Towards personalised therapy and potential disease modification

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USZ Universitäts Spital Zürich

ISAD
INTERNATIONAL SOCIETY OF ATOPIC DERMATITIS

Conflicts of Interests:
Peter Schmid-Grendelmeier

I declare the following, real or perceived conflicts of interest:

Lecture and Consultancy fees from
AbbVIe, Aimunne, Almirall, ALK Abello, Amgen, Astra Zeneca, Biomed, Bühlmann, derma2Go, Euroimmun, Galderma, Glaxo Smith Kline, Jansen, LEO, Lilly, L`Oréal, Novartis, Permamd, Pfizer, Pierre Fabre, Roche Pharma, Ruwag, SanofiGenzyme, Stallergenes, Unifarco, Thermo Fisher

Research collaborations
AbbVie, Bühlmann Diagnostics, LEO, Novartis, Pfizer, Stallergenes,Thermo Fisher

Zürich, 09. Oct 2027

T2T in Atopic Dermatitis

(Treat to target)

Better Access to Treatments for AD on a global scale

Disease modification in other disciplines

TABLE 1 Examples of early intervention trials/studies in non-dermatologic chronic inflammatory diseases.

Author(s)	Condition/population studied	Intervention vs. control	Outcomes/results
Van der Linden et al. (2010)	Rheumatoid arthritis (RA)	Treatment initiation >12 weeks vs. <12 weeks of symptom onset	Lower remission rates in delayed treatment group
Wevers-de Boear et al. (2012)	Rheumatoid arthritis (RA) and undifferentiated arthritis (UA)	Predictors of remission at 4 months from initiation of methotrexate 25 mg/week and prednisone 60 mg/day, which was tapered to 7.5 mg/day in 7 weeks.	Earlier treatment initiation was identified as a predictor of early remission in this cohort of 610 participants.
D'Haens et al. (2008)	Crohn's disease in treatment-naive patients	Corticosteroid vs. treatment with infliximab + azathioprine/ Methotrexate	Early aggressive treatment yielded greater remission rates 2 years post-initiation with similar safety.
Lee et al., 2010	Crohn's disease in paediatric patients naive to therapy	Prednisolone induction therapy + mesalamine & azathioprine for maintenance vs. 'aggressive' infliximab induction therapy & azathioprine for maintenance	Early aggressive intervention showed sig. higher disease remission. Remission persistent at 52 weeks.
Kim et al. (2011)	Crohn's disease in paediatric patients refractory to corticosteroid therapy (step-Up arm) and Crohn's disease in paediatric patients naive to therapy (top-down arm)	Prednisolone followed by maintenance mesalamine and azathioprine vs. 'aggressive' infliximab infusions with maintenance azathioprine	Early aggressive intervention showed sig. higher disease remission. Remission persistent at 52 weeks.

Neurology

Alzheimers disease

M. Parkinson

Pneumology

Cardiology

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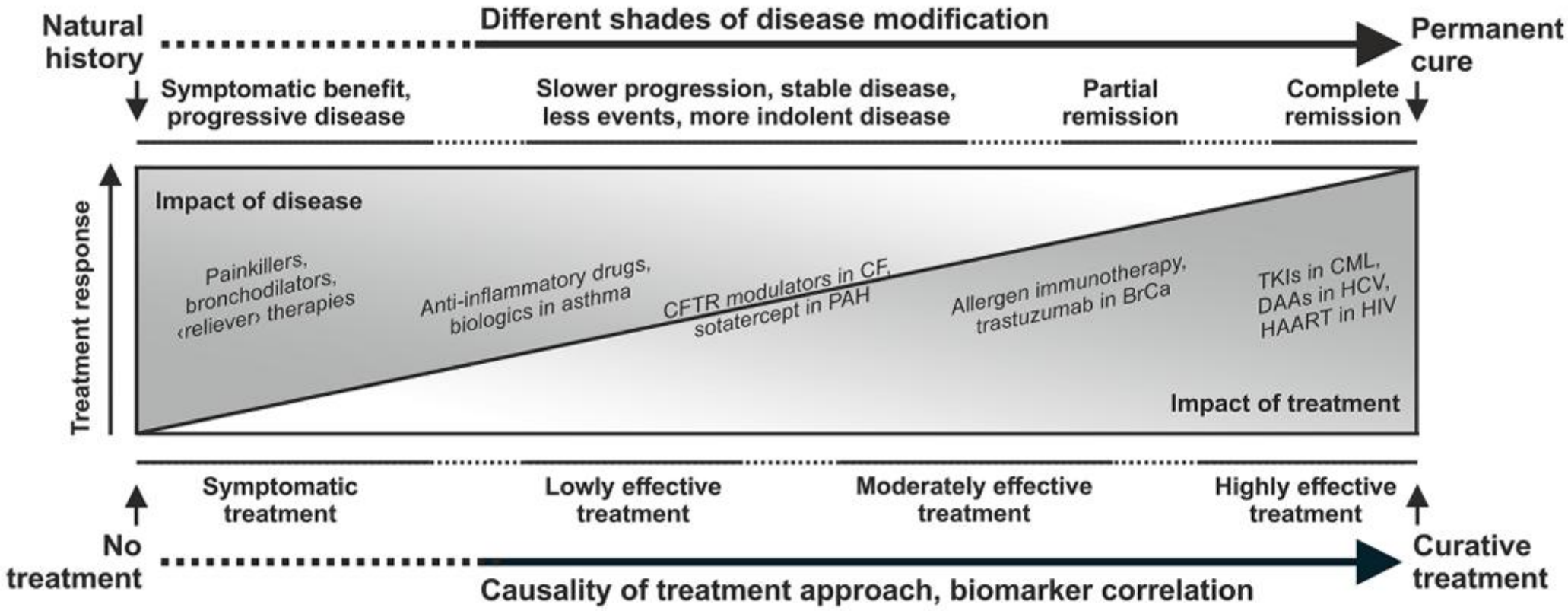
Jacobson Meet al….Simpson EL. Early intervention and disease modification in atopic dermatitis-the current state of the field and barriers to progress. J Eur Acad Dermatol Venereol. 2024 Apr;38(4):665-672

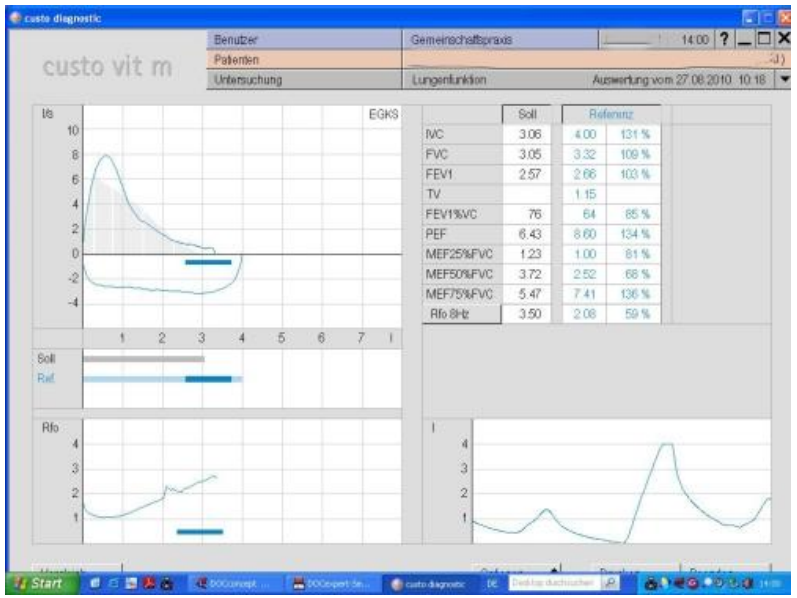
What means disease modification?

A **disease-modifying drug**, or **disease-modifying therapy** is a treatment that delays, slows or reverses the progression of a disease by targeting its underlying cause.[1]
They are distinguished from symptomatic treatments that treat the symptoms of a disease but do not address its underlying cause.[2]

What means disease modification?



Boesch M et al. What is disease modification and is this concept even helpful? Eur J Intern Med. 2024 Jun;124:1-


custo diagnostic
custo vit m
Benutzer
Gemeinschaftspraxis
Patienten
Untersuchung
Lungenfunktion
Auswertung vom 27.08.2010 10:18
EGKS
Soll
Referenz
IVC 3.06 4.00 131 %
FVC 3.05 3.32 109 %
FEV1 2.57 2.66 103 %
TV 1.15
FEV1%VC 76 64 85 %
PEF 6.43 8.60 134 %
MEF25%FVC 1.23 1.00 81 %
MEF50%FVC 3.72 2.52 68 %
MEF75%FVC 5.47 7.41 136 %
Rfo 8Hz 3.50 2.08 59 %
Start

Disease modification in other skin diseases

Author	Condition/Population studied	Intervention	Results
Peck et al. (1979)	Treatment-resistant cystic acne in 8 men and 6 women (average age 24 years)	Oral 13-cis-retinoic acid (daily average 2.0 mg/kg) for 4 months.	13/14 patients were clear at 4 months and the other had 75% improvement, After treatment discontinuation, all patients experienced prolonged remissions (<20 months-end of observation period)
Lebwohl et al. (2017)	Patients with moderate-to-severe psoriasis	Secukinumab treatment of moderate-to-severe psoriasis, PASI 75 responders continued double-blind secukinumab (300 mg) or switched to placebo ($N = 120$).	21 and 10 percent of patients did not relapse for at least 1 or 2 years, respectively, and maintained low mean PASI scores: 2.7 after 1 year and 1.7 and after 2 years off-drug. The longer the duration of psoriasis prior to treatment, the less likely the relapse-free outcome was.
Huang and Tsai (2019)	95 patients with moderate-to-severe psoriasis who completed a biologic or tofacitinib trial and achieved PASI-75 at completion.	No intervention	Median time to relapse was 7.6 months. Patients who received treatment with the study drug within 2 years of diagnosis had lower relapse rates.
Han et al., (2022)	4468 patients with moderate-to-severe psoriasis >20 years old.	Treatment with ustekinumab ($n = 2448$) or anti-TNF-α inhibitors (adalimumab, etanercept and infliximab; $n = 2020$)	Ustekinumab vs. TNF-α inhibitor group Hazard ratio of psoriatic patients developing heart failure: 0.641 (95% confidence interval: 0.415–0.985) vs 1 (reference) of ustekinumab vs. TNF-α inhibitor group
Robbins et al., (2018)	190 psoriasis patients with 1%–15% body surface involvement and Physician Global Assessment (5-point) score ≥2 (mild)	Tapinarof cream (0.5%/1.0% QD/BID; 4 groups) vs. Tapinarof vehicle (QD/BID; 2 groups)	Tapinarof cream was superior to vehicle. Treatment efficacy was generally maintained until the end of the trial (4 weeks post-treatment)

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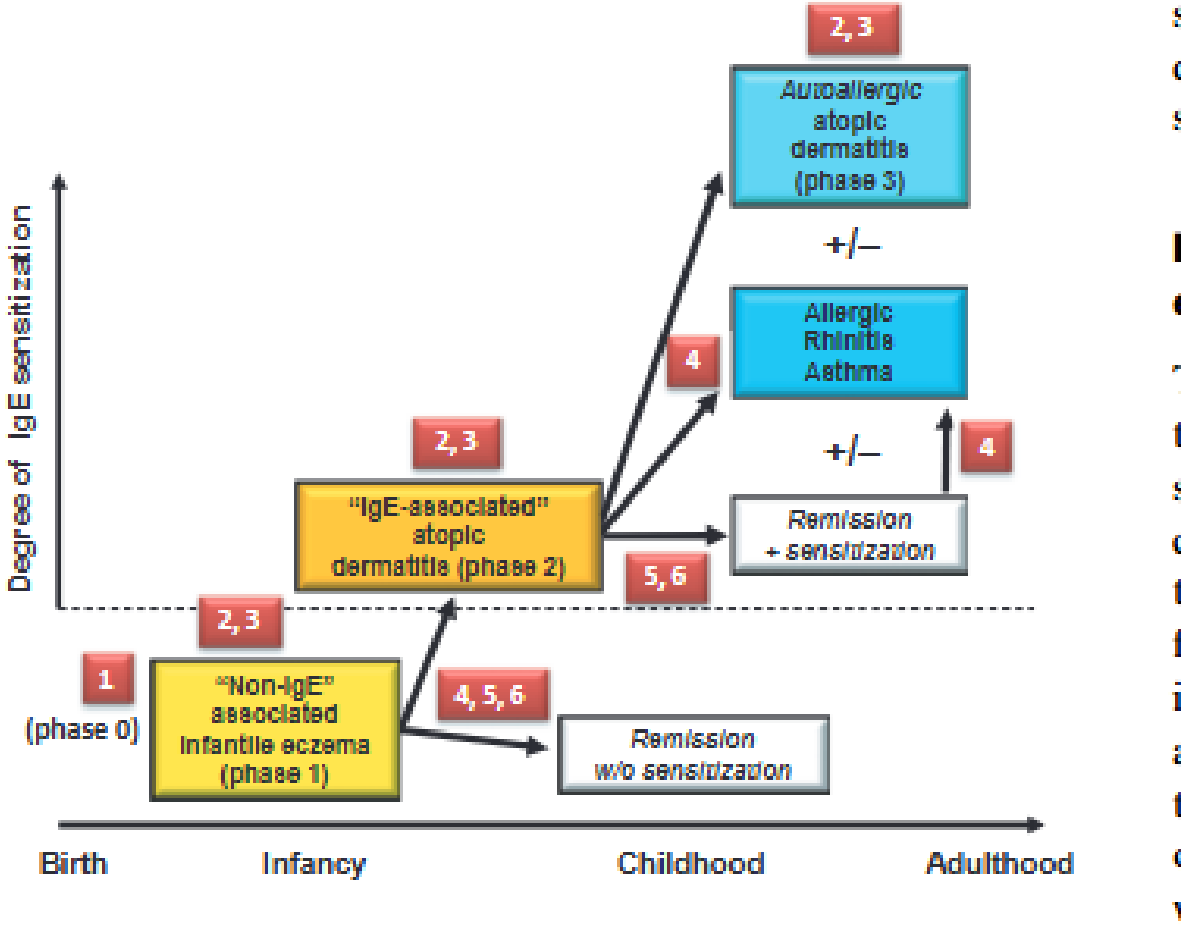


Whether this kindof strategy is already feasible with the arsenal of availablemedical products such as topical steroids or calcineurininhibitors or whether the issue of safety, especially in infancyrequires the further development of new and safe compoundsfor this particular approach need to be clarified. In any case,the scientific community will face a number of new challengesduring this fascinating development ultimately leading to thereduction in the burden of AD and asthma.

Bieber T, Cork M, Reitamo S. Atopic dermatitis: a candidate for disease-modifying strategy. Allergy. 2012 Aug;67(8):969-75

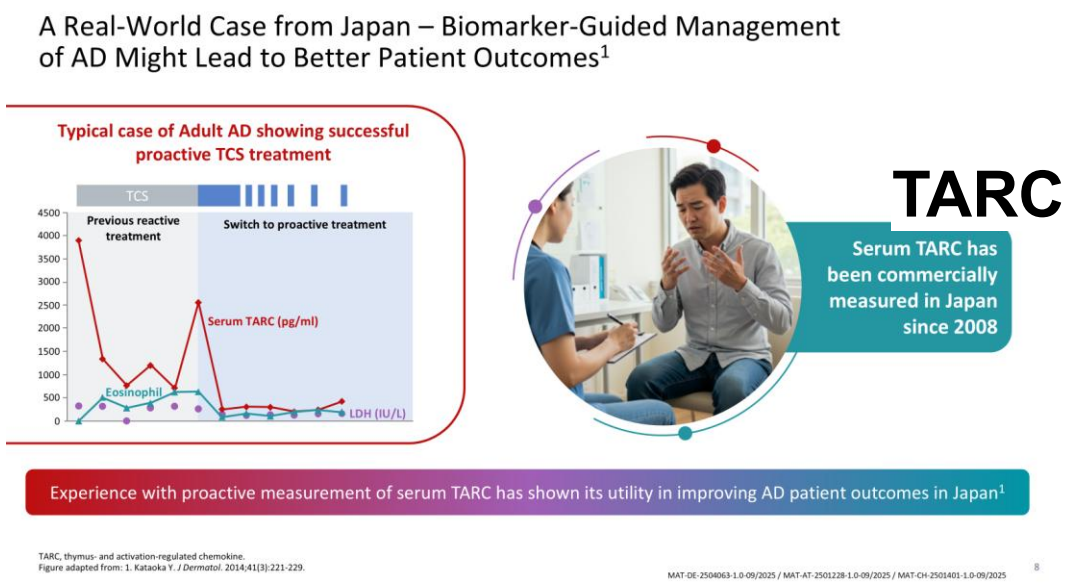
Scores: SCORAD, EASI, IGA

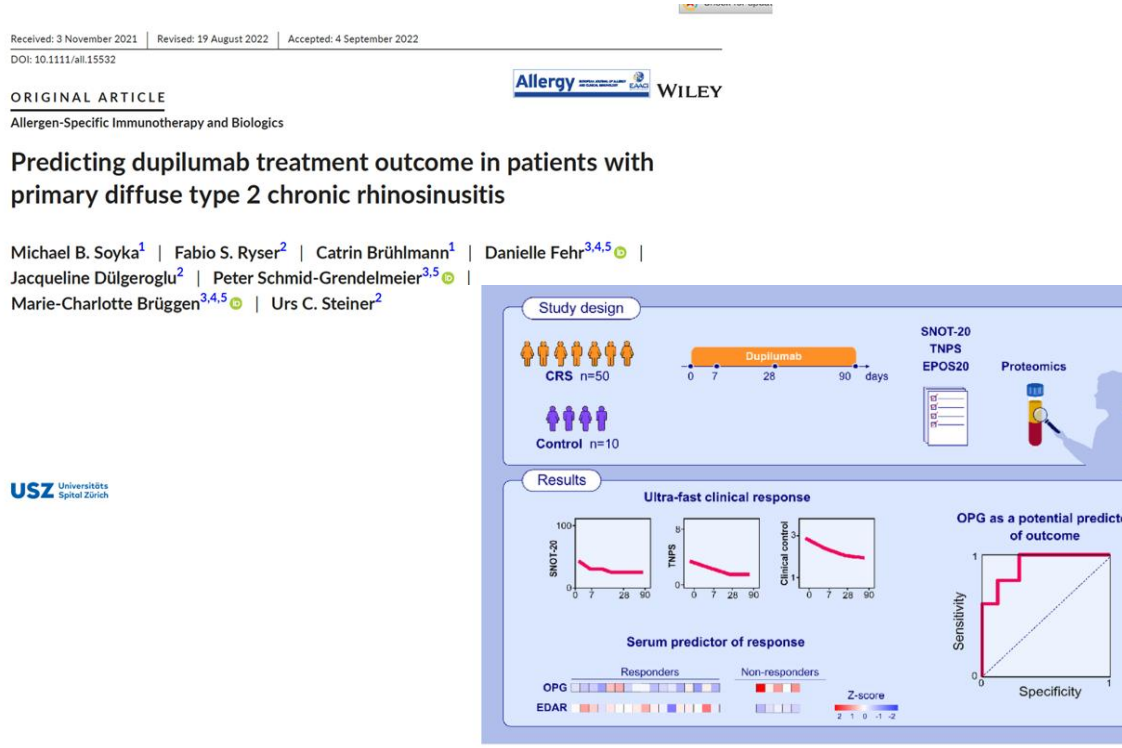
Clinical subtypes
Immunologic sbtypes

Lab parameters: IgE, Sensitizations

TARC?

Osteopotegerin?





