



Organization of Care in AD

Current Status of AD in Africa

G Todd
with apologies

ISAD Global 2019

Atopic dermatitis in sub-Saharan Africa

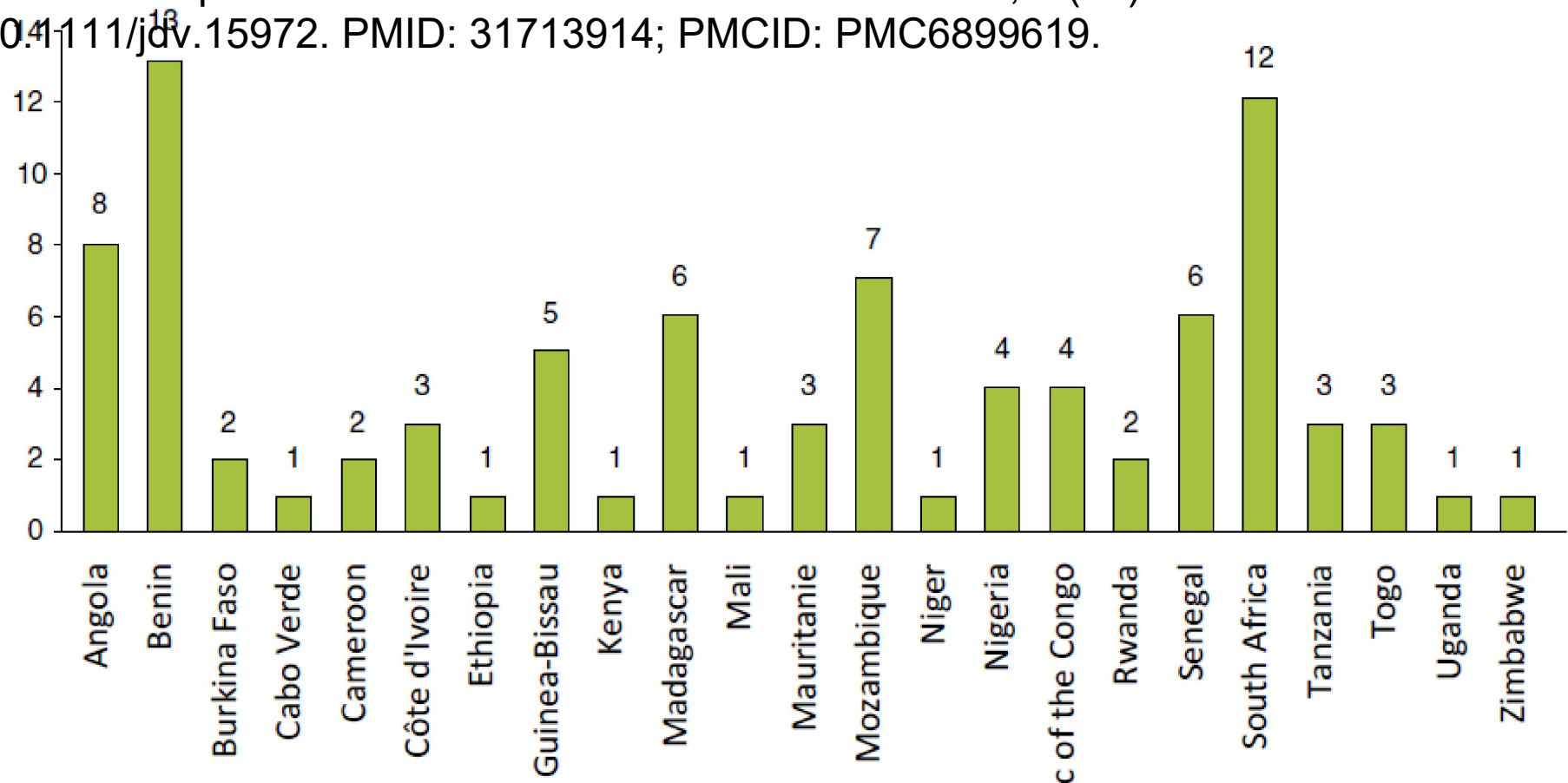
In order to advance the involvement of the ISAD in Africa, a meeting was organized in Geneva to identify research and intervention priorities in Africa and initiate African-led projects for AD (research and care) with the help of international health organizations as the main objectives.



Schmid-Grendelmeier P, Takaoka R, Ahogo KC, Belachew WA, Brown SJ, Correia JC, Correia M, Degboe B, Dorizy-Vuong V, Faye O, Fuller LC, Grando K, Hsu C, Kayitenkore K, Lunjani N, Ly F, Mahamadou G, Manuel RCF, Kebe Dia M, Masenga EJ, Muteba Baseke C, Ouedraogo AN, Rapelanoro Rabenja F, Su J, Teclessou JN, Todd G, Taieb A.

Position Statement on Atopic Dermatitis in Sub-Saharan Africa: current status and roadmap.

J Eur Acad Dermatol Venereol. 2019 Nov;33(11):2019-2028. doi: 10.1111/jdv.15972. PMID: 31713914; PMCID: PMC6899619.

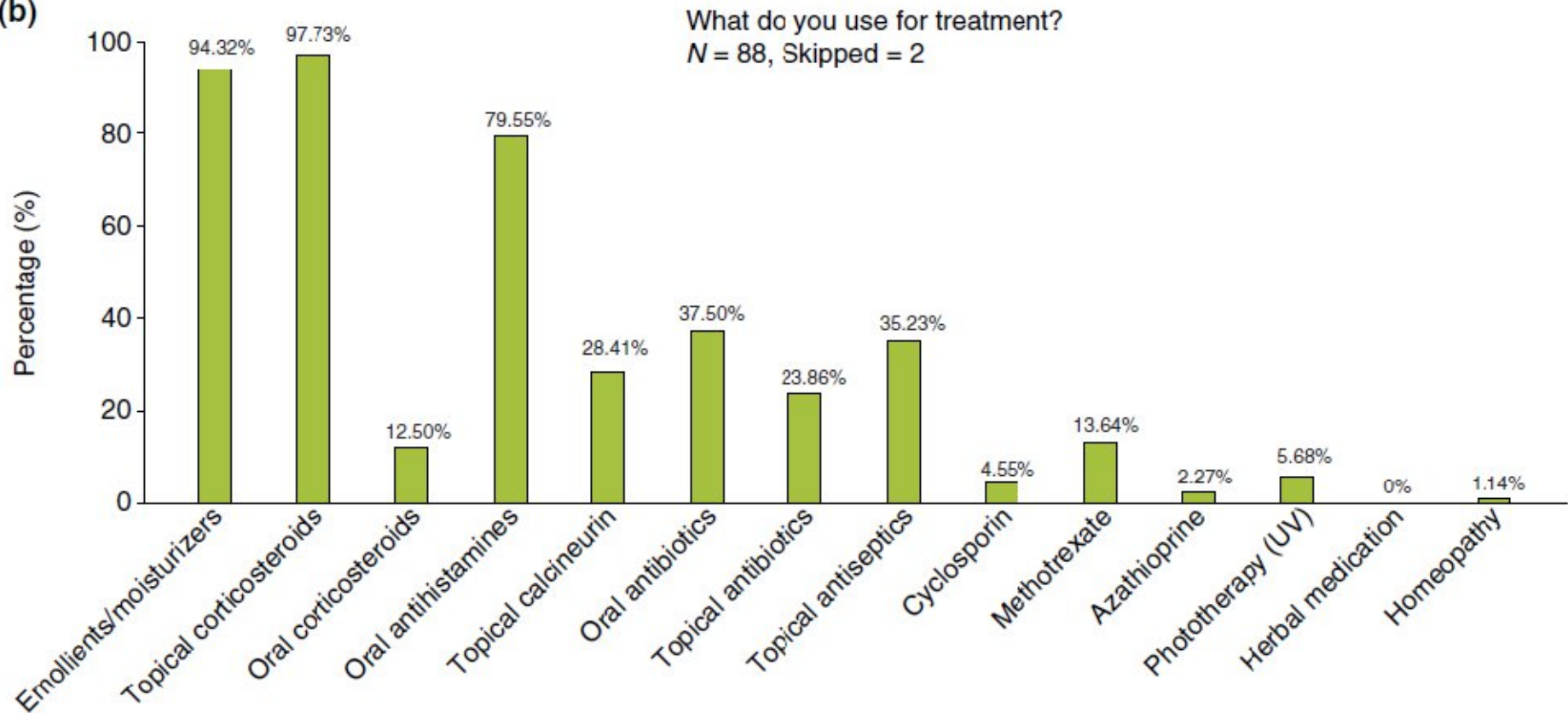


90 responses from 23 countries (52 Francophone, 23 Anglophone and 15 Lusophone); 85% response rate.

