotype analysis of the skin and blood distinguishes AD in infants from adults with serial changes at advancing age.[55,56] Polar T-cell subsets in blood evolve from infancy to adulthood and differences are found between concomitant Th17 expression, more common in children, and Th1 expression (reduced until adulthood). Comparative international studies are needed to better identify differences in the phenotypes/endotypes which may help to better stratify patients and give earlier access to optimal treatments, which will be more effective, safer and more cost-effective for patients.

Loss-of-function filaggrin (FLG) mutations, first linked to ichthyosis vulgaris, were the first genetic endotype to be studied at the global level in the White and Asian populations, showing a clear association with early onset and severe AD phenotypes, as well as an association with food allergy and allergic asthma.[57] However, gaps of knowledge exist in several populations, in which an analogous genetic barrier impairment remains to be found. The FLG2 variants studied in Blacks in the United States do not explain convincingly the skin barrier dysfunction commonly found among black Sub-Saharan Africans.[58] Other genes such as Claudin-1 might be equally important in this setting.[59] In addition, the ichthyosis vulgaris and recessive X-linked ichthyotic phenotype are not well delineated in this population.[60] During evolution, skin pigmentation lightened progressively to a variable extent, as modern humans emigrated out of Africa, but extreme lightening occurred only in northern Europeans. This led to the hypothesis that FLG loss-of-function mutations could have evolved to sustain adequate vitamin D_3 status.[61] Climate adaptation and skin pigmentation were also highlighted for FLG loss of function for Asian skin in Japan, with FLG loss-of-function mutations detected in one study only in northern Japan (Hokkaido) with its cold and dry climate, but not in Ishigaki Island with its subtropical climate at the most southern latitude of Japan.[62]

PERSPECTIVES AND ACTIONS

The panel concluded that the current AD guidelines are not adapted for low resource settings and that a more pragmatic approach, as developed by WHO for skin NTDs, would be advisable. The panel highlighted the need to conduct epidemiological surveys with newly developed, standardized methodology, particularly focusing on geographical areas that lack data. The objective would be to identify factors associated with the rapid changes in prevalence of AD and related allergic disorders in different parts of the world to better target prevention, regardless of existing resources. To fill this gap, the Global Atopic Dermatitis Atlas (GADA) is an international collaboration between the International League of Dermatological Societies (ILDS), the International Eczema Council (IEC), the International Society of Atopic Dermatitis (ISAD), the European Taskforce for Atopic Dermatitis (ETFAD) and the Global Alliance of Dermatology Patient Organizations (IADPO/GlobalSkin). GADA plans three phases: a systematic review of current epidemiological data; reaching international consensus to standardize and improve epidemiological studies; and developing research tools for fieldwork. A recently published report summarizes all known aspects of AD and presents the disparities regarding the burden of disease and care, resulting in unmet needs.[63]

As highlighted during the meeting, the control of AD needs long-term management. In World Bank category 3 countries, such as China, and in most category 4 countries, the main problem is not access to drugs, but rather poor compliance due to insufficient time at visits for education about treatment. Better access to patient therapeutic education remains a challenge in most countries. In Brazil, the AADA has been instrumental to champion 9 AD patients' support groups across the country. These are monthly held meetings for AD patients and their families which aims to provide therapeutic patient education, improve treatment adherence and bridge the gap between patients and healthcare professionals An interesting project is to combine therapeutic education with prevention, as highlighted in China with its multi-disciplinary preventive prenatal education programme for allergic diseases during pregnancy (PAEPAD), which will track the incidence and outcome of allergic diseases in a birth cohort who are offspring of allergic parents.[64]

Collaboration of ISAD with WHO within the new skin NTDs framework programme is ongoing,[65] with: (i) an OpenWHO course, designed jointly with ISAD, for training for community health workers in Sub-Saharan Africa; (ii) the filing of an application for moisturizers adapted for low resources countries for inclusion in the next WHO essential medicines list of 2025; and (iii) improving capacity training through several other initiatives, including improving the WHO skin NTD app[66] with good photographs and access to assistance using artificial intelligence.

Collaboration with patient advocacy groups and industry is also on the agenda to change our vision on a global

scale and fight current inequalities. The predictable growing economy of level 1 and 2 countries offers a good business model to industry partners who market generic products at a reasonable price with many affected patients.[33] AD for most patients of mild-to-moderate severity can be treated as recommended by EU guidelines steps 1–2 with moisturizers and topical anti-inflammatory drugs. With the Accord initiative,[67] Pfizer has committed to provide its entire portfolio, including patented medicines and vaccines available in the United States or EU on a not-for-profit basis to the governments of 45 lower-income countries most vulnerable to healthcare inequalities to support patients through public health systems. This includes all 27 low-income countries plus 18 lower-middle-income countries that have moved from low-income status in the last 10 years, as defined by the World Bank. Other foundations are supporting research and education in Sub-Saharan Africa such as the Pierre Fabre Foundation,[68] the Leo Pharma Foundation[69] or Foundation Sanofi (S)[70] or promote AI in these regions such as the Passion project supported by the foundation Botnar[71] or logistical support such as help logistics.[72] Finally, the prevalence of AD, and its related allergic disorders and comorbidities needs more action at the primary care level, because reaching specialist care is merely aspirational in most settings, including in level 4 countries because of location, time commitments (e.g. work, childcare demands and distance to the specialist), and finances. Primary care empowerment is possible with new tools such as store and forward (SAF) telemedicine for non-urgent care. The rapid advances using augmented intelligence may further simplify the patient journey in the future.

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Data sharing is not applicable to this article as no new data were created or analyzed in this study.

ETHICS STATEMENT

Not applicable.

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