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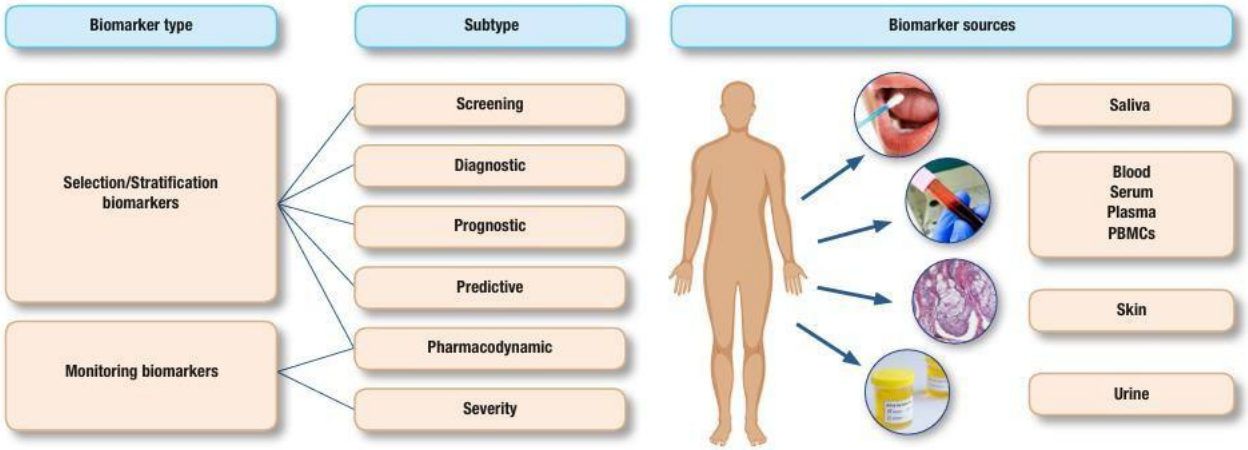
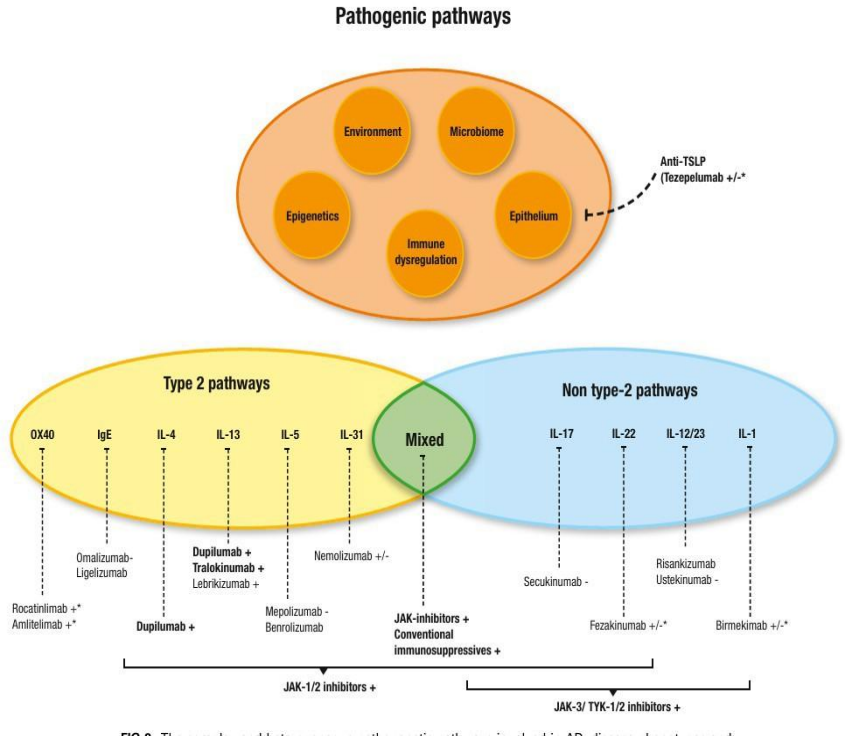
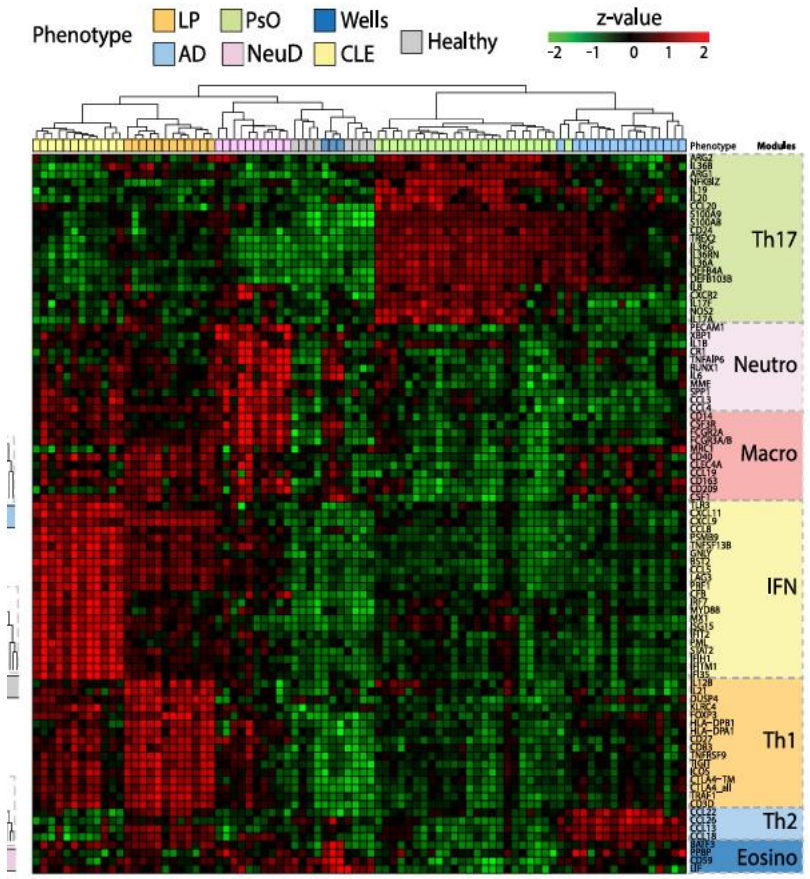
Scores: SCORAD, EASI, IGA

Clinical subtypes
Immunologic sbtypes





Bakker D et al Allergy Clin Immunol. 2023



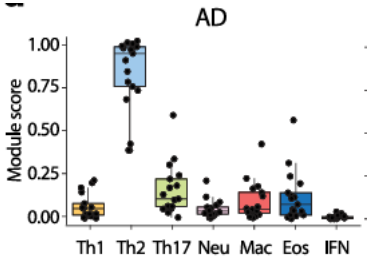


Table 2 | Treatments and module matching of non-responding patients

Patient ID	Age	Gender	Initial Clinical Dx	Treatment	Module scores			Module matching	Re-matched treatment - Response
					Th1	Th2	Th17		
NR_001	67	M	AD	Dupilumab	**0.82**	0.11	0.32	non matched	-
NR_002	66	M	AD	Dupilumab	**0.61**	0.5	0.25	non matched	-
NR_003	66	M	AD	Dupilumab	**0.66**	0.29	0.52	non matched	-
NR_004	79	M	AD	Dupilumab	**0.6**	0.42	0.19	non matched	Baricitinib – 100% response
NR_005	33	M	AD	Dupilumab	**0.43**	0.15	0.03	non matched	Upadacitinib- 90% response
NR_006	88	F	PsO	Tildrakizumab	0.41	**0.95**	0.23	non matched	Dupilumab – 90% response
NR_007	65	M	PsO	Tildrakizumab	0.36	**0.88**	0.38	non matched	Dupilumab – 100% response
NR_008	66	M	PsO	Ixekizumab	0.05	**0.84**	0.33	non matched	Dupilumab – 90% response
NR_009	61	M	AD	Dupilumab	0.51	**0.58**	0.37	matched	-
NR_010	59	M	AD	Tralokinumab	0.25	**0.76**	0.13	matched	-
NR_011	58	M	PsO	Secukinumab	0.1	**0.98**	0.1	non matched	-
NR_012	56	M	PsO	Secukinumab	0.32	**0.96**	0.12	non matched	-
NR_013	65	M	PsO	Ixekizumab	0.19	**0.97**	0.47	non matched	-
NR_014	47	F	AD	Dupilumab	0.17	0.1	**0.38**	non matched	-
NR_015	55	M	AD	Dupilumab	0.19	0.3	**0.55**	non matched	-
NR_016	59	M	AD	Dupilumab	0.1	0.11	**0.36**	non matched	Ixekizumab – 90% response
NR_017	18	F	PsO	Guselkumab	0.04	0.08	**0.72**	matched	-

Bold scores correspond to the dominant module score for each patient.

Seremet T….Gilliet M. Immune modules to guide diagnosis and personalized treatment of inflammatory skin diseases. Nat Commun. 2024 Dec 18;15(1):10688

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- 1: We have to define/consider subtypes

The immuno-development of Atopic Dermatitis

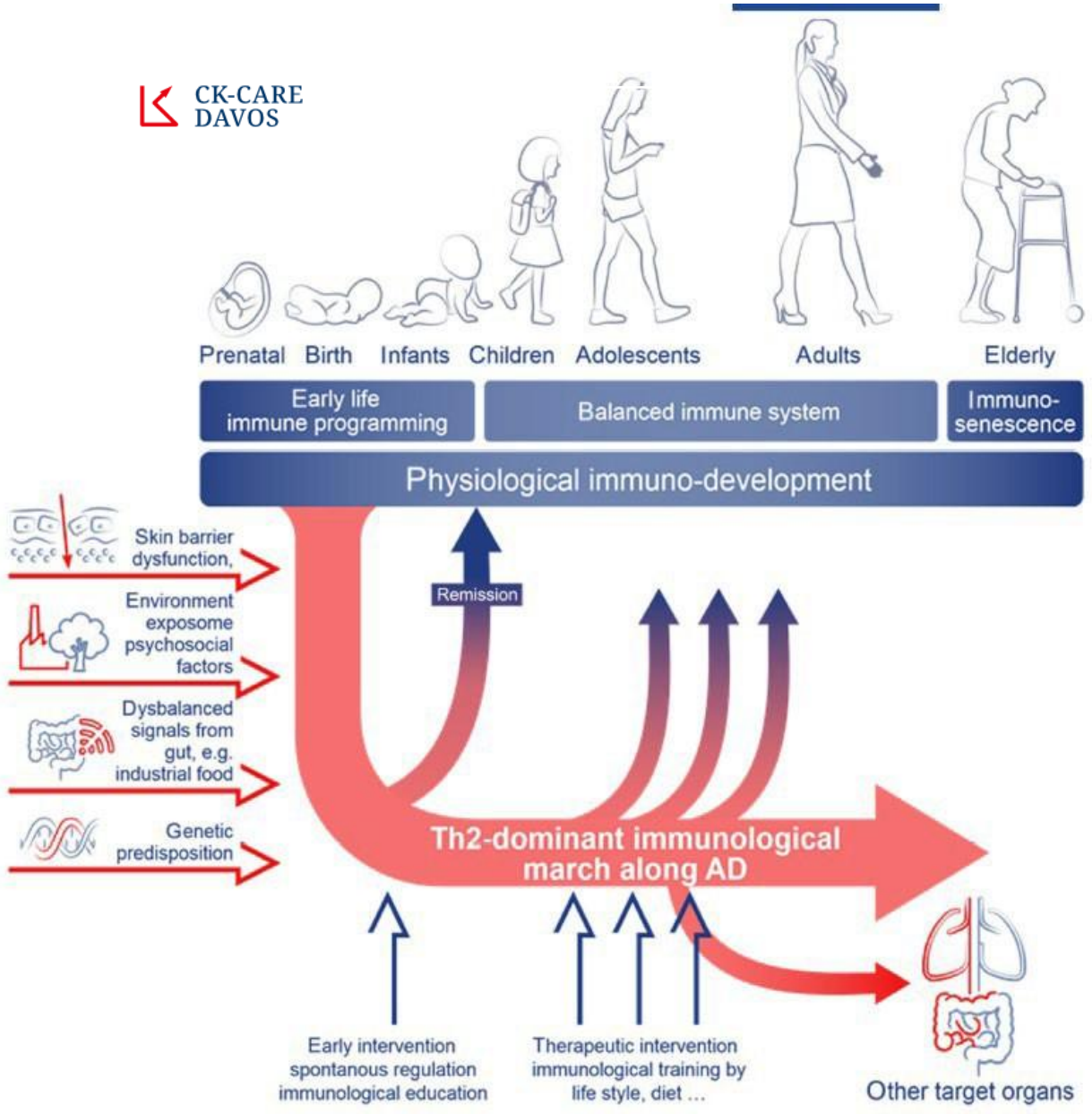
Traidl-Hoffmann C.....Schmid-Grendelmeier P. Navigating the evolving landscape of atopic dermatitis: Challenges and future opportunities: The 4th Davos declaration. Allergy. 2024 Aug 4

a) Neonates;

b) Infants

c) Adolescents and adults

Adapted from Weidinger & Novak Lancet 2015



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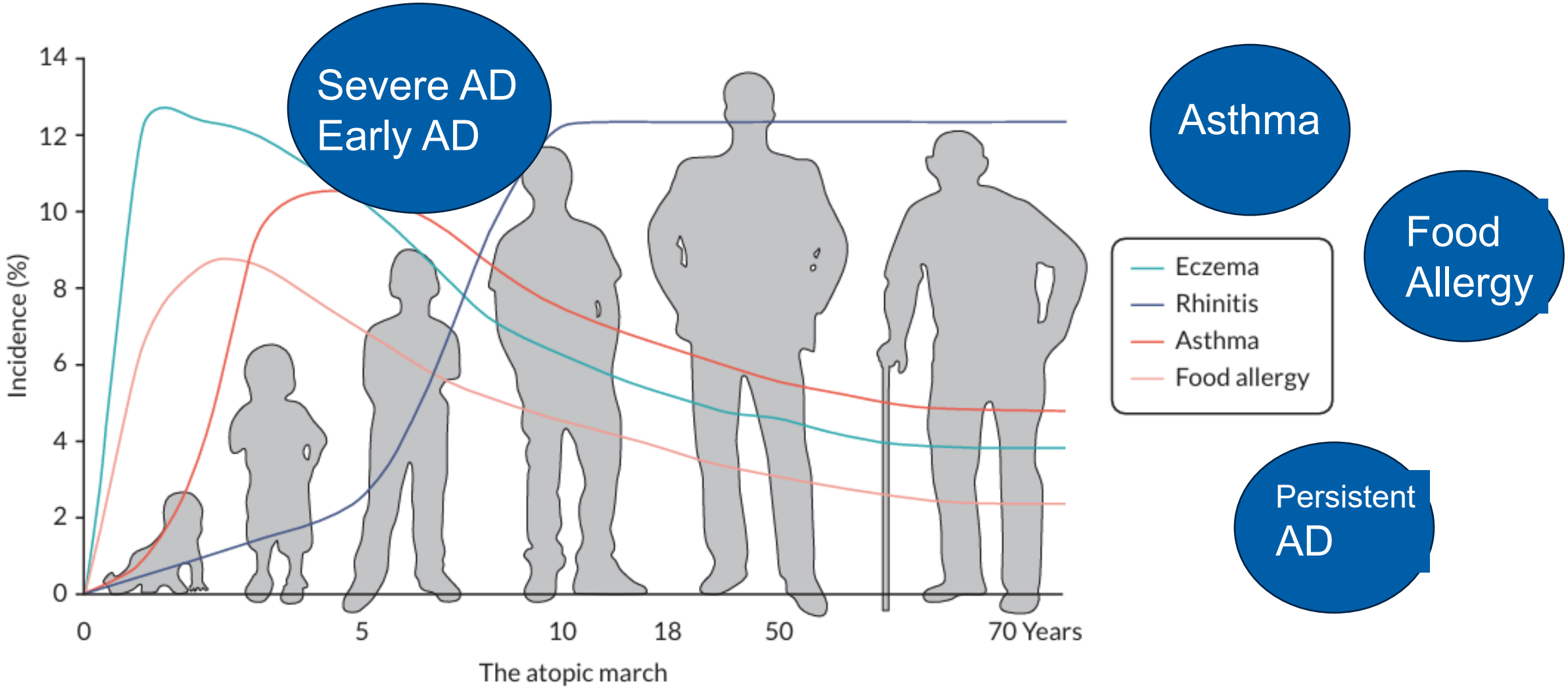
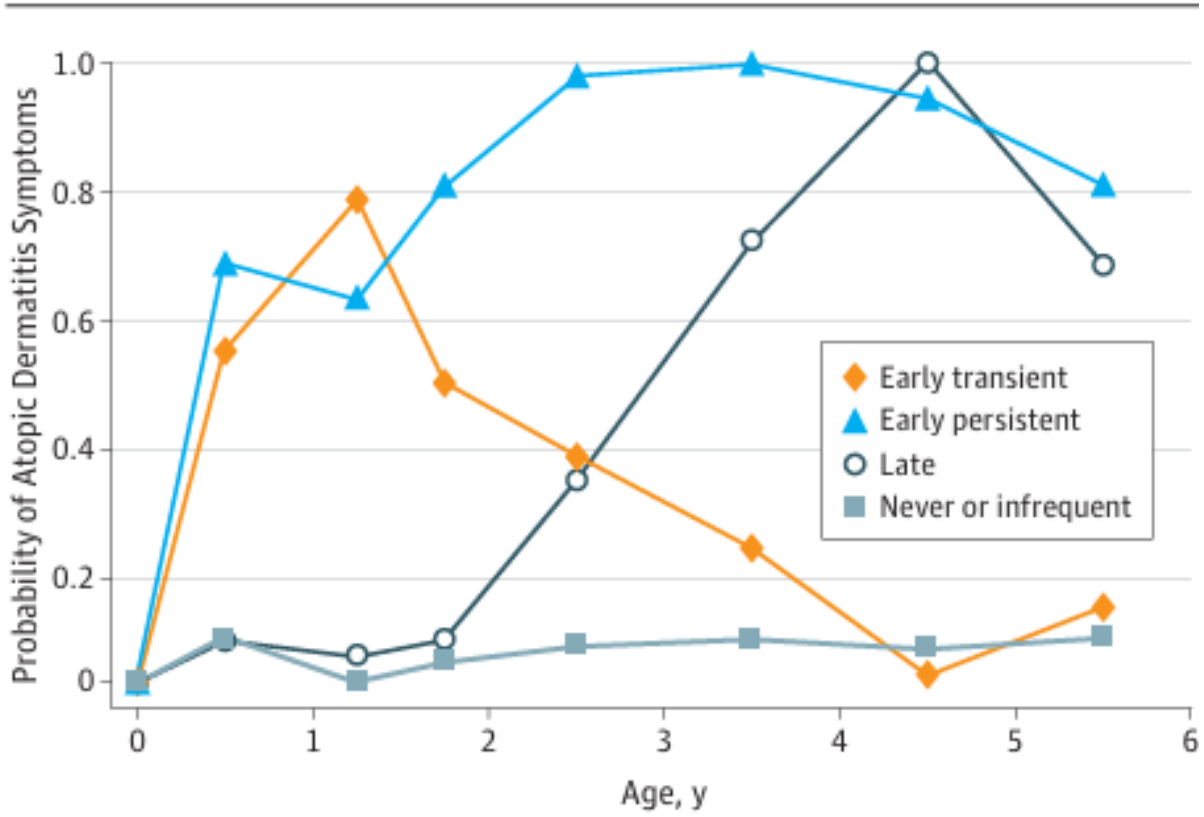
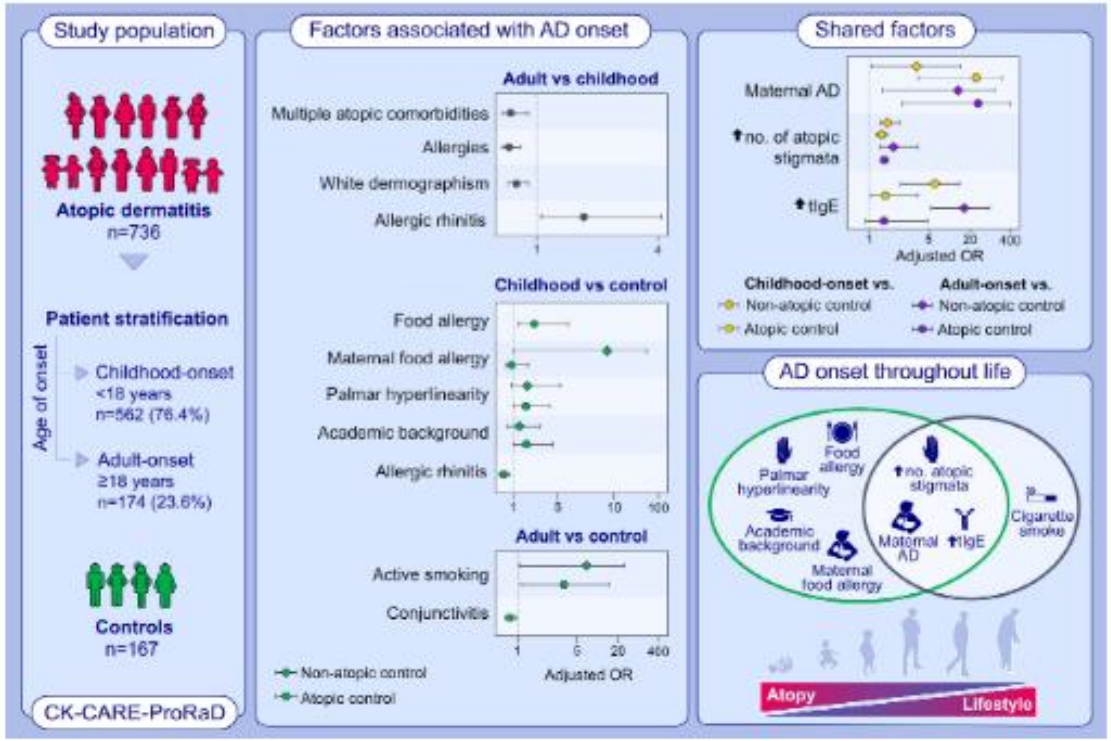


FIGURE 1 Illustration of the typical onset of symptoms of allergic diseases during childhood. Reprinted from Davidson*et al.* (2019),[15] Copyright (2023), with permission from Elsevier.