- 52 dermatologists (58%)
- 11 resident dermatologists (12%)
- 9 paediatricians
- 6 general practitioners (most with training in allergy)
- 2 allied health workers
- 1 patient serving as an ambulance paramedic (South Africa)

Democratic Republic of the Congo

(b)



- The majority (69.7%) were seeing **1–10 AD patients/week** in a regional/central centre.
- Most were using **emollients/moisturizers** and **topical corticosteroids**.
- Systemic therapies, **oral antihistamines**, **oral antibiotics** (secondary infections), **systemic corticosteroids** and **methotrexate**.
- Dermatology or allergy societies **guidelines** (South Africa, foreign countries) were used by roughly half of the practitioners

Problems related to AD that were considered common or very common in Africa

- lack of medication
- limited access to medical care
- lack of proper training of healthcare professionals
- lack of information about AD amongst the local population
- lack of information about AD amongst primary care workers

Lack of education materials and educational programs for patients with AD in most African countries.

Recommendations

Make specific pan African surveys

- Comparing recommended diagnostic and outcome criteria and tool relevance to Africa
- AD prevalence
- Patient desires/needs
- Education programmes for skin disease especially for primary care workers
- Emollients

Atopic eczema clinical
features in Africa

A systematic review and meta-analysis of the regional and age-related differences in atopic dermatitis clinical characteristics

Yew YW, Thyssen JP, Silverberg JI

J AM ACAD DERMATOL 2019, 80(2):391-401

101 studies, 28 countries, 7 Africa and Australia
Considerable heterogeneity of atopic dermatitis
78 different signs and symptoms identified
Notable differences by study region and age group.

The most prevalent AD features were pruritus, lichenification, and xerosis




Cohort of 1019 tertiary atopic eczema patients in Nigeria
Overall 70% had extensor involvement

	Flex	Ext	Flex	Ext
Knee	18%	37%	47%	16%
Wrist	17%	27%	11%	8%
Elbow	40%	39%	57%	17%

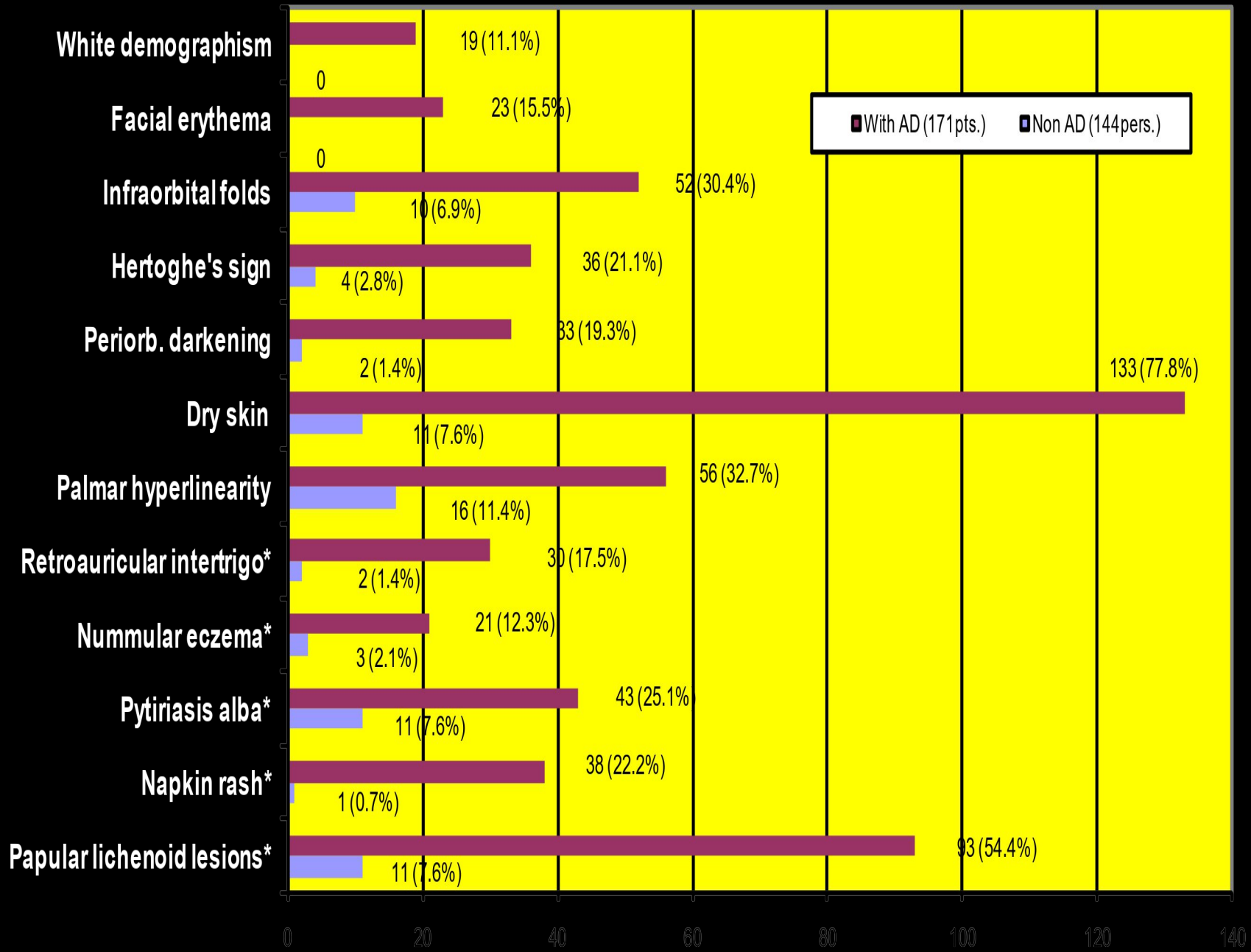
Table 5 Frequency of associated minor criteria observed in AD patients compared to controls

Skin condition (minor features)	AD patients (<i>n</i> = 1012)	Controls (<i>n</i> = 726)
Xerosis	719 (71%)	31 (4.3%)
Periorbital darkening	550 (54.3%)	0
Papular lichenoid lesions	547 (54.1%)	15 (2.1%)
Palmar hyperlinearity	524 (51.8%)	6 (0.8%)
Infraorbital folds	498 (49.2%)	9 (1.3%)
Itch on sweating	398 (39.3%)	12 (1.7%)
Ichthyosis	217 (21.4%)	0
Hand and foot eczema	204 (20.1%)	0
Shiny nails	204 (20.0%)	0
Keratitis pilaris	171 (16.7%)	0
Pytirisias alba	134 (13.1%)	0
Forehead lichenification	109 (10.7%)	0
Palmar erythema	87 (8.5%)	0
Retro/infra-auricular intertrigo	86 (8.4%)	0
Nipple eczema	76 (7.5%)	0
White dermographism	75 (7.4%)	0
Fissured heels	53 (5.2%)	5 (0.7%)
Nail pitting	44 (4.3%)	0
Cheilitis	41 (4.0%)	0
Knuckle dermatitis	39 (3.8%)	0
Pitted keratolysis	19 (1.7%)	0

The image shows two children's knees, one on the left and one on the right. Both knees exhibit a large, circular, red, and irritated skin lesion, characteristic of scabies. The lesions are raised and have a slightly scaly texture. The children's hands are visible, resting on their knees. The background is dark, and the children are wearing a yellow shirt and blue shorts.