Roduit C et al. Phenotypes of Atopic Dermatitis Depending on the Timing of Onset and Progression in Childhood. JAMA Pediatr. 2017 Jul 1;171(7):655-662



Maintz L et al, Atopic dermatitis: Correlation of distinct risk factors with age of onset in adulthood compared to childhood. Allergy. 2023 Aug;78(8):2181-2201

- 1: We have to define/consider subtypes
- 2: Different approaches for childhood and adult AD

Pathophysiology and mechanism of AD

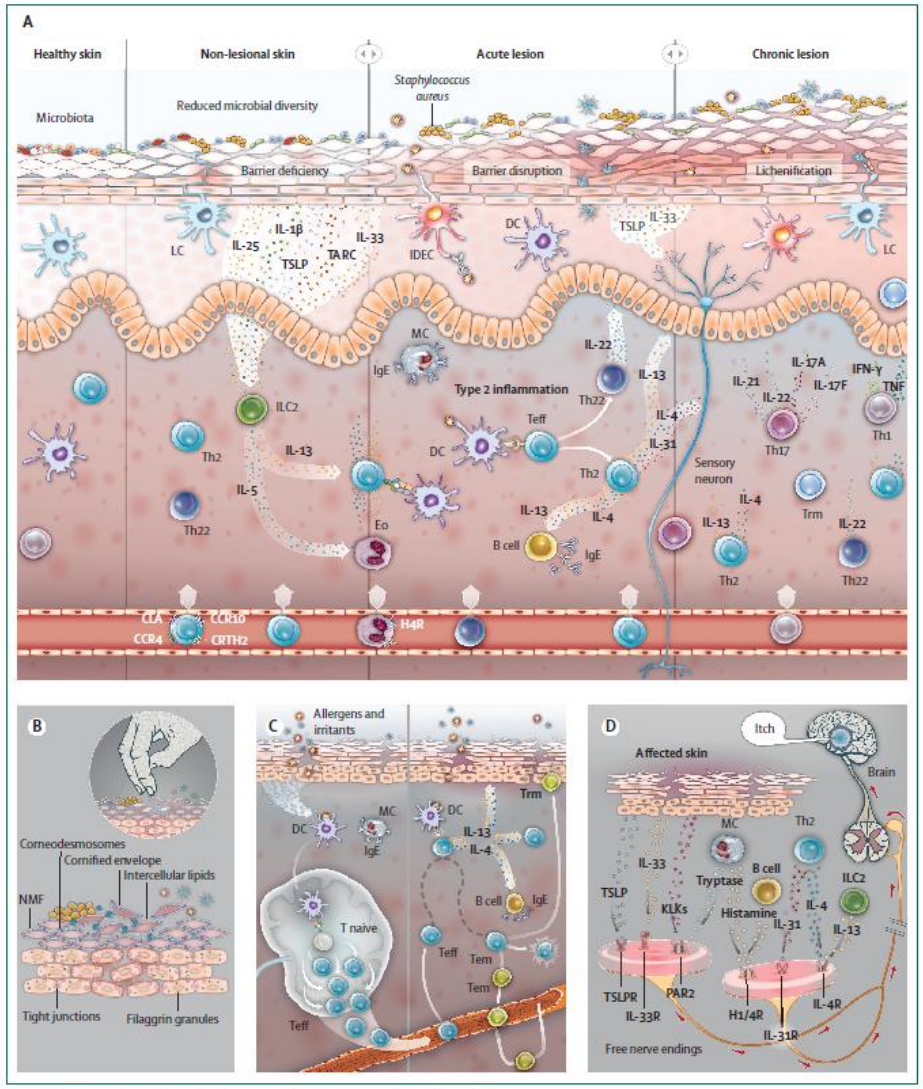


Figure 2: Pathogenesis, main mechanisms, and pathophysiology of atopic dermatitis

Immune **D**eviation **IBD-DDD**

Barrier **D**disruption

Microbe **D**ysbiosis

Many new insights:

- Role of mediators and cell function
- Disrupted barrier function
- Role of environment
  - Allergens (Food?)
  - Microbiome
  - Mycobiome

Adapted from:

Sinéad M Langan, Alan D Irvine, Stephan Weidinger.
Atopic dermatitis. *Lancet* 2020; 396: 345–60

Trigger factors in AD

Guttman-Yassky E, Renert-Yuval Y, Brunner PM.
Atopic dermatitis.
Lancet. 2025 Feb 15;405:583-596

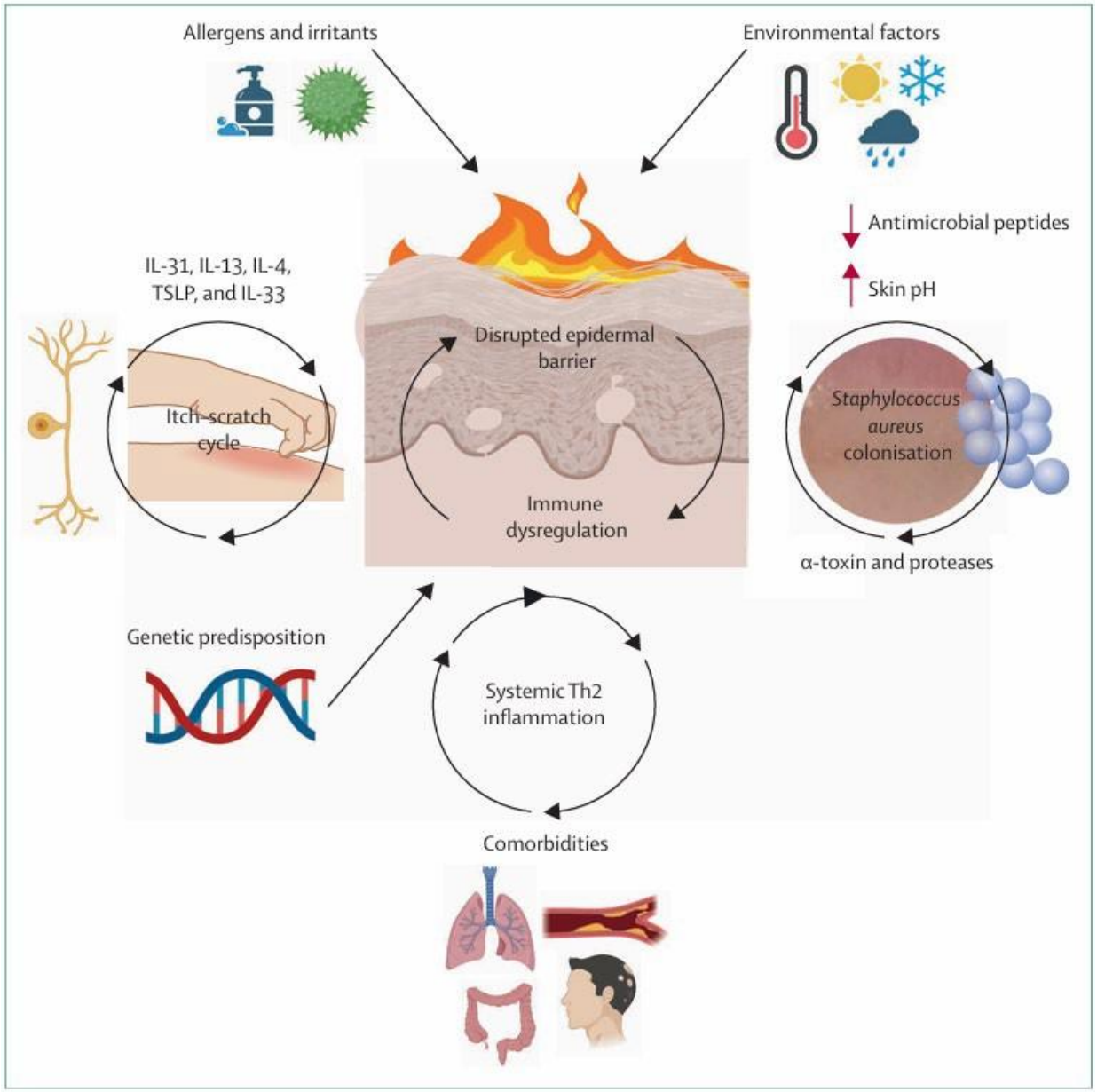


Figure 3: **Common triggers and drivers of atopic dermatitis skin inflammation and barrier disruption**

Trigger factors in AD

Guttman-Yassky E, Renert-Yuval Y, Brunner PM.
Atopic dermatitis.
Lancet. 2025 Feb 15;405:583-596

Clinical history:
- Provoking factors
- Allergologic work up
- Dietary habits
- Sleeping behaviour
- etc

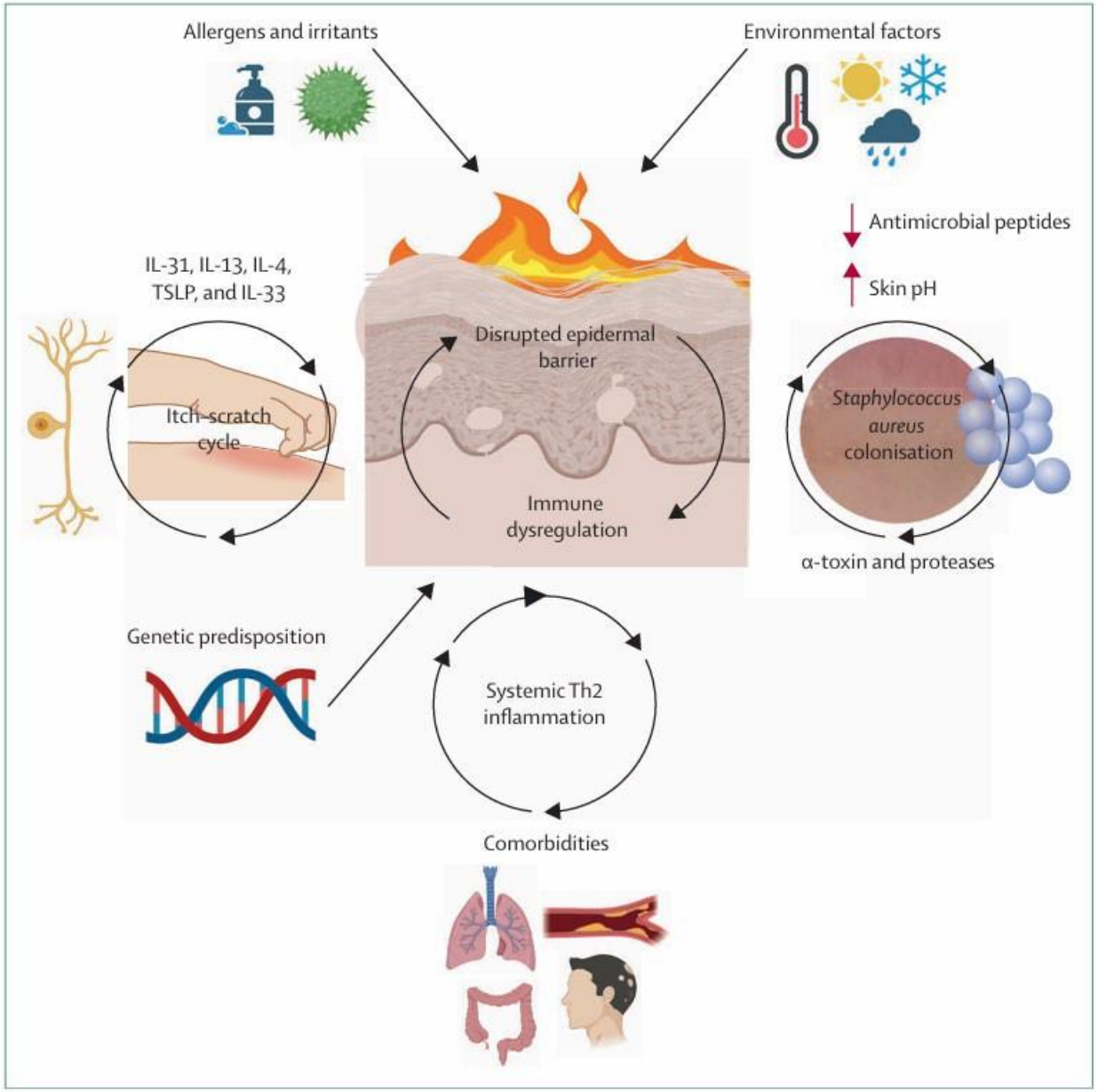
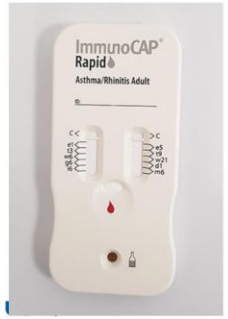


Figure 3: **Common triggers and drivers of atopic dermatitis skin inflammation and barrier disruption**

How to detect IgE in the serum

Detection of Specific IgE by bedside testing

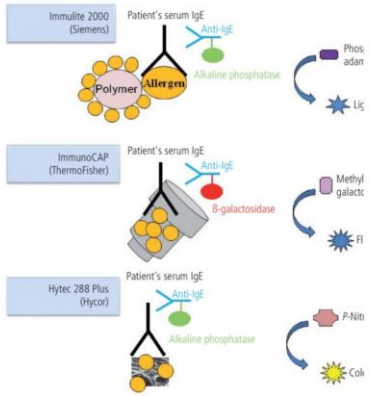


There are three different test panels available, each holding a fixed set of 10 different allergens.*

ImmunoCAP Rapid Wheeze/Rhinitis Child	ImmunoCAP Rapid Asthma/Rhinitis Adult	ImmunoCAP Rapid Rhinitis/Asthma 1*
Cat	Cat	Cat
Birch	Birch	Mold
Mugwort	Mugwort	Cocksfoot
Timothy	Timothy	Common ragweed
Egg White	Cockroach	Mugwort
Dog	Dog	Dog
Olive pollen	Olive	Cockroach
Wall pellitory	Wall pellitory	Japanese Cedar
House dust mite	House dust mite	
Cow's milk	Mold	

*ImmunoCAP Rapid Rhinitis/Asthma 1 holds eight different allergens.

Detection of Specific IgE by ImmunoCAP®



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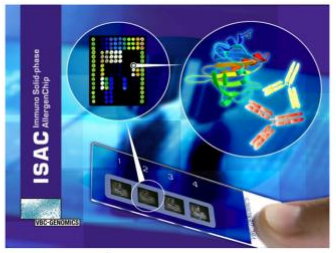
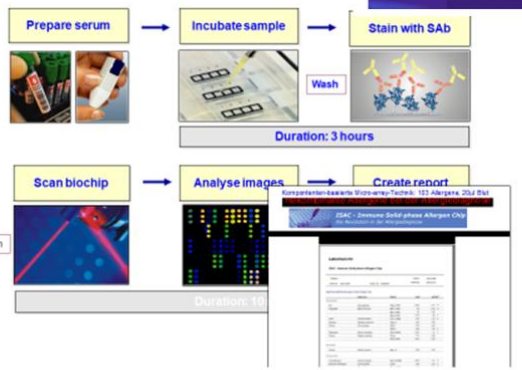
Platforms for MicroArray IgE

(110-250 spec IgE values from 20-30 µl Serum)



113 AllergenS, 20µl Blut

ISAC® technology in the lab - Summary



ALEX Allergy Explore

Vaules of >280 spezifischen IgE
- Allergens (zb Birch)
- Molecular Allergens (zB Bet v 1, Bet v 2)

Total IgE

02.05.2023

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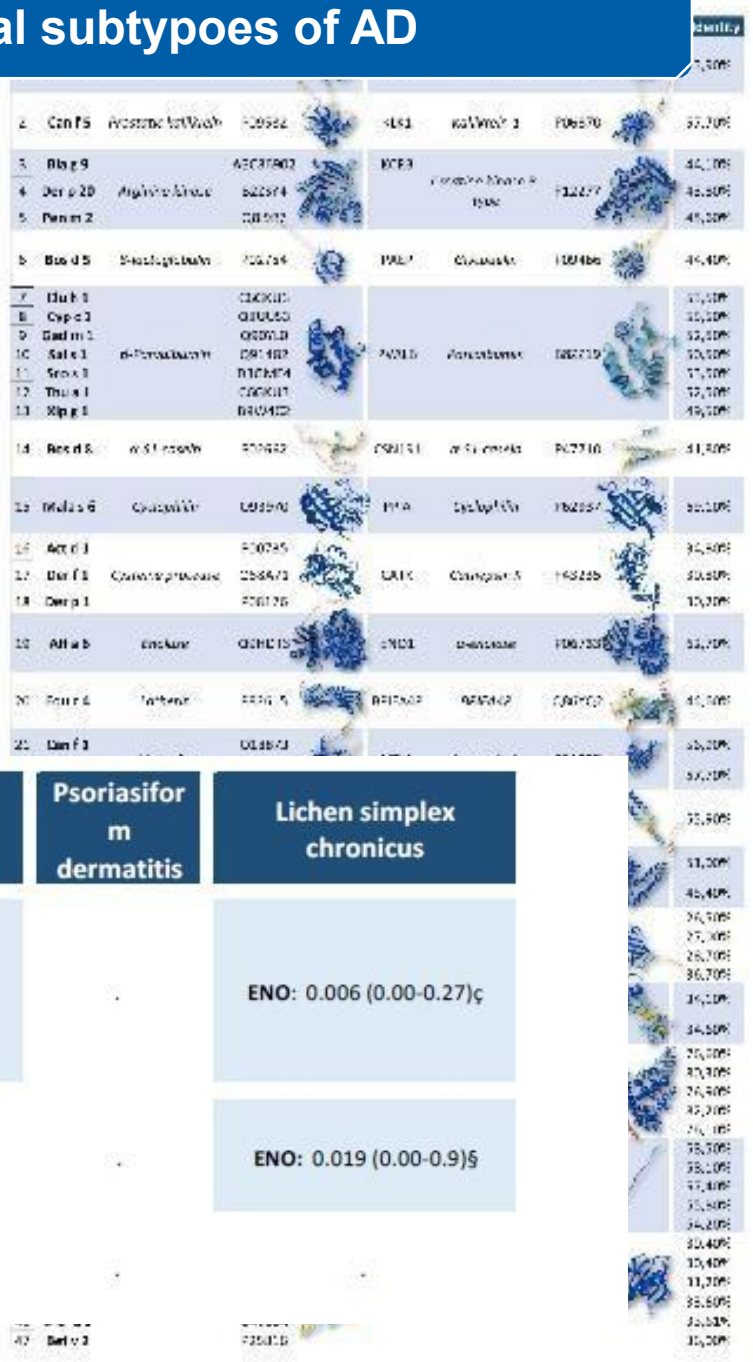
Patterns of molecular sensitization allow to differentiate different clinical subtypoes of AD

Allergy EUROPEAN JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY EAACI

Scala E, et al
A microarray-based IgE-molecular mimicry index (IgE-MMI): A biomarker for disease severity, clinical phenotypes, and therapeutic response in atopic dermatitis?
Allergy. 2024 Nov 4



B	Generalized eczema	Prurigo-like AD	Nummular eczema	Erythroderma	Psoriasiform dermatitis	Lichen simplex chronicus
Flexural dermatitis	**PRV**: 8.248 (1.65-41.20)ç **SA**: 0.202 (0.06-0.65)^ **PSA**: 3.268 (1.27-8.44)§	**MnSOD**: 8.672 (1.04-72.39)§ **AK**: 0.164 (0.05-0.52)ç	.	**Casein**: 0.033 (0.00-0.74)§	.	**ENO**: 0.006 (0.00-0.27)ç
Head and neck dermatitis	**PSA**: 5.351 (1.48-19.39)§	**MnSOD**: 19.637 (2.01-192.30)§	.	.	.	**ENO**: 0.019 (0.00-0.9)§
Portrait dermatitis	**CYP**: 32.067 (4.45-231.23)^	**CYP**: 17.719 (1.86-168.67)§	**NPC-2**: 17.669 (1.53-203.82)§	.	.	.

Food diversity prevetns food allergy

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 26, 2015 VOL. 372 NO. 9

Randomized Trial of Peanut Consumption in Infants at Risk for Peanut Allergy

George Du Toit, M.B., B.Ch., Graham Roberts, D.M., Peter H. Sayre, M.D., Ph.D., Henry T. Bahnson, M.P.H., Suzana Radulovic, M.D., Alexandra F. Santos, M.D., Helen A. Brough, M.B., B.S., Deborah Phippard, Ph.D., Monica Basting, M.A., Mary Feeney, M.Sc., R.D., Victor Turcanu, M.D., Ph.D., Michelle L. Sever, M.S.P.H., Ph.D., Margarita Gomez Lorenzo, M.D., Marshall Plaut, M.D., and Gideon Lack, M.B., B.Ch., for the LEAP Study Team*

No peanut — higher rate of panut allergy

Regular peanut consumption — lower risk of peanut allergy

CONCLUSIONS

The early introduction of peanuts significantly decreased the frequency of the development of peanut allergy among children at high risk for this allergy and modulated immune responses to peanuts. (Funded by the National Institute of Allergy and Infectious Diseases and others; ClinicalTrials.gov number, NCT00329784.)

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Food intake — Prevention of food allergy

Emollients use: — no additional use for Food allergy

AD: — Prevetion does not work

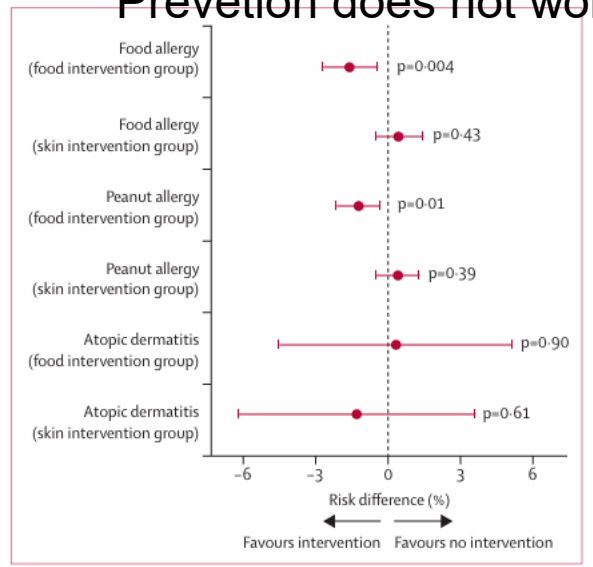
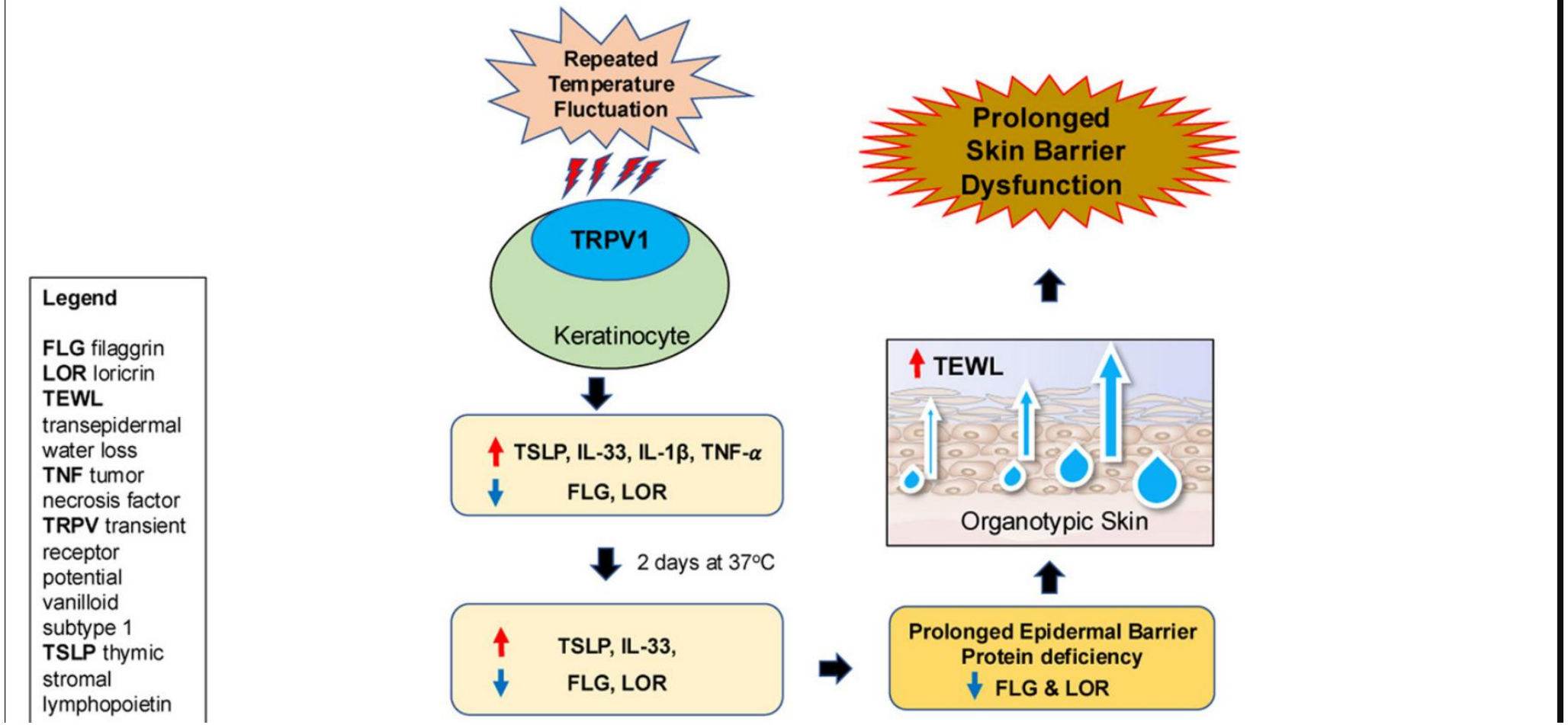


Figure 3: **Risk reduction of food allergy for each primary prevention strategy**
Error bars show 95% CIs. Food allergies are presented as main effects, whereas atopic dermatitis is presented as a marginal estimate.

Early regular use of skin emollients did not reduce food allergy at 36 months.

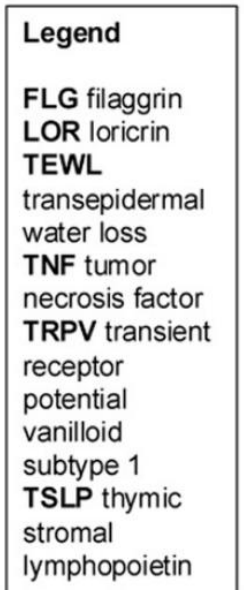
Skjerven HO et al Early food intervention and skin emollients to prevent food allergy in young children (PreventADALL): a factorial, multicentre, cluster-randomised trial. Lancet. 2022 Jun 25;399(10344):2398-2411

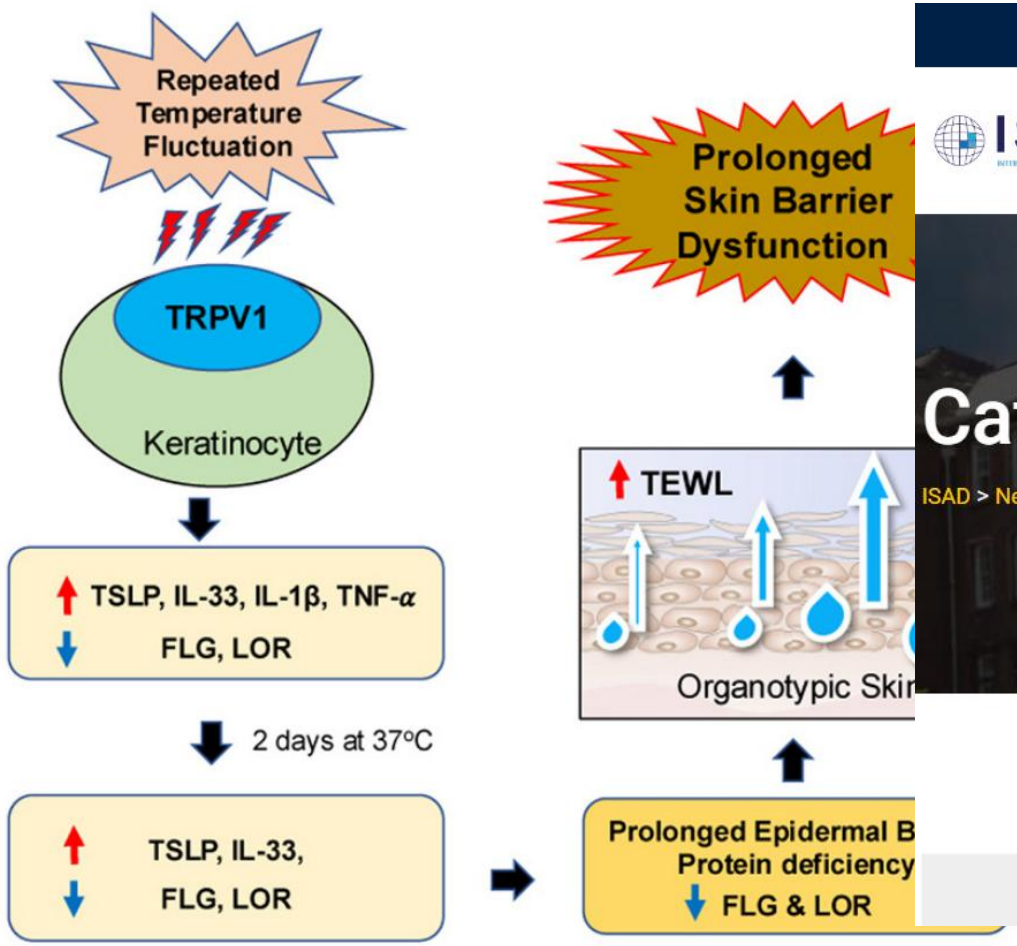
Repeated temperature fluctuation causes prolonged skin barrier dysfunction through TRPV1



Hui-Beckman JW, et al,. Repeated Temperature Fluctuation Exposure Causes Prolonged Skin Barrier Dysfunction. J Invest Dermatol. 2025 Oct;145(10):2626-2628

Repeated temperature fluctuation causes prolonged skin barrier dysfunction through TRPV1





Hui-Beckman JW, et al,. Repeated Temperature Fluctuation Exposure Causes Prolonged Skin Barrier Dysfunction. J Invest Dermatol. 2025 Oct;145(10):2626-2628

- 1: We have to define/consider subtypes
- 2: Different approaches for childhood and adult AD
- 3. We have to define (and exclude/avoid) Trigger factors

T2T from the patient perspective

Itch

T2T from the patient perspective

Itch

Unpredictable flares

T2T from the patient perspective

It

Sleep disturbance

Unpredictable flares

T2T from the patient perspective

Itch

Hand eczema

Sleep distur

Unpredictable flares

T2T from the patient perspective

Face involvement

Hand eczema

Itch

Sleep disturbance

Unpredictable flares

T2T from the patient perspective

Face involvement

Isolation

Hand eczema

Itch

Sleep disturbance

Unpredictable flares

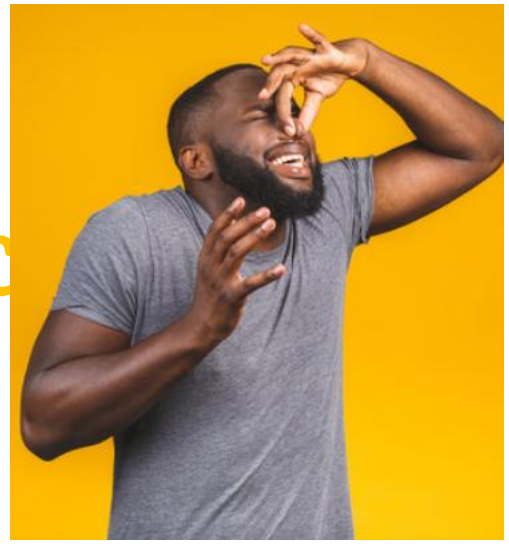
T2T from the patient perspective

Face involvement

Isolation

Hand eczema

Itch



Sleep disturbance

Unpredictable flares

Smell

T2T from the patient perspective

Face involvement

Isolation

Hand eczema

Itch

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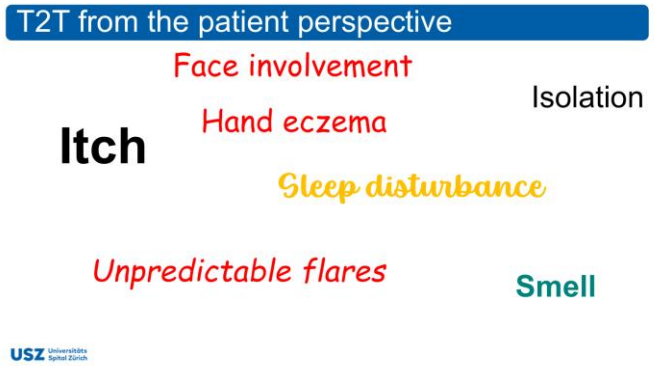
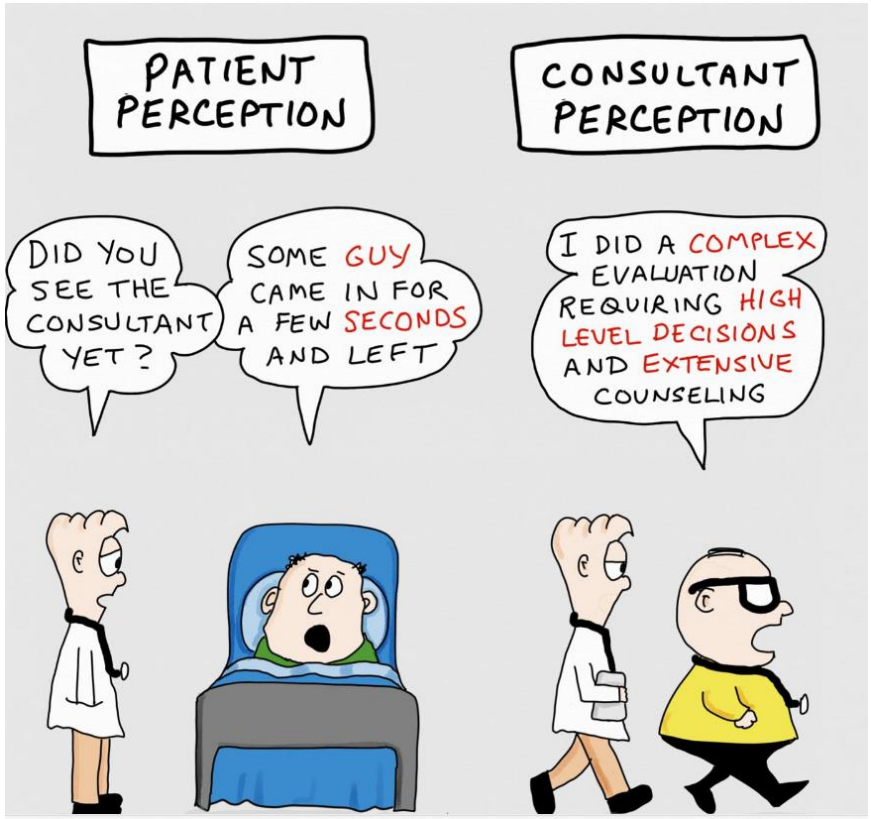
T2T from the patient perspective





SCORAD
EASI
IGA

Biomarkers

T2T from the doctor's perspective

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- 1: We have to define/consider subtypes
- 2: Different approaches for childhood and adult AD
- 3. We have to define (and exclude/avoid) Trigger factors
- 4. We have to integrate tne needs and expections of our patients

Disease modification in AD

Author	Intervention vs. control	Outcomes	Results
Schneider et al. (2016)	Pimecrolimus vs. standard of care	Development of asthma	50% dropout rate. No significant difference.
Van der Aa et al. (2010)	Synbiotic-enriched formula vs. placebo	Incidence of asthma symptoms and use of asthma medication at 1-year follow-up.	Synbiotics were superior to placebo in both outcomes.
Warner et al. (2001)	Cetirizine vs. placebo	Incidence of asthma over three-year follow-up	No difference between cetirizine and placebo.
Fukiuie et al. (2016)	Proactive topical steroid vs. standard of care	AD control, quality of life, aeroallergen IgE sensitization	Proactive therapy was superior to standard of care for AD control, QoL and levels of house mite-specific IgE despite no difference in amount of medication used with similar safety profile.
Miyaji et al. (2019)	Proactive aggressive topical steroid therapy 4 months before vs after diagnosis (retrospective).	Food allergy at 2 years of age (defined as a positive oral food challenge and/or history of anaphylaxis).	Patients treated within 4 months of diagnosis had lower levels of food allergy at 2 years of age by -DBPCFC
Nadeau et al. (enrolling) SEAL Study	Proactive topical steroid with or without ceramide emollient vs. standard of care	Food allergy determined by oral food challenges.	Anticipated results in 2027
Yamamoto-Hanada et al. (2023)	Proactive topical steroid (full body) vs. standard of care	Food allergy (oral food challenge-proven IgE-mediated hen's egg allergy at 28 weeks of age)	Proactive therapy was superior to conventional treatment in reducing hen's egg allergy. Proactive therapy-treated participants had lower body weight and height at follow-up