	Flex	Ext
Knee	29%	31%
Wrist	16%	22%
Elbow	49%	33%

Cross-sectional survey in one village (Miembeni) in the Kilimanjaro region, Tanzania. The general population was 6953. There were 3427 children aged 0-15 years



Atopic eczema
diagnostic criteria
and scoring tools
relevance in Africa

Validation of ISAAC and UK criteria for atopic eczema in Ethiopian children

Cross sectional screening survey, children 1-5 years, Ethiopia
7915 interviewed, 506/590 cases, 438 controls

Prevalence 4.4% (ISAAC) 1.8% (UK criteria)

Validity of the ISAAC criteria

PPV 33% (95% CI 28.0-38.6)

NPV 91% (95% CI 88.4-93.8)



Validity of the UK criteria

PPV 56% (95% CI 10.4-28.9)

NPV 91% (95% CI 99.0-99.6)

Visible flexural eczema alone

PPV 57% (95% CI 48.2-65.9)

NPV 91% (95% CI 88.0-93.5)

Validation of the U.K. Working Party diagnostic criteria for atopic eczema in a Xhosa-speaking African population

D.A. Chalmers, G. Todd, N. Saxe, J.T. Milne, S. Tolosana, P.N. Ngcelwane, B.N. Hlaba, L.N. Mngomeni, T.G. Nonxuba and H.C. Williams*

Department of Dermatology, Faculty of Health Sciences, University of Cape Town, South Africa

*Centre of Evidence-Based Dermatology, Queen's Medical Centre, University of Nottingham, Nottingham, U.K.

Brit J Dermatol 2007

Prevalence 1.0% (dermatologist) 1.8% (VFE), 2.5% (UK)

Full UK criteria

Sensitivity 43.7% (95% CI 26.3-62.3)

Specificity 97.9% (97.3-98.4)

PPV 18.4% (95% CI 10.4-28.9)

NPV 99.4% (95% CI 99.0-99.6)

Visible flexural eczema alone

Sensitivity 81.2% (95% CI 63.5-92.7)

Specificity 99.0% (95% CI 98.6-99.3)

PPV 48.1% (95% CI 34.3-62.1)

NPV 99.8% (95% CI 99.5-99.9)



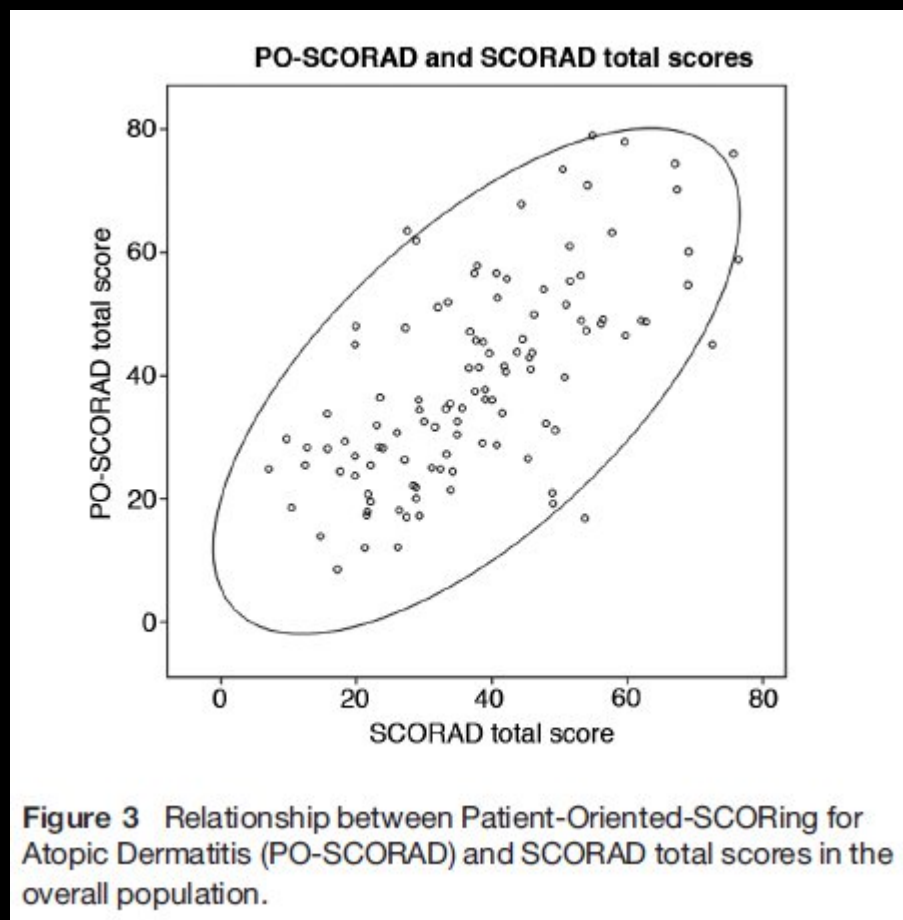
Validation of the Patient-Oriented SCORing for Atopic Dermatitis tool for black skin

JEADV 2019 DOI:

10.1111/jdv.15999

O. Faye,¹ A.P. Meledie N'Djong,² S. Diadie,³ S. Coniquet,⁴ P.A. Niamba,⁵ F. Atadokpede,⁶ P. Yao Yoboue,⁷ M. Thierno Dieng,³ A. Zkik,⁸ C. Castagne,⁸ F. Zumaglini,⁹ A. Delarue^{9,*}

Benin, Burkina Faso, Cameroon, Ivory Coast, Gabon, Mali, Senegal



What is atopic eczema
prevalence/incidence
in Africa?

Atopic eczema in Tanzania - clinical features

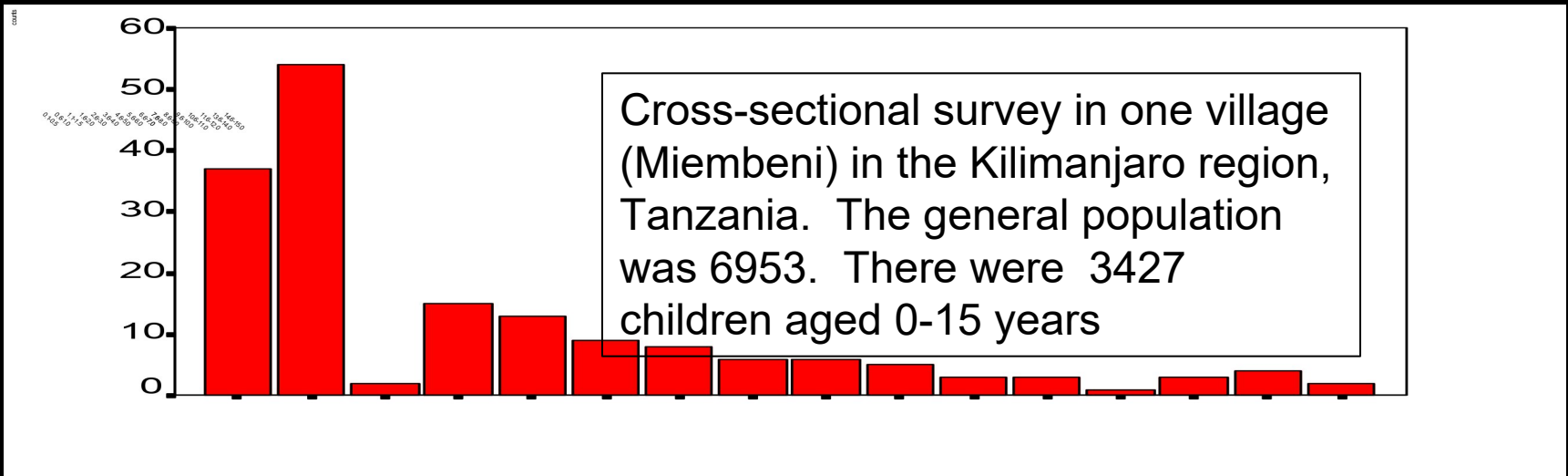
3427 children, 3268 took part, participation rate 92.2%

0 - 15 years, Female 94/171=55% Male 77/171=45%

Children with AD 171/3268 = 5.2%

Age 2 yrs. and below 106/171=62%

Age 2-15 65/171=38%



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Worldwide Variation of asthma, allergic rhinitis and atopic dermatitis

ISAAC Study I and III

	ISAAC Study I	ISAAC Study III
Ethiopia	11.4 (3.2-19.9)	19.0
Kenya	10.4 (9.4-11.4)	15.2 (14.9-15.5)
Nigeria (13-14yr)	17.7	7.7
Nigeria (6-7yr)	4.5	5.0
South Africa	8.3	13.3
Morocco	8.7 (5-12)	21.8 (20.5-23)
Algeria	5.2	6.5
Tunisia	8.0	9.4

AD is an emerging public health problem in Africa
Large variations within countries and centres in same country

Non-allergic factors (EPAAC)
Urban living

What are African
atopic eczema triggers
and risk factors?

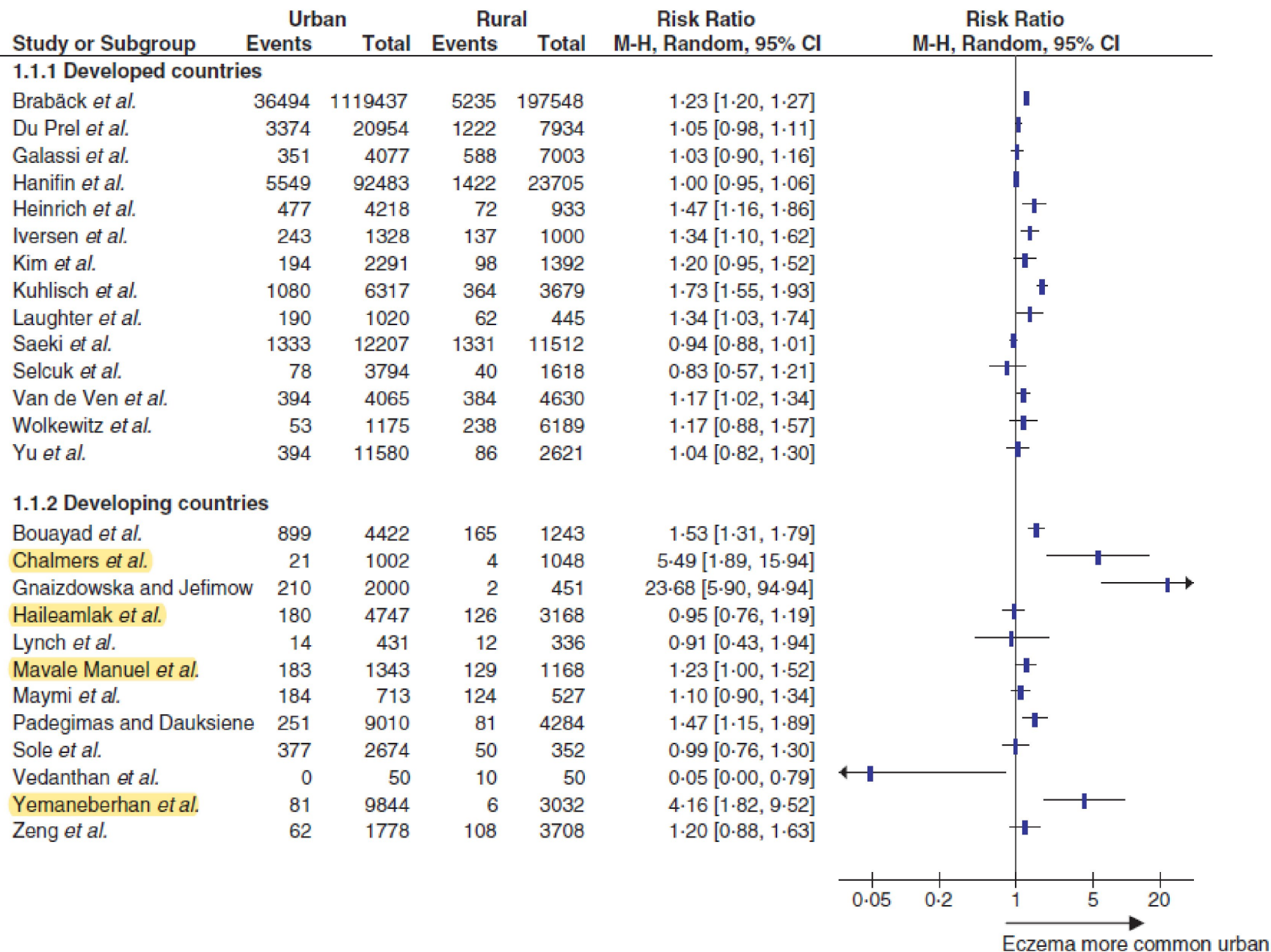


Table 5. Final logistic regression model

Risk factor	Odds ratio (95 % CI)	P-value	Effect on atopic dermatitis risk
Age			
0–19	1	<0.001	↑
20–39	1.49 (0.97–2.30)		
40–59	2.03 (1.24–3.35)		
60+	3.69 (2.10–6.49)		
Male sex	1.56 (1.12–2.16)	0.008	↑
Urban residence	3.74 (1.82–7.75)	<0.001	↑
Domestic kerosene use	2.32 (1.40–3.83)	0.001	↑
Indoor DDT use	0.35 (0.19–0.64)	0.001	↓
Lived elsewhere	2.08 (1.39–3.12)	<0.001	↑
Tigrean ethnic group	2.77 (1.46–5.25)	0.001	↑
Socio-economic status			
None of the below	1	0.46	
Radio (but none of below)	1.84 (0.79–4.33)		
Telephone			
(but none of below)	1.46 (0.73–2.94)		
TV (but no car)	1.67 (0.88–3.16)		
Car	1.13 (0.74–1.73)		
Wooden floor	6.12 (2.19–17.13)	0.008	↑
Parental smoking as a child	2.22 (1.35–3.63)	0.002	↑

CI, confidence interval.

Yemaneberhan H, Flohr C, Lewis SA, Bekele Z, Parry E, Williams HC, Britton J, Venn A.

Prevalence and associated factors of atopic dermatitis symptoms in rural and urban Ethiopia.

Clin Exp Allergy. 2004 May;34(5):779-85. doi:

10.1111/j.1365-

2222.2004.1946.x. PMID:

15144471.

Prospective study of 12876 participants 1996

General population of Jimma (80 000)

9844 urban, 3032 rural
0 to 120 years

Prevalence 1.2%
(ISSAC Questionnaire)
urban 1.5%, rural 0.3%

Haileamlak A, Dagoye D, Williams H, Venn AJ, Hubbard R, Britton J, Lewis SA.
Early life risk factors for atopic dermatitis in Ethiopian children.

J Allergy Clin Immunol. 2005 Feb;115(2):370-6. doi: 10.1016/j.jaci.2004.10.024. PMID: 15696097.

Prospective study of 7915 children
General population of Jimma
1-5 years, patients and controls
Prevalence 4.4% (ISAAC)

Parasites (Trichuris) (1.61, 95% CI 1.14-2.26)
Access to piped drinking water cf. river water
Fruit >1/week (2.29, 95% CI 1.40-3.77)
Malaria history (2.18, 95% CI 1.53-3.10)

Vaccination (DPT, polio)

Family size, crowding, breast feeding, income,
education, sensitization patterns, animals type
of dwelling etc

Current epidemiology of atopic dermatitis in south-eastern Nigeria.

Nnoruka EN.

Int J Dermatol. 2004 Oct;43(10):739-44. doi: 10.1111/j.1365-4632.2004.02360.x. PMID: 15485531.