Jacobson Meet al….Simpson EL. Early intervention and disease modification in atopic dermatitis-the current state of the field and barriers to progress. J Eur Acad Dermatol Venereol. 2024 Apr;38(4):665-672

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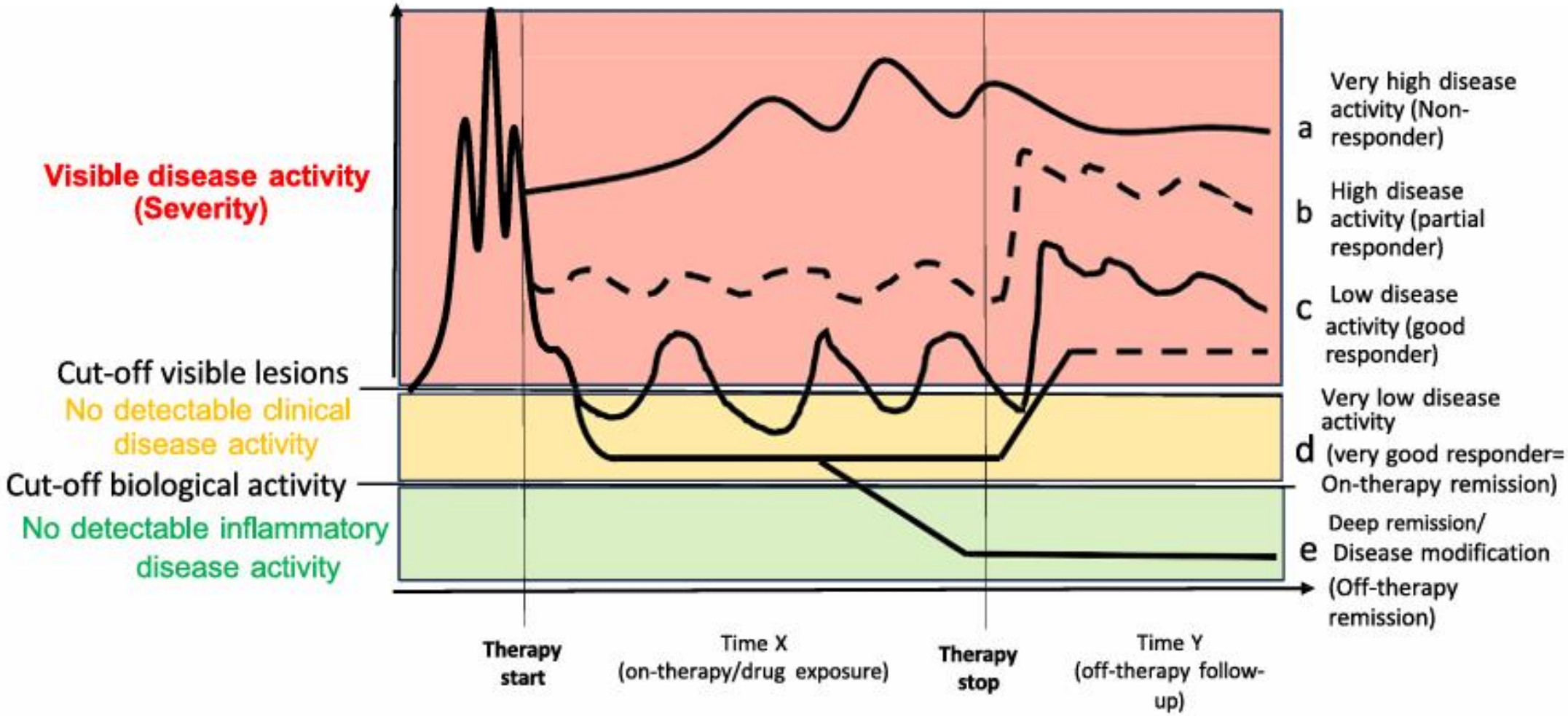
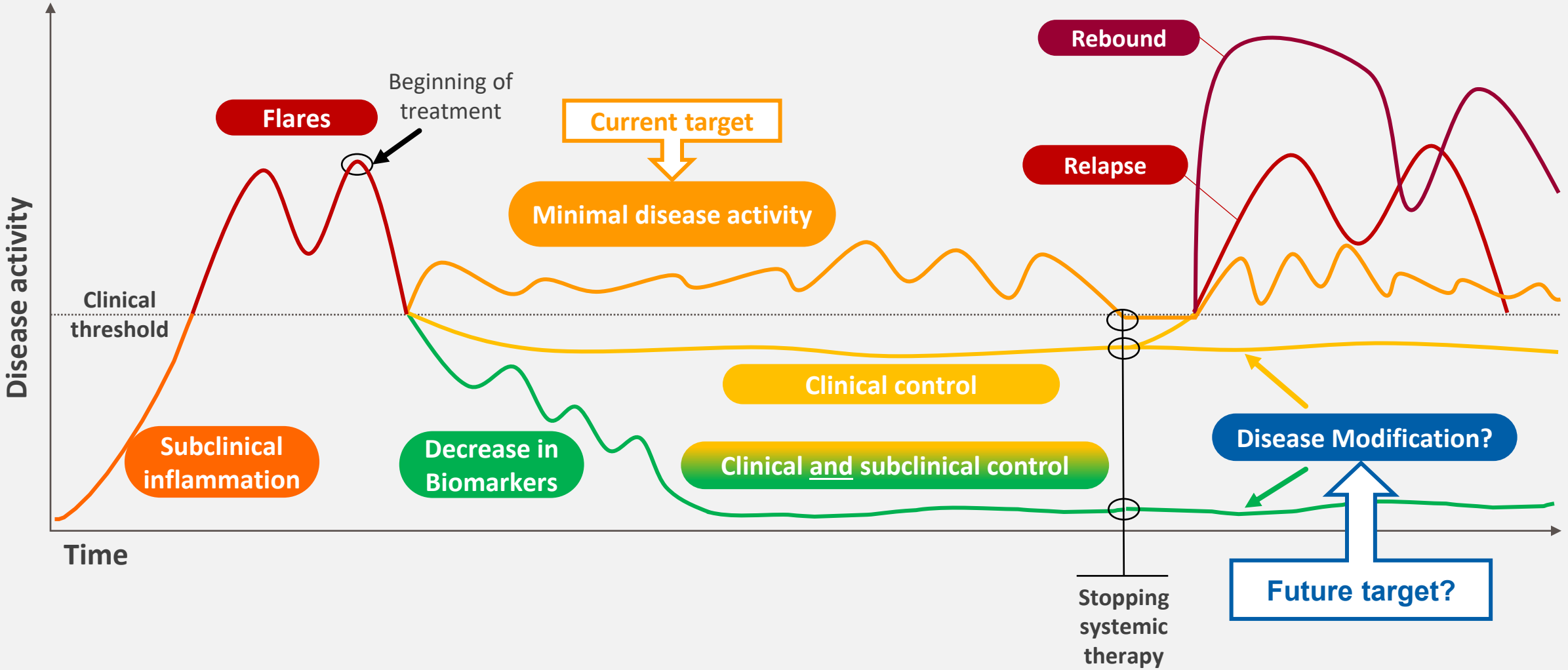


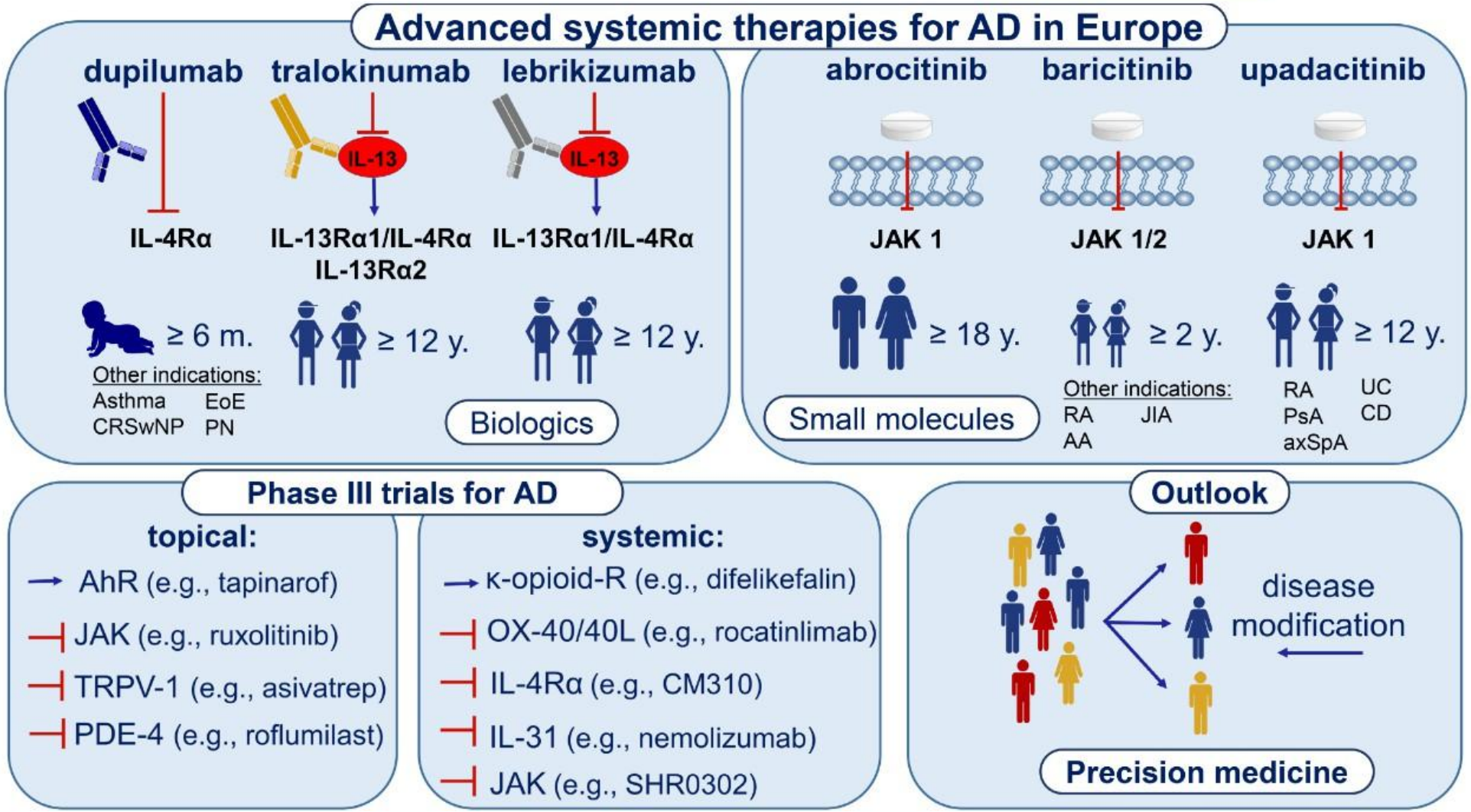
Bieber T, Maintz L, Phad GE, Brüggen MC. From Disease Control to Disease Modification: The Atopic Dermatitis Disease Activity Index. Allergy. 2025 Aug 29

To Achieve Modification of Disease Course, Both Clinical and Subclinical Control of AD Might Be Required



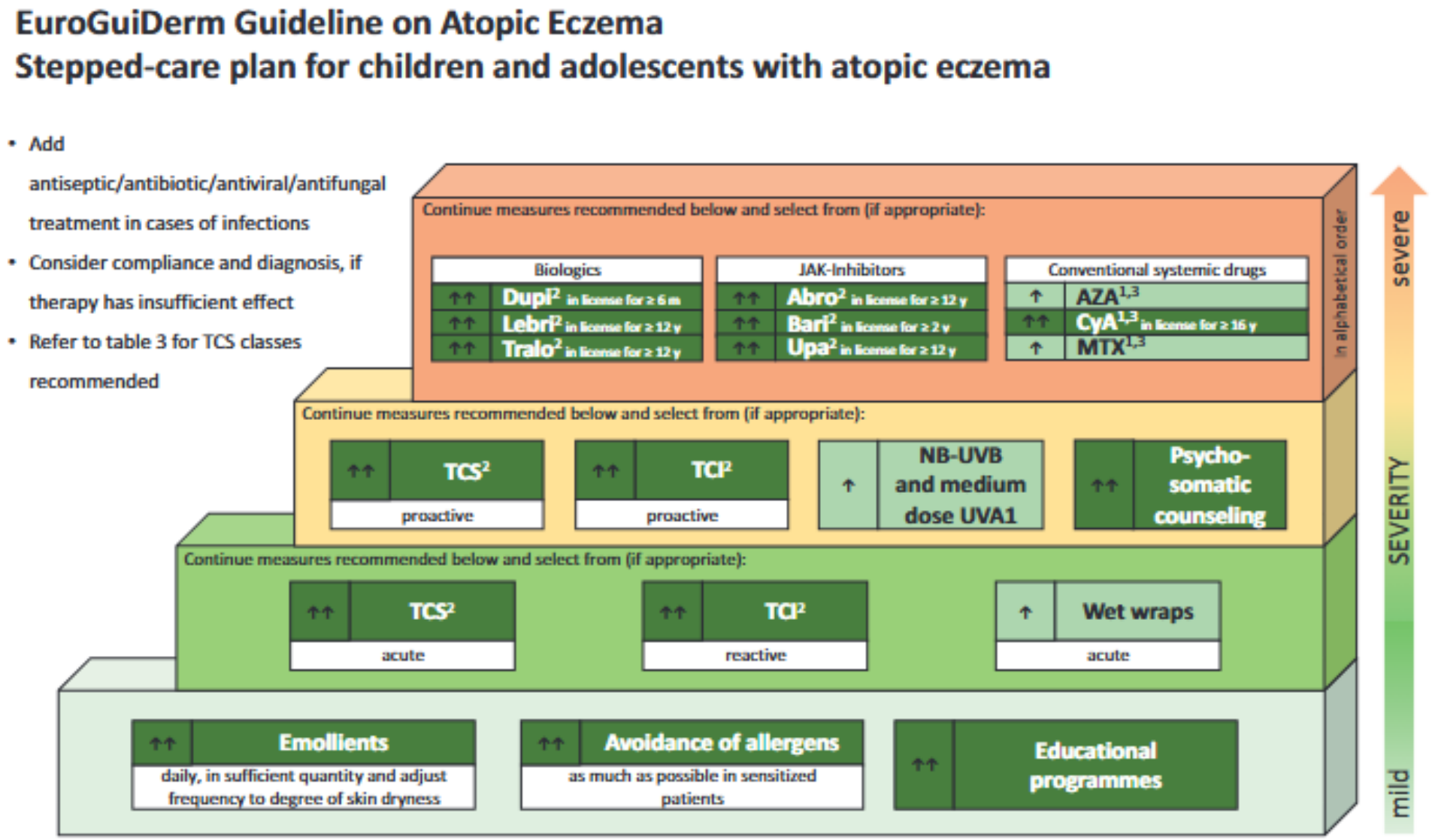
Not drawn to scale.

Figure adapted from: 1. Elaine C. Siegfried, et al. Clinical Remission and Off-treatment Remission in Pediatric Patients with Moderate-to-Severe Atopic Dermatitis Treated with Dupilumab: Preliminary Data from an Open-label Extension Study. *WCPD, April 8-11,* 2025, Buenos Aires, Argentina, Poster ID: 339. Graphic designed by Dr Ana Rossi (Sanofi) and Sonya Cyr (Regeneron) ©



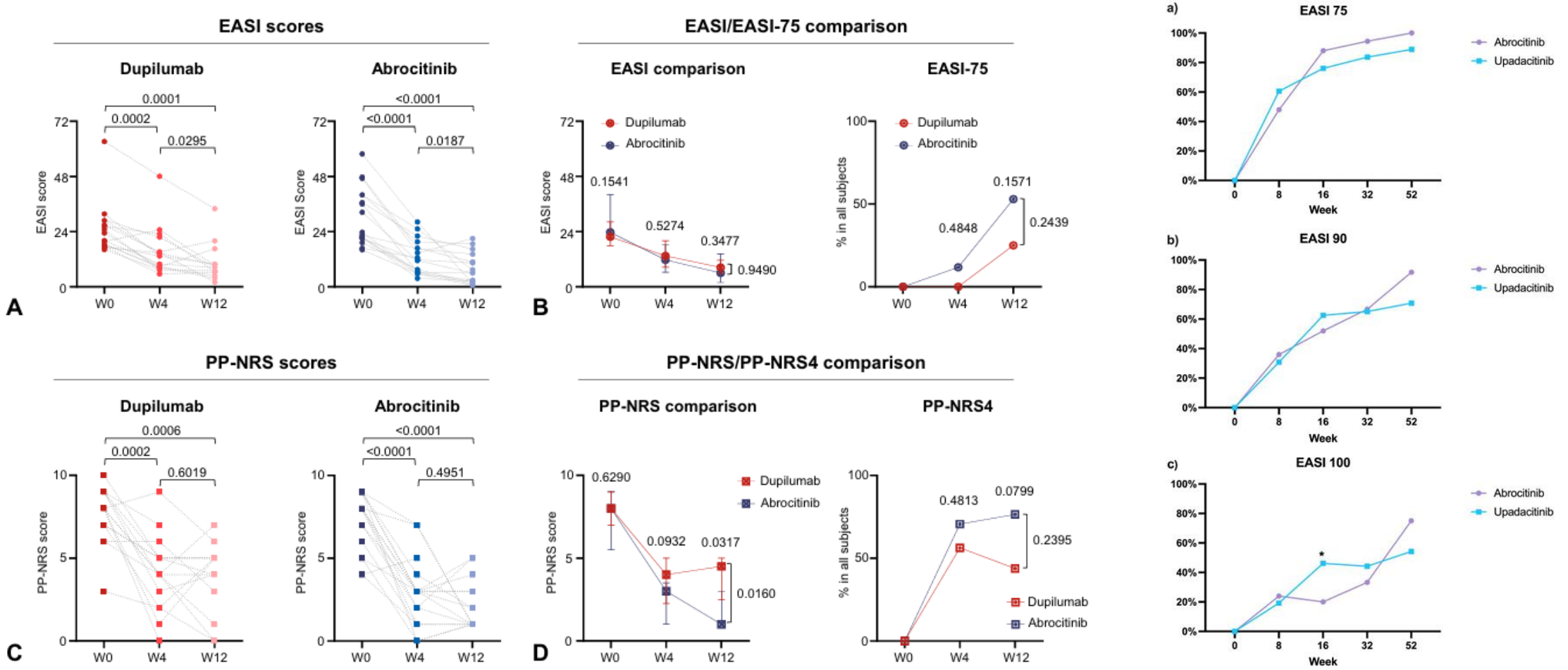
Müller S, Maintz L, Bieber T. Treatment of atopic dermatitis: Recently approved drugs and advanced clinical development programs. Allergy. 2024 Jan 8. doi: 10.1111

Wollenberg A et al. European Guideline (EuroGuiDerm) on atopic eczema: Living update. J Eur Acad Dermatol Venereol. 2025 May 2. doi: 10.1111



Chang JW et al……., Wang F. Abrocitinib versus dupilumab: Impact on skin barrier function and proteomics in atopic dermatitis. J Am Acad Dermatol. 2025 Apr 15:S0190-9622(25)00621

Ibba L et al.. Gargiulo L.
Real-World Effectiveness and Safety of Upadacitinib and Abrocitinib in Moderate-to-Severe Atopic Dermatitis: A 52-Week Retrospective Study.
J Clin Med. 2025 Apr 24;14(9):2953



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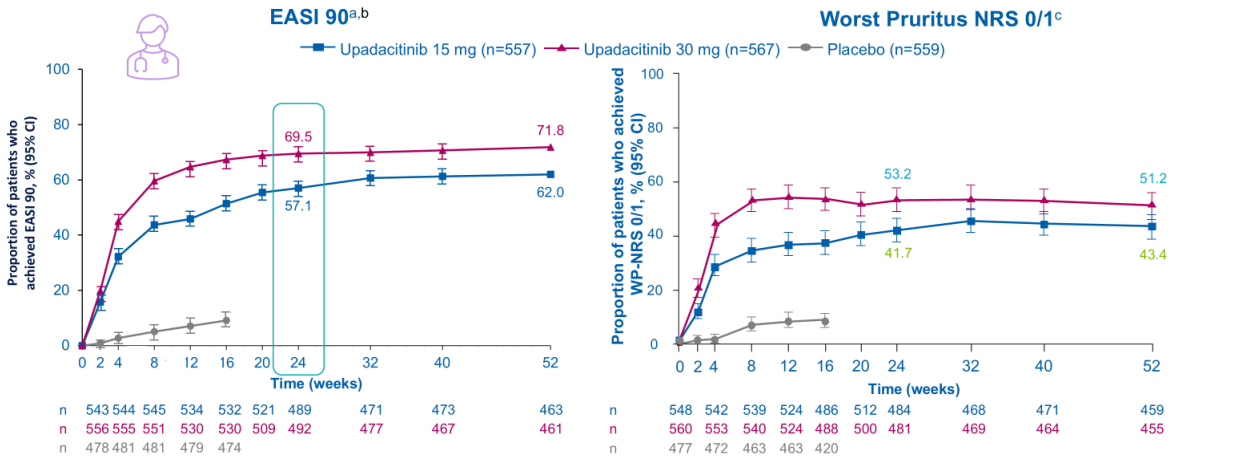
Reaching the optimal target with Upadacitinib



[a]Combined data from Measure Up 1 and Measure Up 2 studies (ITT population, NRI-C analysis). [b]Response rates at each visit. Weeks 2 and 16 were multiplicity controlled. Missing due to COVID-19 which were imputed by MI: 1 in upadacitinib 15 mg, 5 in upadacitinib 30 mg, and 1 in placebo at Week 12; and 1 in upadacitinib 15 mg, 6 in upadacitinib 30 mg, and 5 in placebo at Week 16. [c]For patients with Worst Pruritus NRS >1 at baseline
CI, confidence interval; COVID-19, coronavirus disease 2019; EASI 90, ≥90% improvement in Eczema Area and Severity Index; WP-NRS, Worst Pruritus Numeric Rating

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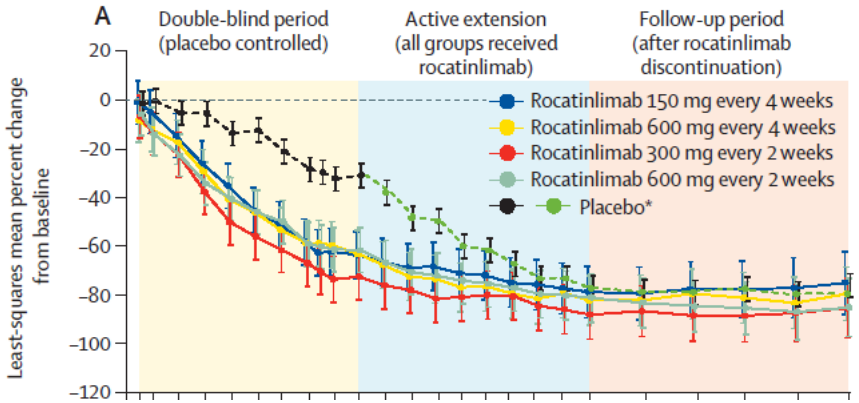
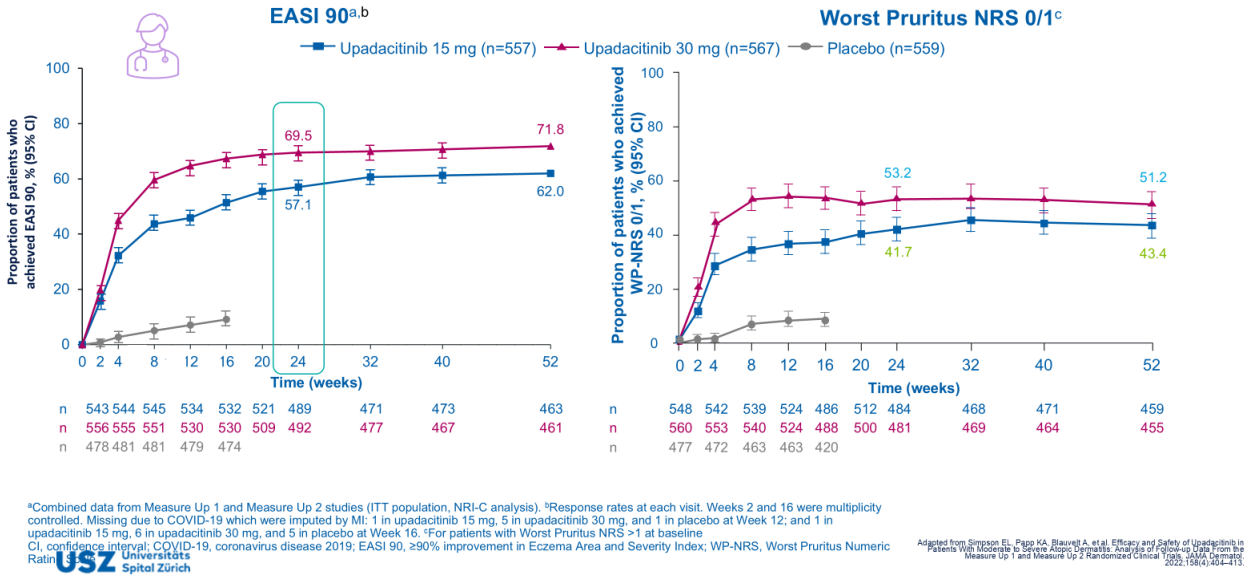
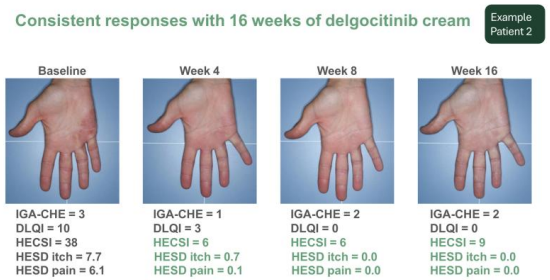
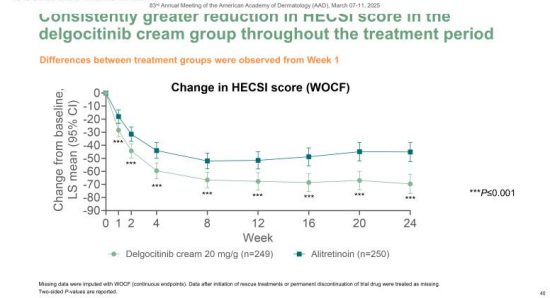
Adapted from Simpson EL, Papp KA, Blauvelt A, et al. Efficacy and Safety of Upadacitinib in Patients With Moderate to Severe Atopic Dermatitis: Analysis of Follow-up Data From the Measure Up 1 and Measure Up 2 Randomized Clinical Trials. JAMA Dermatol. 2022;158(4):404–413.

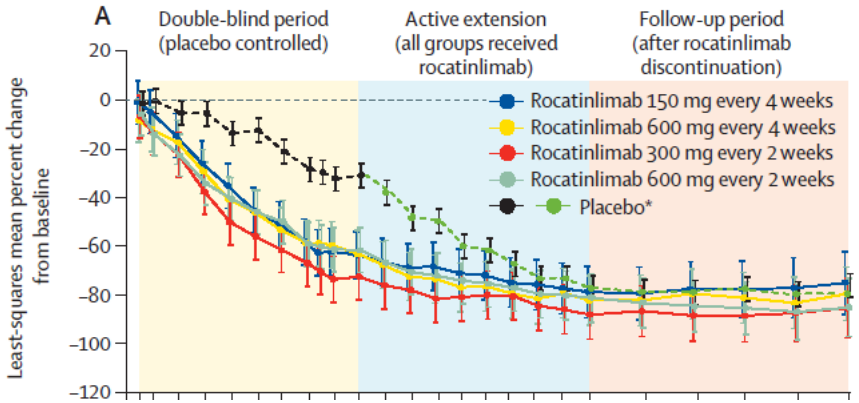


Guttman-Yassky E. et al An anti-OX40 antibody to treat moderate-to-severe atopic dermatitis: a multicentre, double-blind, placebo-controlled phase 2b study. Lancet. 2023 Jan 21;401(10372):204-214









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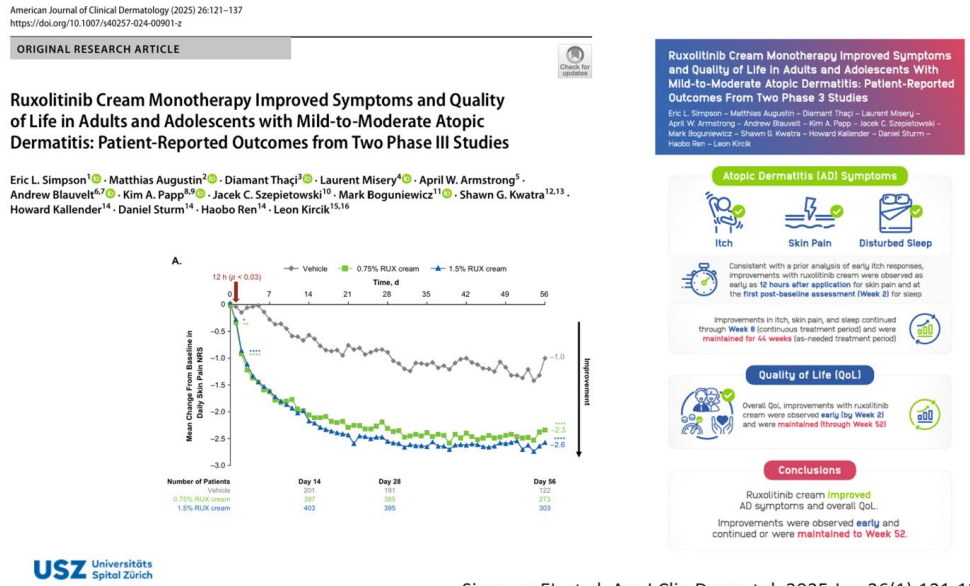
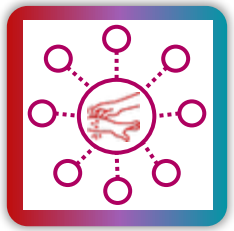


Simpson EL et al. Am J Clin Dermatol. 2025 Jan;26(1):121-137

Disease Modification in AD – A Complex and Evolving Definition*[1,2]

Modification of the disease itself[1]

*"Any intervention that endurably impacts the **pathomechanisms** and the **natural course of the disease** leading to a **sustained remission** after cessation of treatment"*



Impact on associated comorbidities[1]

*"Any intervention successfully **preventing the development or the progression of atopic comorbidities** (food allergy, allergic asthma and/or allergic rhinitis, before or during their development)"*

Unique disease characteristics make it difficult to clearly define what disease modification means for AD

AD is not universally progressive in nature[2]

Disease course varies widely by individual[2]

Spontaneous remission is common in pediatric patients[2]

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*There is currently no agreed upon definition for disease modification. The concepts provided here are to facilitate discussion.
Figures adapted from: 1. Bieber T. *Nat Rev Drug Discov*. 2023;22:662–680 and 2. Jacobson ME, et al. *J Eur Acad Dermatol Venreol*. 2024;38(4):665-672.

Can we achieve a preventive effect on AD or on the Atopic march?

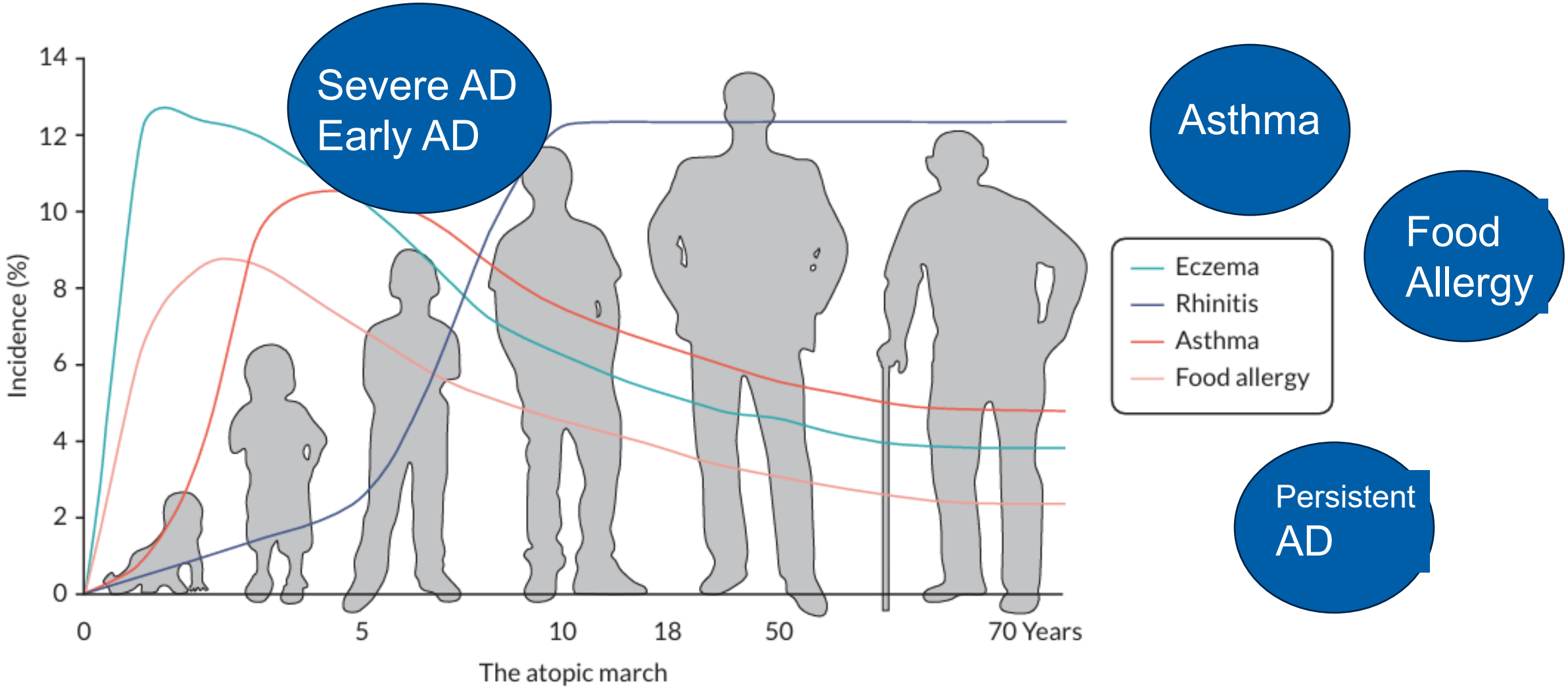
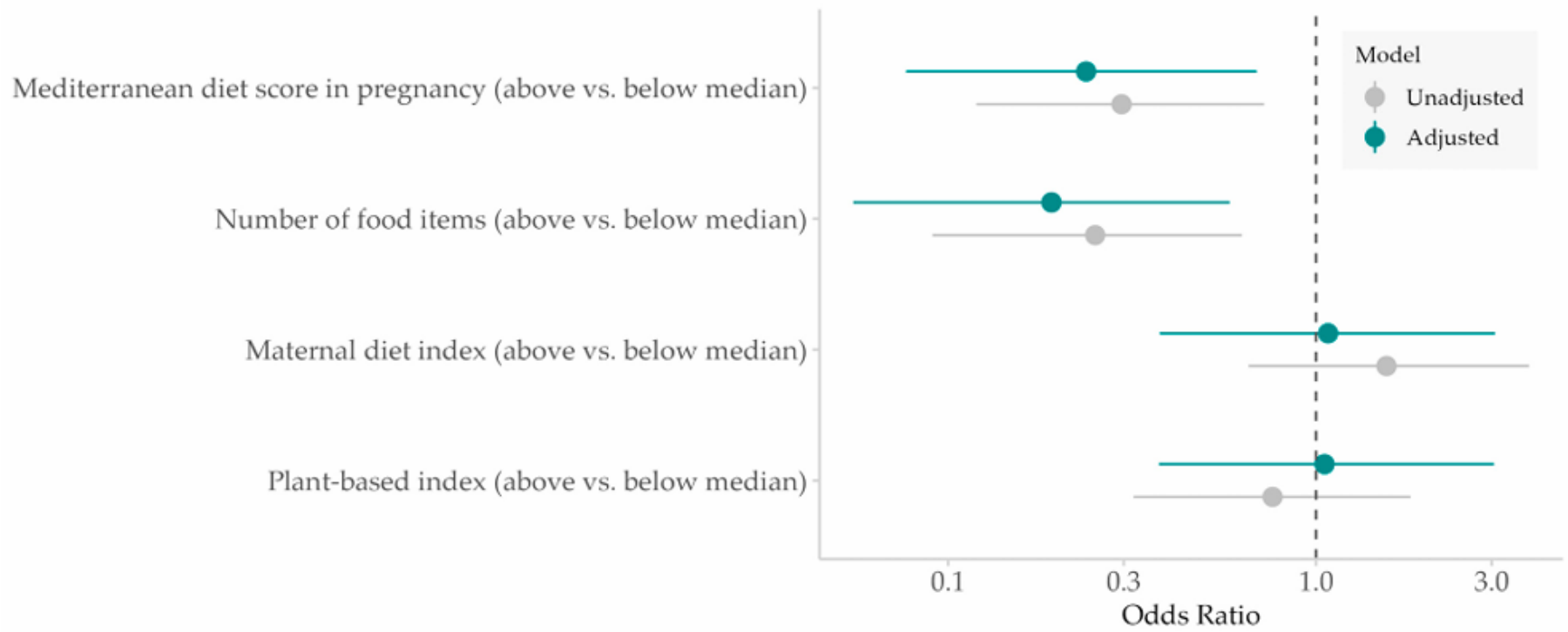


FIGURE 1 Illustration of the typical onset of symptoms of allergic diseases during childhood. Reprinted from Davidson*et al.* (2019),[15] Copyright (2023), with permission from Elsevier.

Influence on diet during pregnancy on the development of AD in the child

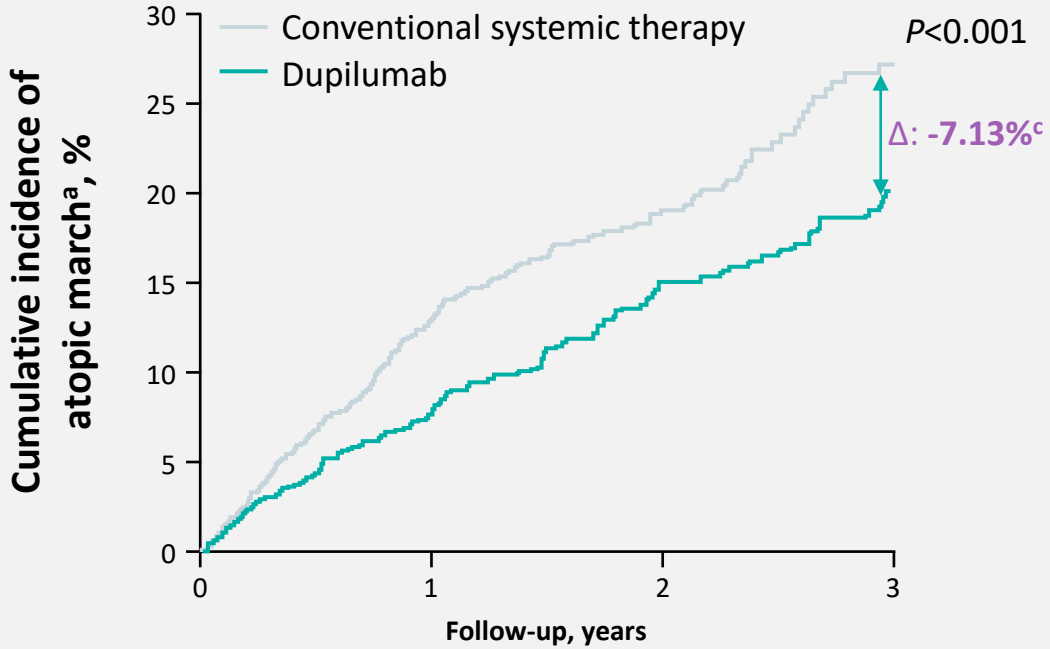


Heye KN et al. Diet Diversity and Adherence to a Mediterranean Diet Pattern in Pregnancy Is Protective Against the Development of Early-Childhood Atopic Dermatitis. Nutrients. 2025 Jul 7;17(13):2243.