Prospective study. 12013 patients, teaching hospital, 1998 to 2000
1019 patients with AD (8.5% prevalence) and 726 controls

Age: 4 weeks to 57 years

AD Onset: before 10 years 51.3%
 teens/early adulthood 25.6%
 after 21 years 24.5%

First degree family member with atopy 42% cf 13.3% controls
Weather (30.4%), heat intolerance, humidity, perspiration, grass
intolerance, thick woolen clothing, drug reactions, stress

Food intolerance, (egg, crayfish, artificial milk), 3.5%

Parasites in stool (n=100) 2% cf. 3%

HIV (n=67) 1.3%

TABLE 2 Filaggrin null mutations in individuals of African Ancestry

Race	Number studied	% with R501X	% with 2282del4	% with R2447X	% with S3247X	New (% affected)	Ethnic group	Ref.
Black	370 AD	3.2%	0.5%	0.7%	1.5%	N/A	African American	[43]
White	433 AD	13.8%	12.0%	1.4%	2.8%	N/A		
Black	60 AD	0	0	0	0	Q507X (1.7%) R3409X (1.7%) S3707X (1.7%)	African American	[44]
Black	187 AD/ADLII 152 C	3.2% Aa 0	3.2% Aa* 1.3%	N/A	N/A	None	African American	[42]
White	278 AD/ADFH 157 C	14% Aa, 1.4% aa 2.6% Aa	13.9% Aa, 1.8% aa 3.2% Aa					
Black	18 AD + IV 17 C	5.6%	11.1%	N/A	N/A	R826X (5.6%) R826X (5.6%)	African American	[60]
Black	12 AD 11 C	0	0	N/A	N/A	None	African American	[50]
White	17 AD 27 C	0	8.8% Aa 0					
Black	69 AD	0	0	0	0	N/A	South African amaXhosa	[45]
Black	103 AD 7 IV 103 C	0 0 0	0 0 0	0 0 0	0 0 0	632del2 (0.009%) 0 0	Lthiopian	[47]

Atopic dermatitis in diverse racial and ethnic groups —Variations in epidemiology, genetics, clinical presentation and treatment

Kaufman BP, Guttman-Yassky E, Alexis AF

Experimental Dermatology. 2018;27:340-357

Novel filaggrin mutation but no other loss-of-function variants found in Ethiopian patients with atopic dermatitis

M.C.G. Winge,* K.D. Bilcha,† A. Liedén,‡ D. Shibeshi,† A. Sandilands,§ C-F. Wahlgren,* W.H.I. McLean,§ M. Nordenskjöld‡ and M. Bradley*‡

*Dermatology Unit, Department of Medicine Solna, Karolinska Institutet, Karolinska University Hospital Solna, SE-171 76 Stockholm, Sweden

†Department of Dermatovenereology, Faculty of Medicine, Addis Ababa University, Addis Ababa, Ethiopia

‡Department of Molecular Medicine & Surgery and Center for Molecular Medicine, Karolinska Institutet, Karolinska University Hospital Solna, SE-171 76 Stockholm, Sweden

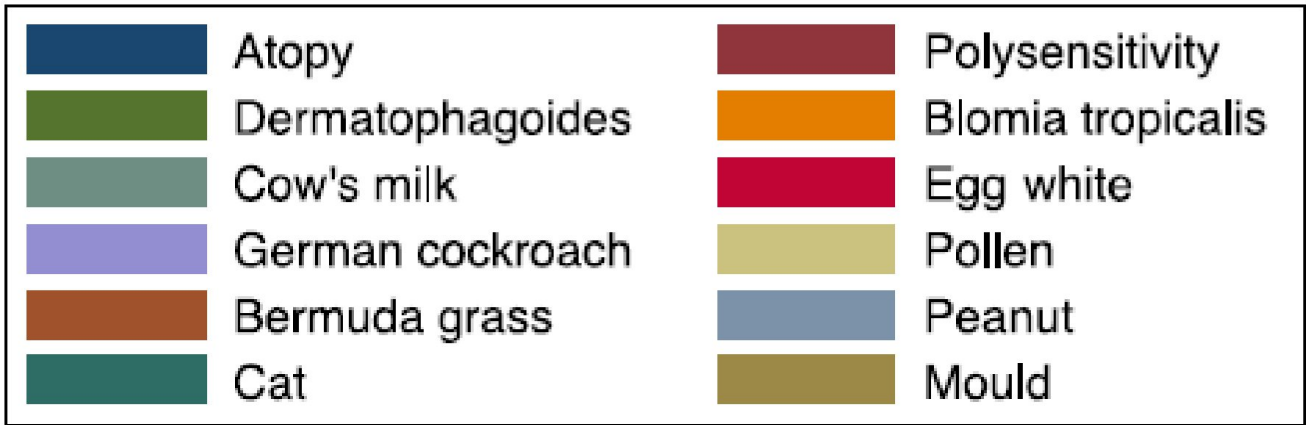
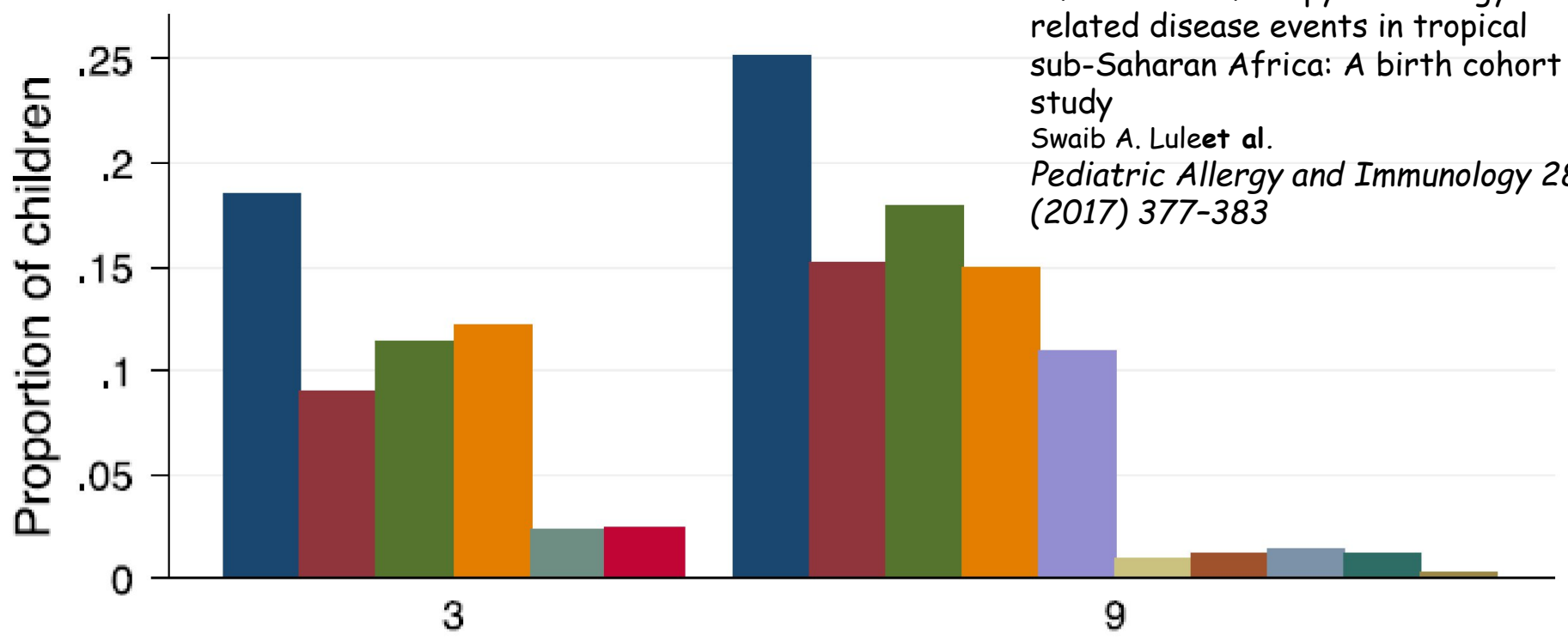
§Epithelial Genetics Group, Human Genetics Unit, Division of Pathology and Neuroscience, University of Dundee, Ninewells Hospital and Medical School, Dundee DD1 5EH, U.K.