Early Intervention with Dupilumab May Be Associated with Reduced Risk of Atopic Comorbidities in Pediatric Patients With AD[1]

TriNetX

Cumulative incidence of atopic march progression[a] in pediatric AD patients (≤18 years) treated with dupilumab vs conventional systemic therapy[b,1]

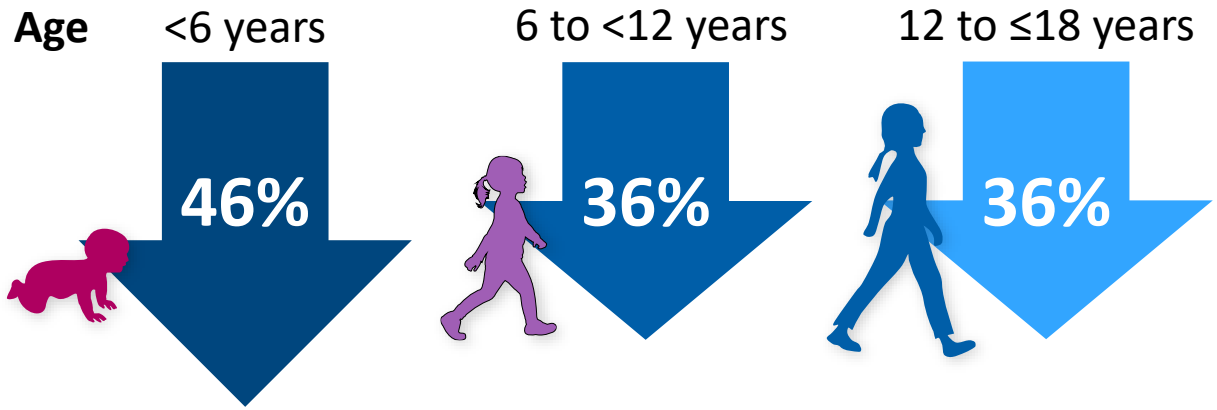


Number at risk

Dupilumab	2190	2097	2022	1943	1861	1823	1752
Conv Ther	2192	2043	1905	1831	1774	1690	1595

Risk of atopic march progression[a] with dupilumab vs conventional systemics stratified by age during the 3-year observation period[1]

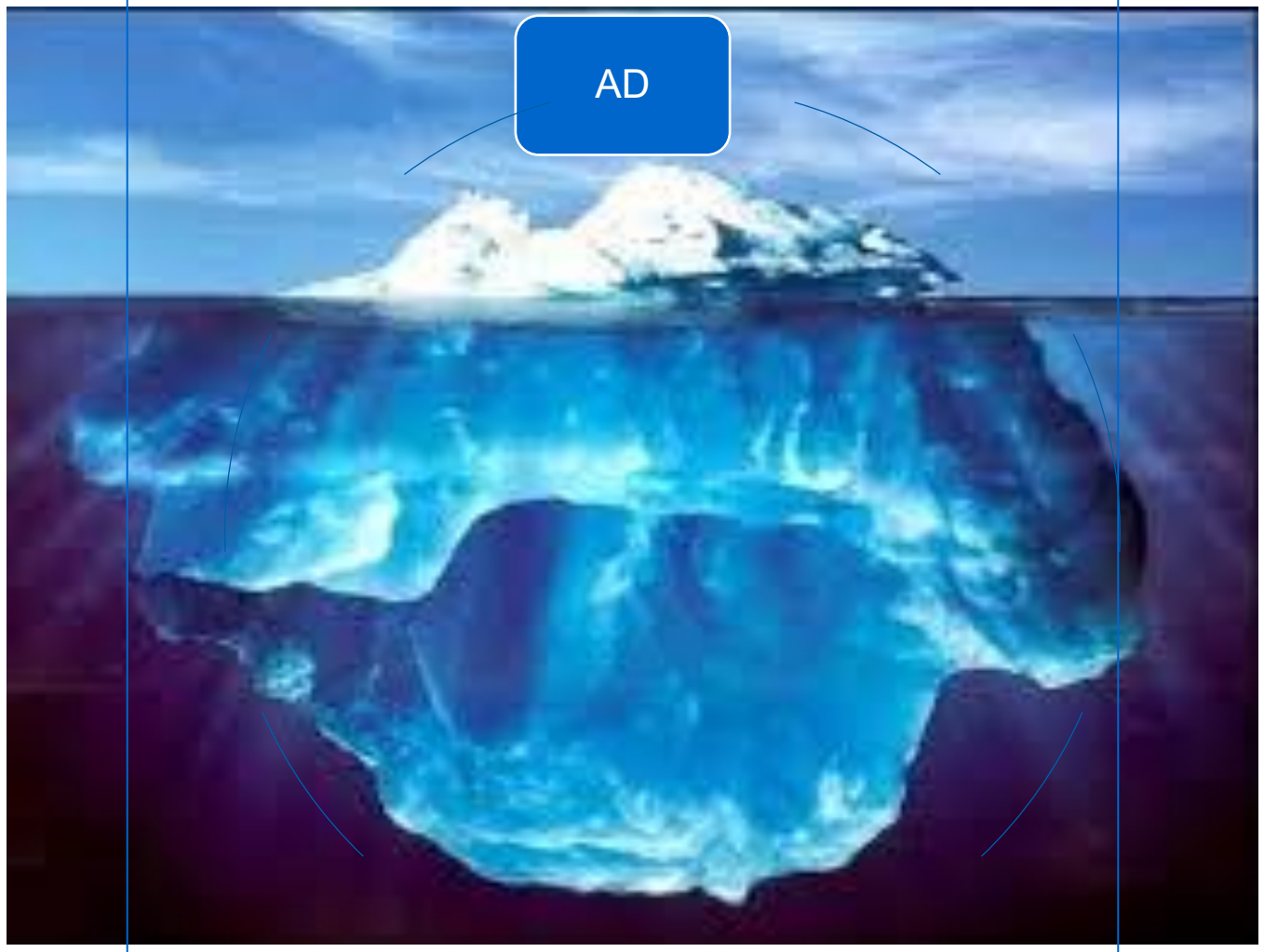
Reduced risk of **atopic march progression** in patients treated with dupilumab across age groups, with younger patients showing a greater reduction[d,1]



Graph adapted with permission from Lin T-L, et al. 2024.

Figures adapted from: 1. Lin T-L, et al. *J Am Acad Dermatol*. 2024;91:466–473.

Comorbidities in Atopic Dermatitis:



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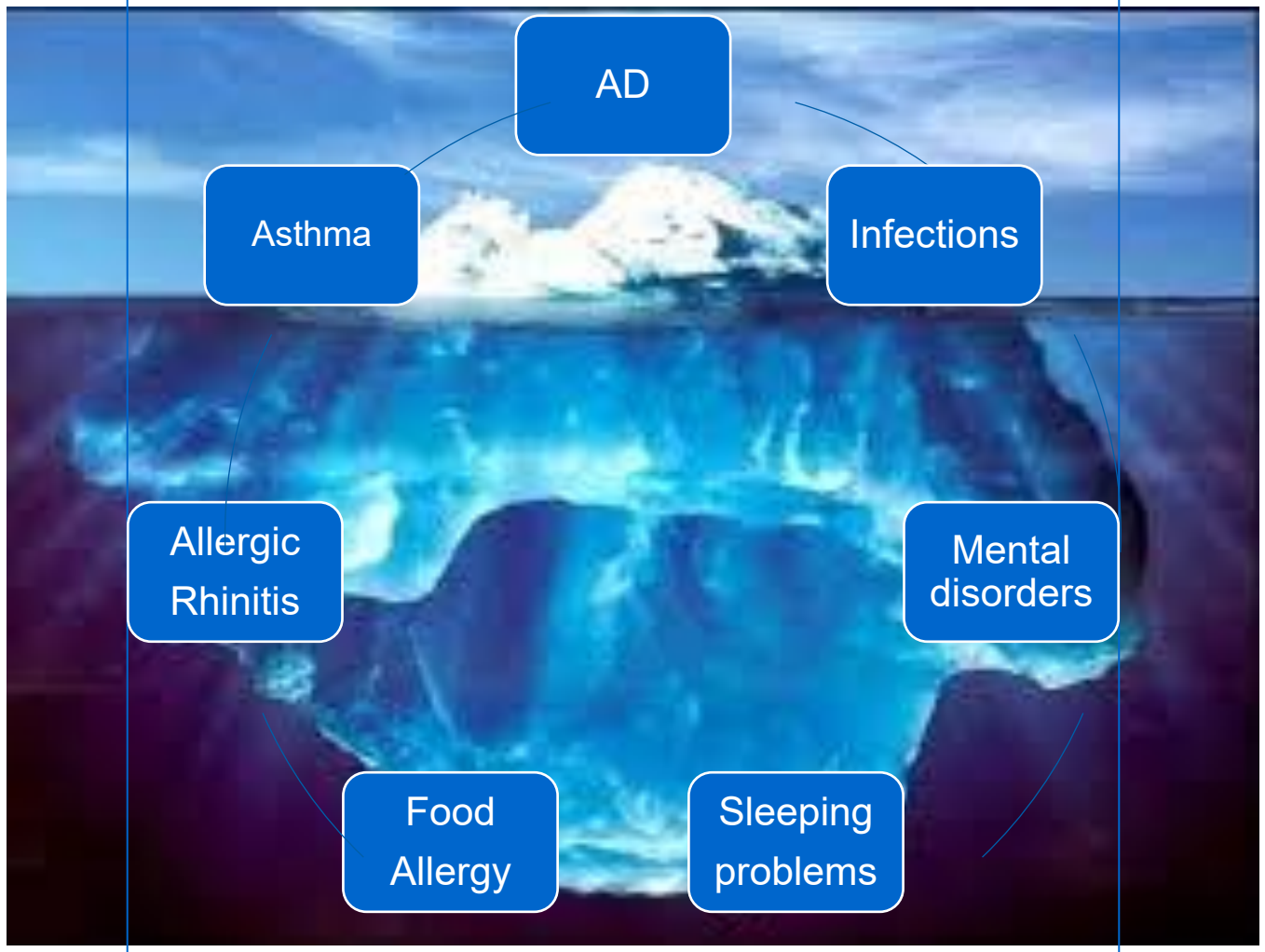

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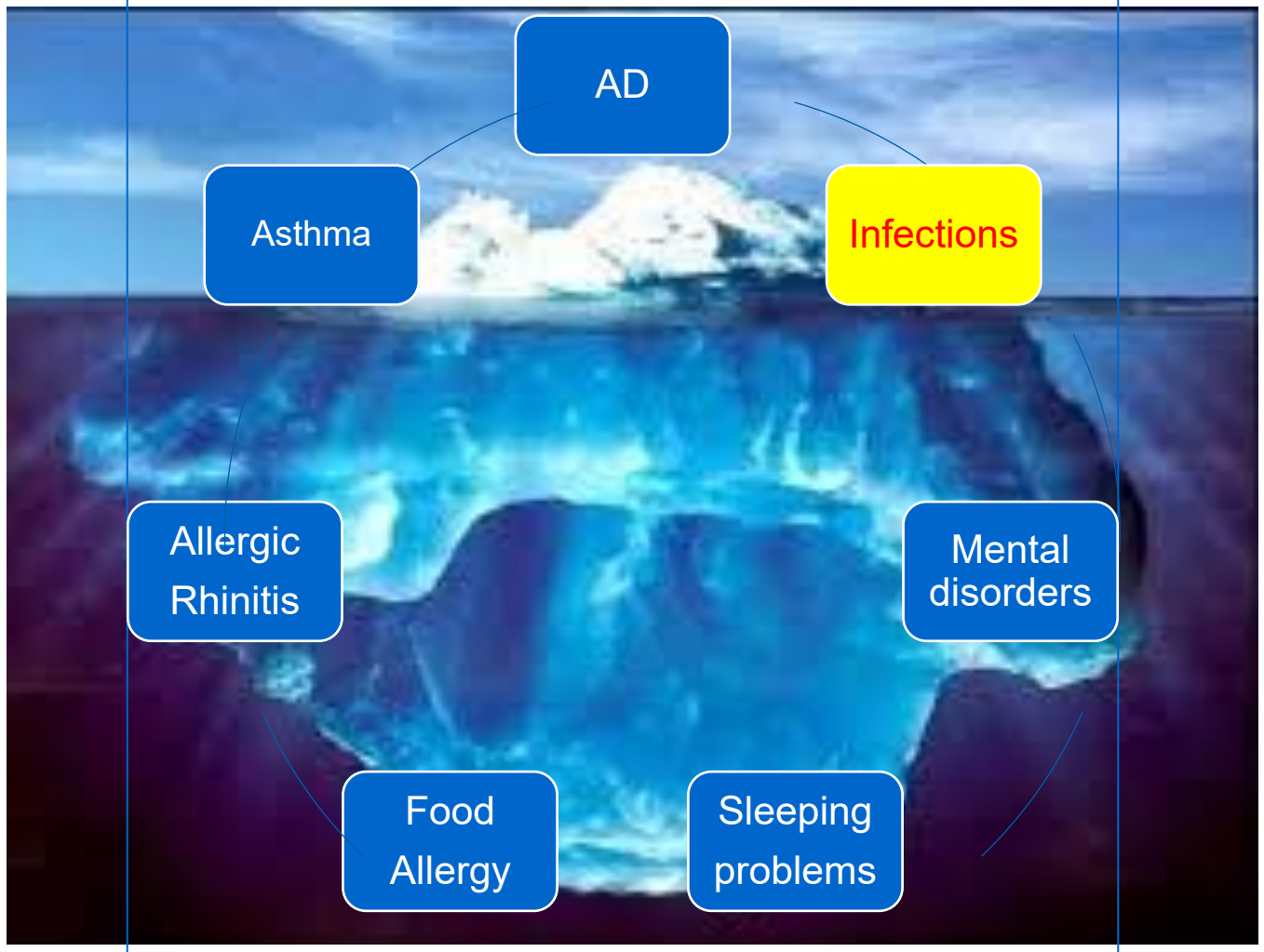


Patients With Moderate-to-Severe AD Have an Increased Risk of Skin Infection, Including Infections With *S. aureus*[1,2]

Bacterial infections

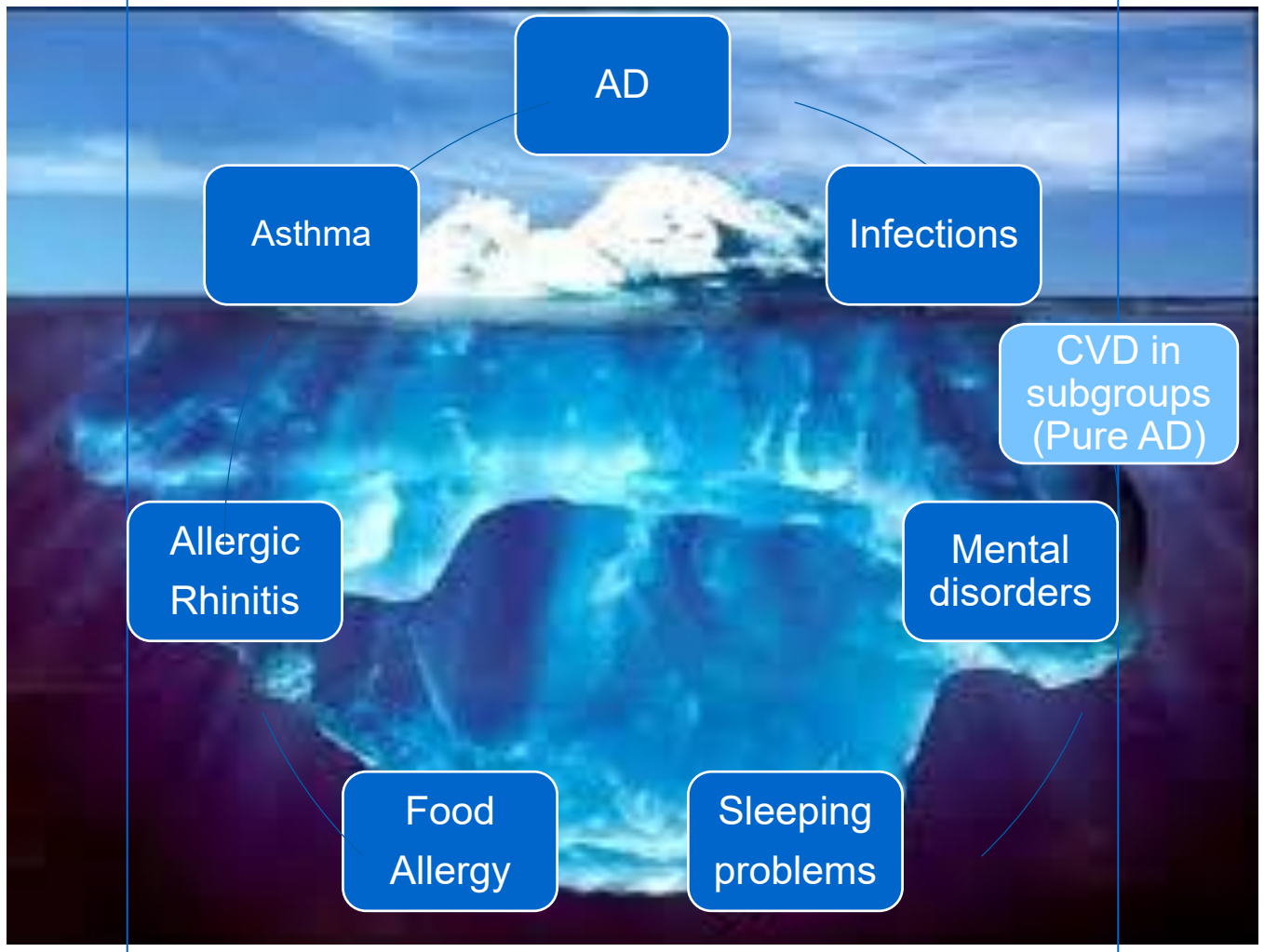
***S. aureus* infections**

Viral infections

Photo courtesy: Dr Vania Carvalho for viral infections; Prof. Peter Schmid for S.aureus and bacterial infections

1. Wang V. *Ann Allergy Asthma Immunol*. 2021;126:3–12. 2. Alexander H, et al. *British J Dermatol*. 2020;182:1331–1342.

Comorbidities in Atopic Dermatitis:



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Review

Current updates in the epide dermatitis

Shanthi Narla, MD*; Jonathan I. Silv

* Department of Dermatology, Medical College of Wisconsin, M
† Department of Dermatology, The George Washington Univer