The **tight junction gene Claudin-1** is associated with atopic dermatitis among Ethiopians

S. Asad, M.C.G. Winge, C.-F. Wahlgren, K.D. Bilcha, M. Nordenskjöld, F. Taylan, M. Bradley

JEADV 2016, 30, 1939-1941

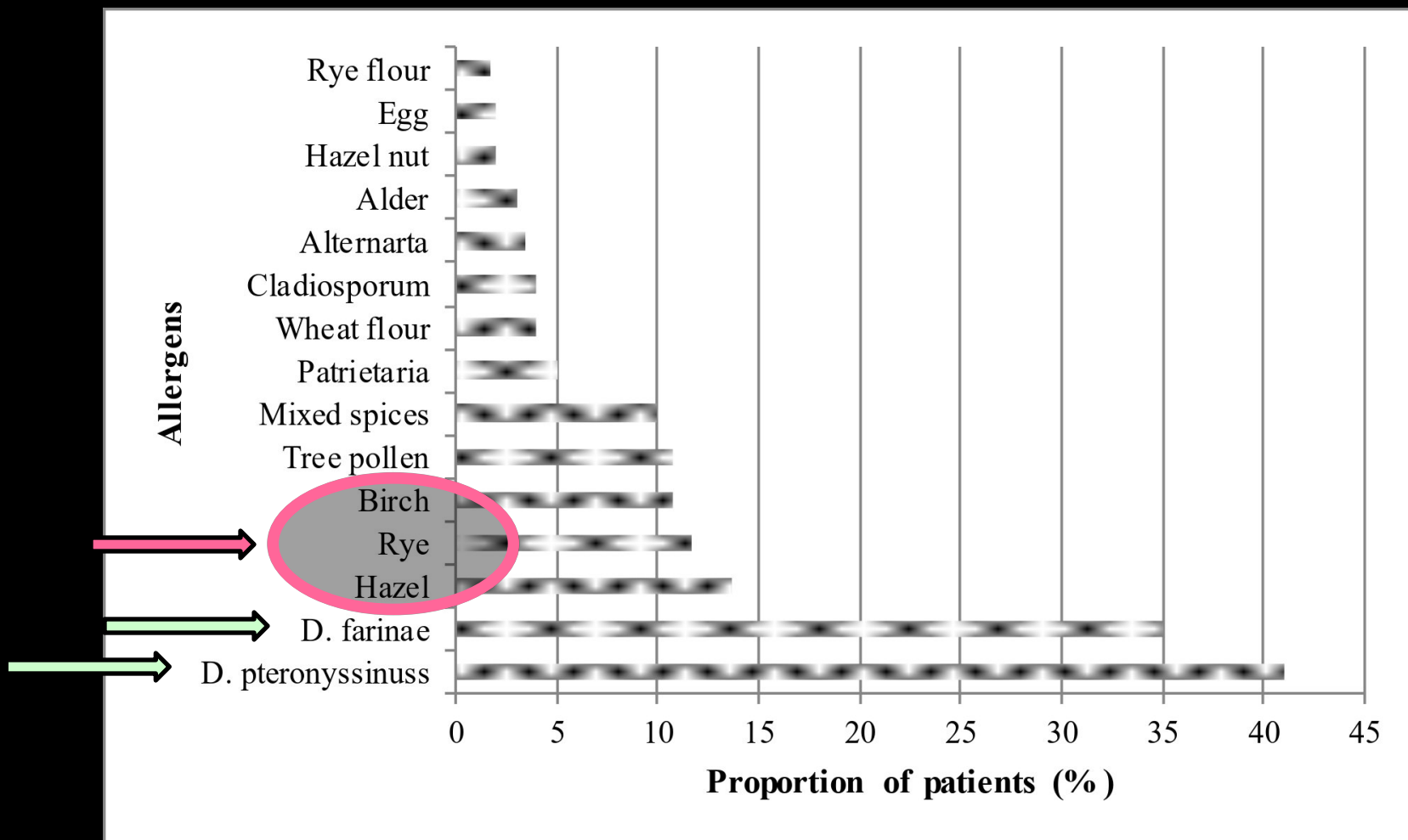
Life-course of atopy and allergy-related disease events in tropical sub-Saharan Africa: A birth cohort study
 Swaib A. Lule et al.
Pediatric Allergy and Immunology 28 (2017) 377-383



2345 live-born children, 1214 (52%) were seen at 9 years.

SENSITIZATION PROFILE ON ALLERGENS OF ADULT PATIENTS HAVING ATOPIC AND NON-ATOPIC DIATHESIS ATTENDING KCMC, NORTHERN TANZANIA

JULIETH K. KABAGIRE



Allergen

Prevalence % (n)

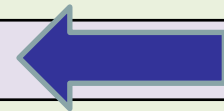
Cases

Controls

(N=76)

(N=148)

nDer p 1	79 (60)	7 (10)
nDer p 2	74 (56)	7 (10)
nDer f 1	78 (59)	7 (10)
rDer f 2	70 (53)	7 (10)
rEur m 2	62 (47)	4 (6)
rPhl p 1	43 (33)	4 (6)
nCyn d 1	43 (33)	5 (7)
nMus m 1	39 (30)	0 (0)
nPhl p 4	30 (23)	3 (4)
nGal d 1	26 (20)	0 (0)
nAra h 2	25 (19)	0 (0)
rPhl p 2	20 (15)	2 (3)
nPla a 2	20 (15)	2 (3)



Analysis of the sensitization profile towards allergens in central Africa.

Westritschnig K, Sibanda E, Thomas W, Auer H, Aspöck H, Pittner G, et al.

Clin Exp Allergy. 2003 Jan 1;33(1):22-7

Table 3. Origin, characteristics and IgE recognition frequency of purified allergens from timothy grass, birch pollen and house dust mites. The table displays allergen sources, allergen names (n, natural; r, recombinant), molecular weights (MW) and biological functions of the allergens. The IgE recognition frequency determined in central Europe (Austria) was compared with that found for the patients from Zimbabwe

Allergen source	Allergen	MW (kDa)	Biological function	Frequency of IgE recognition Austria (%)	Frequency of IgE recognition Zimbabwe (%)
<i>Phleum pratense</i> (timothy grass)	rPhl p 1	26.1	Similar to expansins	96	80
	rPhl p 2	10.7	Unknown	68	0
	nPhl p 4	55	Unknown	84	92
	rPhl p 5a	31	Ribonuclease (putative)	100	27
	rPhl p 6	11.8	P-particle associated	52	15
	rPhl p 7	8.6	Calcium-binding	8	0
	rPhl p 12	14	Actin-binding (profilin)	24	7
<i>Betula verrucosa</i> (birch)	rBet v 1	17.4	IPR-protein	95	0
	rBet v 2	14	Actin-binding (profilin)	10	100
<i>Dermatophagoides pteronyssinus</i> (house dust mite)	rDer p 2	14.1	Unknown	80	70
	rDer p 5	14	Unknown	15	45
	rDer p 7	23.7	Unknown	0	35
	rDer p 10	36	Tropomyosin	10	55

Sensitization profiles of 650 allergy patients

Allergen profiles in Africans differed from Europeans

What about therapies
and their relevance to
African patients?

EDL - Skin conditions

amoxicillin

aqueous cream

benzathine penicillin

6% benzoic acid 3% salicylic acid

5% benzoyl peroxide

25% benzyl benzoate

calamine lotion

chlorpheniramine

clotrimazole

doxycycline

emulsifying ointment

erythromycin

ethyl chloride

0.5% gentian violet

flucloxacillin

griseofulvin

1% hydrocortisone

2% miconazole

monosulfiram

nystatin

1% & 5% permethrin

polyvidone iodine

selenium sulphide

zinc oxide

TABLE 1 Reviewed publications

Countries represented	Organization or author affiliation	Publication
Canada	Eczema Society of Canada	Atopic Dermatitis: A Practical Guide to Management
Germany	AWMF: Association of the Medical Societies in Germany	S2k guideline on diagnosis and treatment of atopic dermatitis—short version
Italy	Italian Society of Pediatric Dermatology, Italian Society of Pediatric Allergology and Immunology	Consensus Conference on Clinical Management of pediatric atopic dermatitis
Japan	Japanese Dermatological Association	Clinical Practice Guidelines for the Management of Atopic Dermatitis
Korea	Dept. of Dermatology, Gachon University Gil Medical Center	Consensus Guidelines for the Treatment of Atopic Dermatitis in Korea: Parts I and II
Poland	Dermatological Section, Polish Society of Allergology, and the Allergology Section, Polish Society of Dermatology	Atopic dermatitis: current treatment guidelines. Statement of the experts of the Dermatological Section, Polish Society of Allergology, and the Allergology Section, Polish Society of Dermatology
Serbia	The Serbian Association of Dermatologists	National Guidelines for the Treatment of Atopic Dermatitis
Singapore	Dept. of Dermatology, Changi General Hospital, Singapore	Guidelines for the management of Atopic Dermatitis in Singapore
South Africa	Dermatological Society of South Africa	Management of atopic dermatitis in adolescents and adults in South Africa
Taiwan	Taiwanese Dermatological Association	Taiwanese Dermatological Association consensus for the management of atopic dermatitis
UK	National Collaborating Centre for Women's and Children's Health	Atopic eczema in children: management of atopic dermatitis in children from birth up to the age of 12 y
U.S.A.	American Academy of Dermatology	Guidelines of care for the management of atopic dermatitis: Sections I-IV
Asia-Pacific; Australia, Hong Kong, India, Indonesia, Malaysia, the Philippines, Singapore, and Taiwan	Japanese Dermatological Association—An Asia-Pacific Perspective	Consensus guidelines for the management of atopic dermatitis: An Asia-Pacific perspective
Europe: Germany, Spain, Denmark, Italy, the Netherlands, Croatia, Switzerland, Austria, Hungary, Poland, and France	European Academy of Dermatology and Venereology	Guidelines for treatment of atopic eczema (atopic dermatitis): Parts I and II

Atopic dermatitis in diverse racial and ethnic groups — Variations in epidemiology, genetics, clinical presentation and treatment

Kaufman BP, Guttman-Yassky E, Alexis AF

Experimental Dermatology. 2018;27:340-357

A thorough understanding of the unique genetic, clinical and molecular features of AD across a broad range of racial/ethnic AD subtypes is critical as we care for an increasingly multinational patient population.

- Under representation of some races in clinical trials as well as lack of subset analyses by race
- Of AD clinical trials published between 2000 and 2009, only 59.5% of studies included race and ethnicity as baseline demographic information
- The majority of patients included were White (62.1%), followed by 18.0% Black, 6.9% Asian and 2.0% Hispanic.
- Only 10.3% of studies commented on race or ethnicity in the interpretation of results, making it difficult to extrapolate the results to other ethnic groups
- Crisaborole, pimecrolimus, topical steroids, phototherapy

African Journals Online (AJOL)

African Journals OnLine (AJOL) is the world's largest online library of peer-reviewed, African-published scholarly journals

- AJOL hosts **523 journals**, including **253 open access journals**.
- The site has 13 633 Issues containing 163 024 Abstracts.
- **32 African countries are represented**

Historically, scholarly information has flowed from North to South and from West to East. It has also been difficult for African researchers to access the work of other African academics. In partnership with hundreds of journals from all over the continent, AJOL works to change this, so that **African-origin research output is available to Africans and to the rest of the world.**

<https://www.ajol.info/>

What about education
and training in Africa?

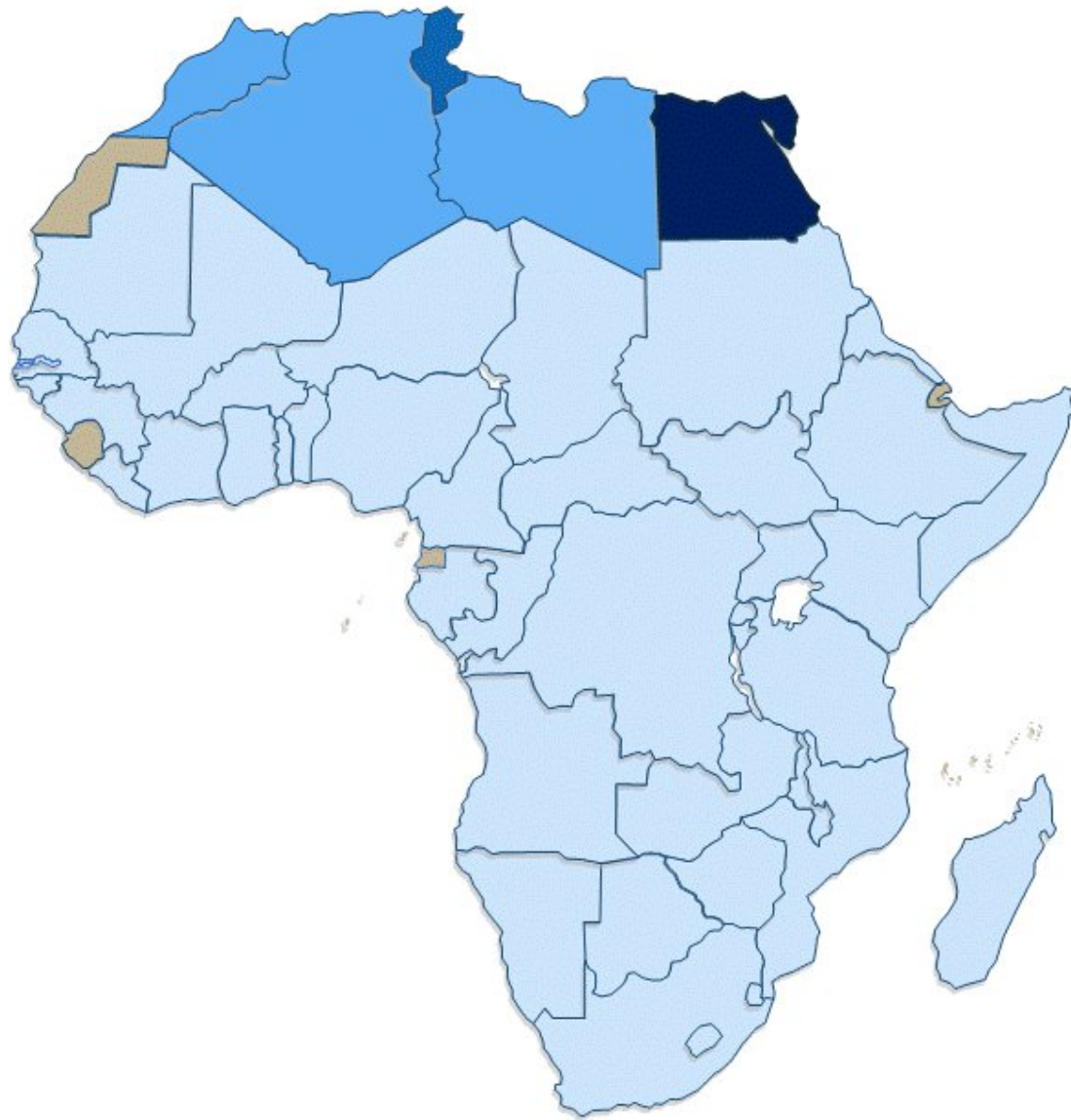
Dermatology Training in Africa: Successes and Challenges.

Mosam A, Todd G.

Dermatol Clin. 2021 Jan;39(1):57-71.

doi: 10.1016/j.det.2020.08.006. PMID: 33228862.

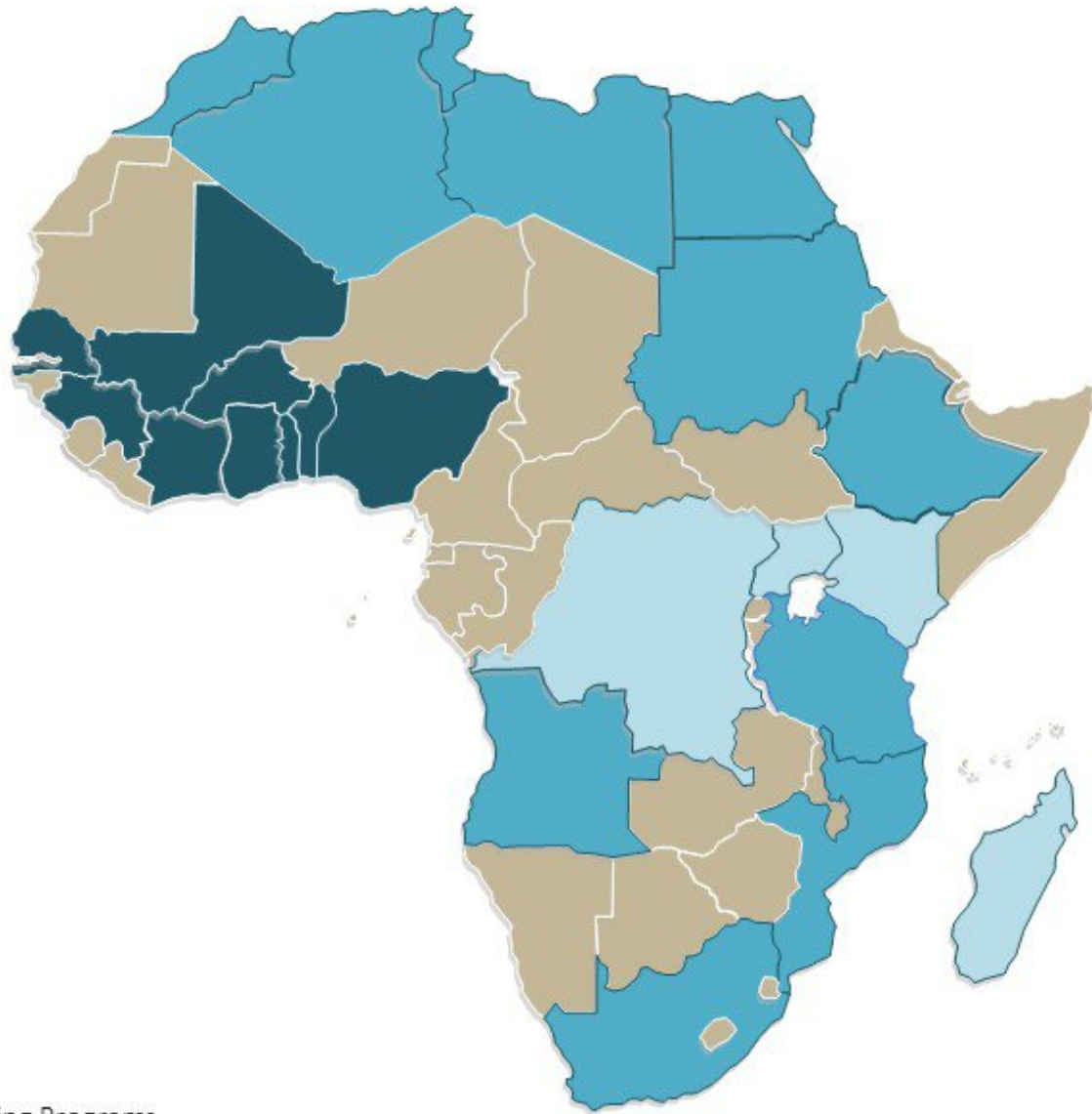
- **Africa:** 55 independent nations, population 1.2 billion, 30.5 people/km²
- **Prevalence** of skin disease ranges
 - **Rural Africa** 26.9% (Tanzania) to 80.4% (Ethiopia).
 - **New consultations** 6.9% (all levels of public health care, Mali) to 13% for primary care in 83 villages in Cameroon (WHO report).
- **Dermatologists** <1 per million population (except for North Africa).
- **Dermatology training programs** 25/55 countries
 - 10 regional, 10 national, 5 university based.
- **Training programmes are of international standard.** Graduates are competent clinicians, knowledgeable of local customs and needs.
- **Training programmes** designed in the "global north" and transplanted into African universities emphasize practices, which are not available, cost-effective, or based on evidence from Africa. **These programs often reflect colonial roots and need de-colonisation to make them relevant to Africa.**



KEY:
= No information

Dermatologists per 1 million people





KEY:

 = No training programs

Training Programs

University

National

Regional

What do African
patients and care
givers want?

The quality of life of caregivers of children with atopic dermatitis in a South African setting

Singh B, Thandar Y, Balakrishna Y, Mosam A

S Afr J Child Health 2019;13(2):63-68. DOI:10.7196/SAJCH.2019.v13i2.1544

119 (84%) black, 20 (14%) Indian and 3 (2%) mixed origins patients

QOL (DFI) factors significantly affected were **emotional distress** of the caregiver ($p < 0.0001$), **tiredness** of the caregiver ($p < 0.0001$) and **family leisure activities** ($p < 0.0001$). Involvement in **treatment** ($p = 0.016$), **food preparation and feeding** ($p = 0.003$), the **family's sleep** ($p = 0.001$) and the **caregiver's relationships** ($p = 0.025$) were moderately affected.

The unique sociodemographic and economic factors in countries globally warrant an assessment of factors that particularly affect AD in each setting to offer patients more holistic care.



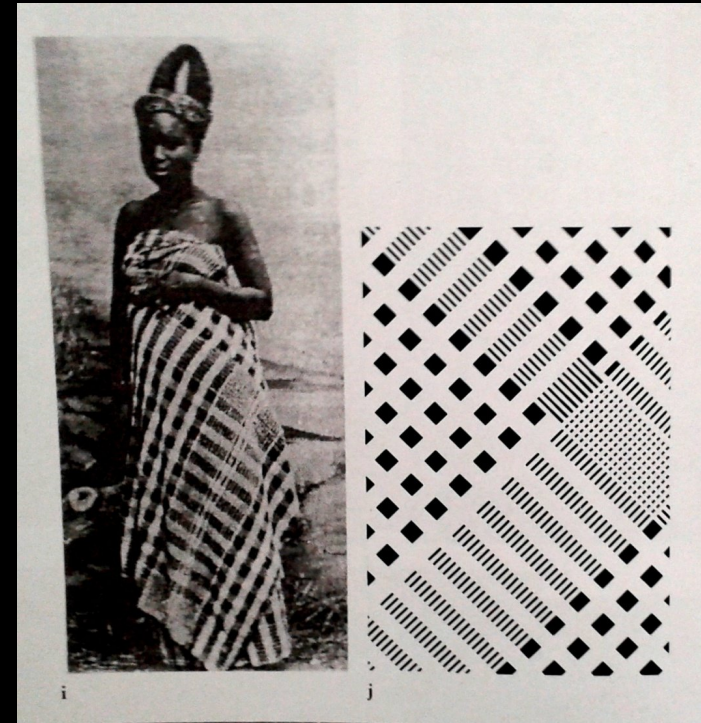
<http://www.asdvafrica.org/>

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AFRICAN SOCIETY
OF DERMATOLOGY & VENEROLOGY

SOCIÉTÉ AFRICAINE DE
DERMATOLOGIE ET VÉNÉRÉOLOGIE

EST. 2015



When "Europeans" first came to Africa, they considered the architecture very disorganised and thus primitive even though it was done according to careful rules of symmetry, proportionality and repetition now known as **fractal design** a form of mathematics that hadn't been "discovered yet."



Thank

you