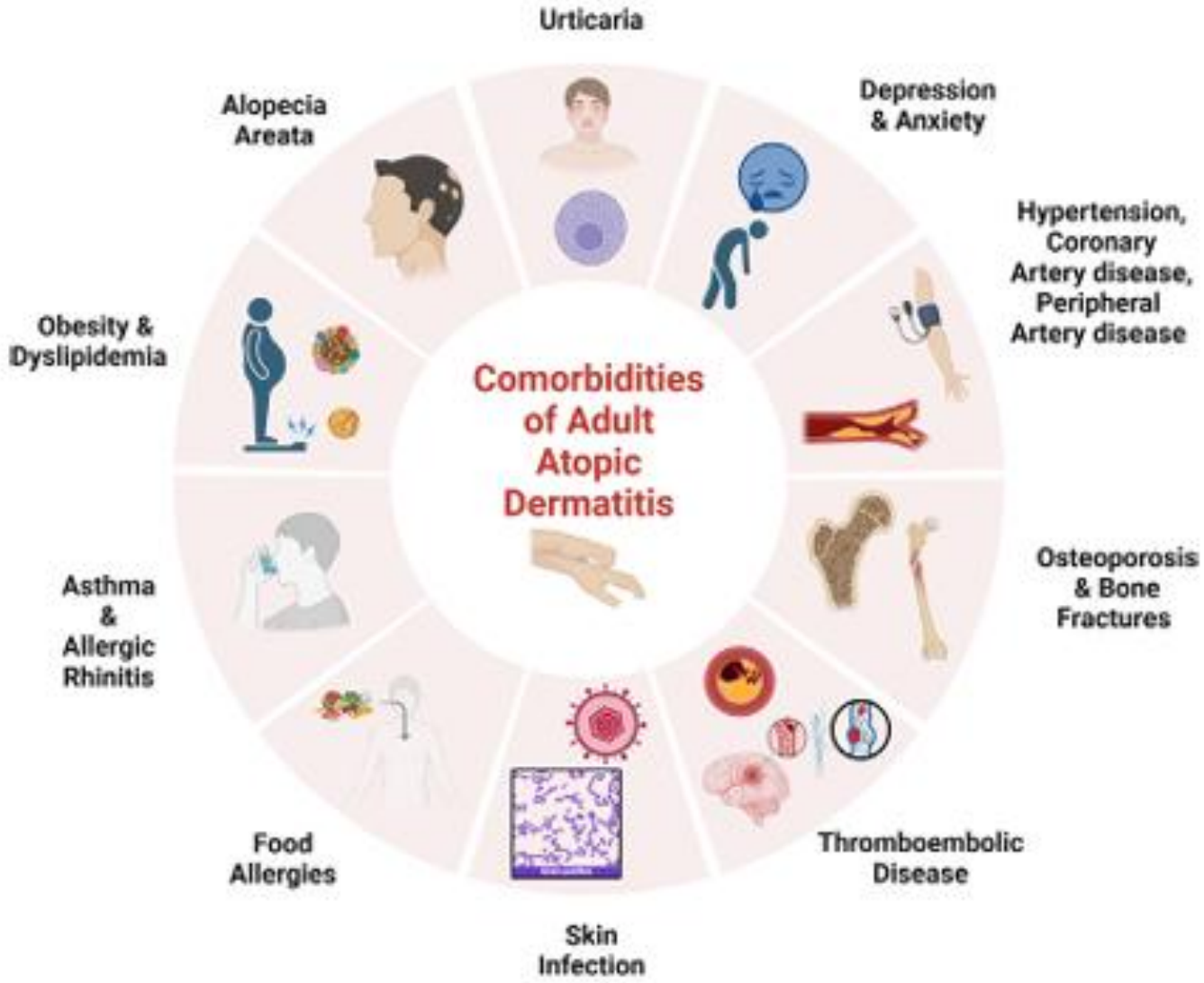

Figure 2. Comorbidities deemed moderately to highly probably associated with adult atopic dermatitis according to the American Academy of Dermatology guidelines on comorbidities. Created in BioRender.

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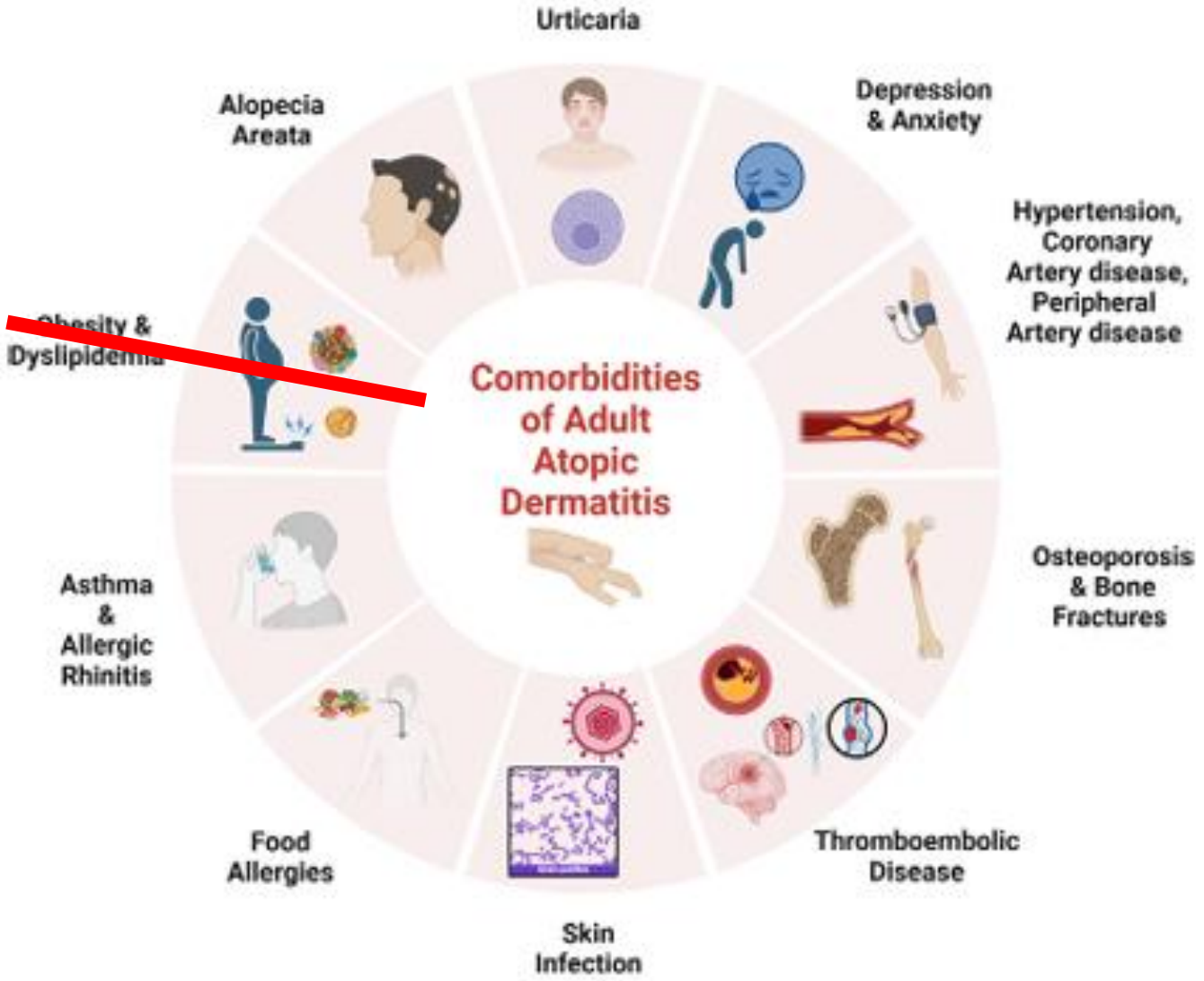

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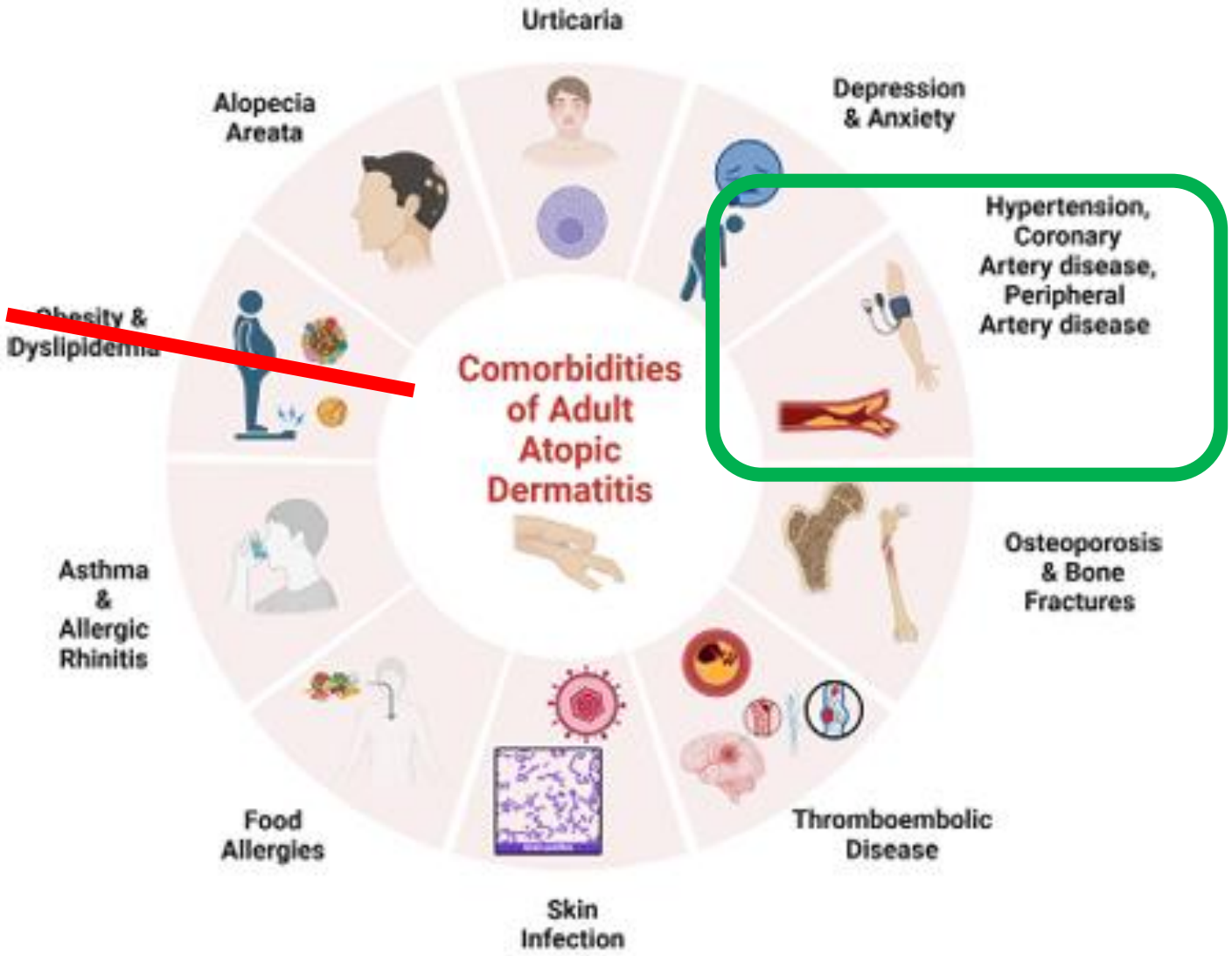

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Allergy EUROPEAN JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY

EAACI

ORIGINAL ARTICLE | Full Access

Deciphering the Connection Between Atopic Dermatitis and Cardiovascular Diseases: Analysis of Clinical Associations and Cardiometabolic Proteins

Danielle Fehr, Van Hung Huynh-Tran, Laura Maintz, David Niederseer, Milad Ameri, Anita Dreher, Cezmi A. Akdis, Roger Lauener, Claudio Rhyner, Claudia Traidl-Hoffmann, Peter Schmid-Grendelmeier, Thomas Bieber, Marie-Charlotte Brüggen ... See fewer authors

- 677 AD patients and 79 nonatopic controls from an observational multicenter case–control study (ProRaD:Prospective longitudinal study investigating the remission phase in patients with atopic dermatitis and other allergy-associateddiseases).
- AD severity and atopic metabolic, and cardiovascular conditions as well as risk factors
- Serum samples: targeted proteomics (cardiometabolics panel, Olink)

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Fehr D et al. Deciphering the Connection Between Atopic Dermatitis and Cardiovascular Diseases: Analysis of Clinical Associations and Cardiometabolic Proteins. Allergy. 2025 May 19

Disease severity may be a risk factor for CVD in pure AD patients, but not in those with atopic comorbidities

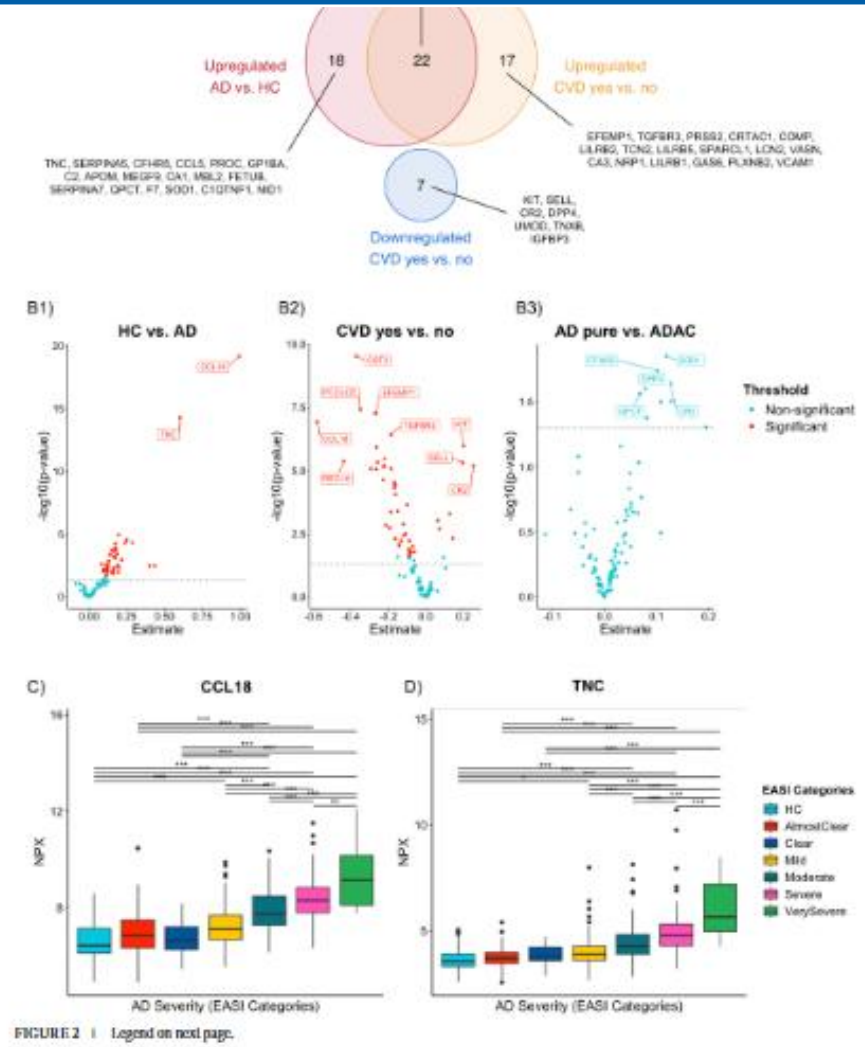
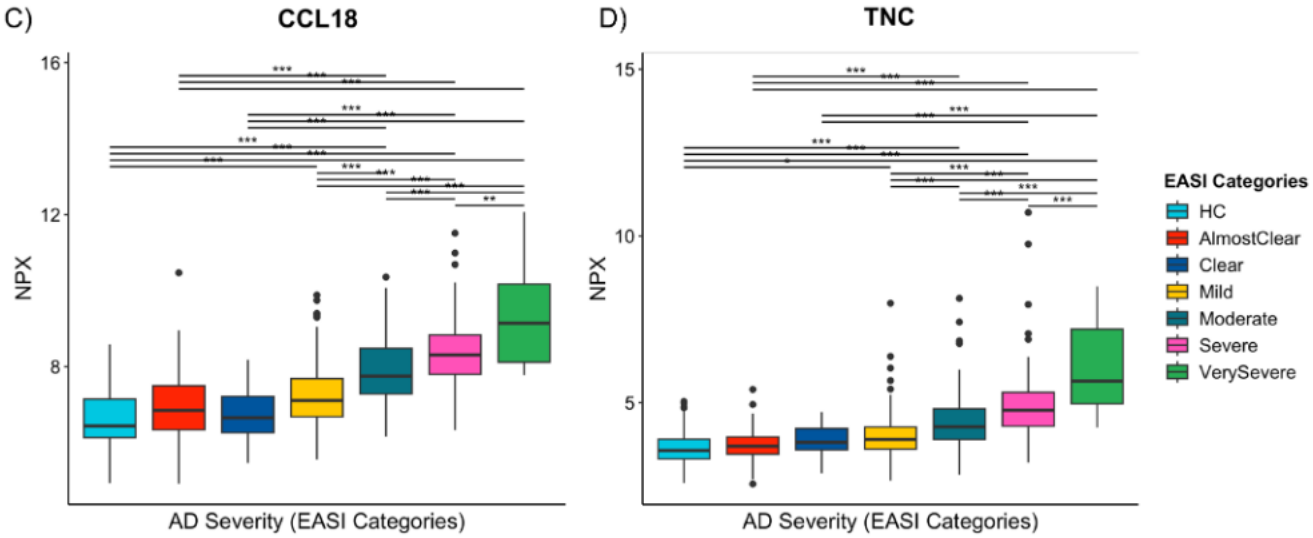


FIGURE 2 | Legend on next page.



TNC, tenascinC;

USZ Universitäts Spital Zürich

Fehr D et al. Allergy. 2025 May 19

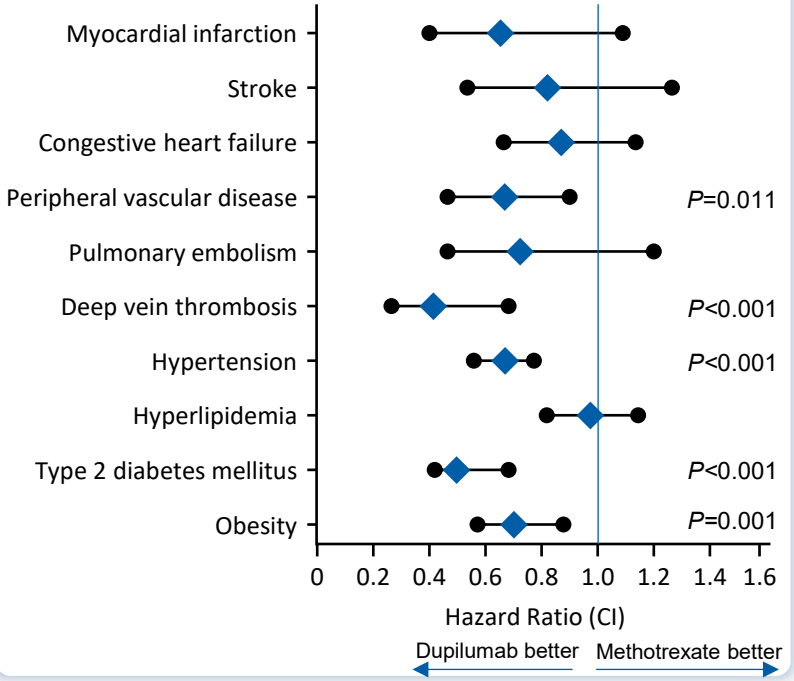
Targeting IL-4 and IL-13 Was Associated with Decreased Cardiometabolic Risk in Adult AD Patients Compared to Conventional Systemics and Oral JAK Inhibitors

TriNetX

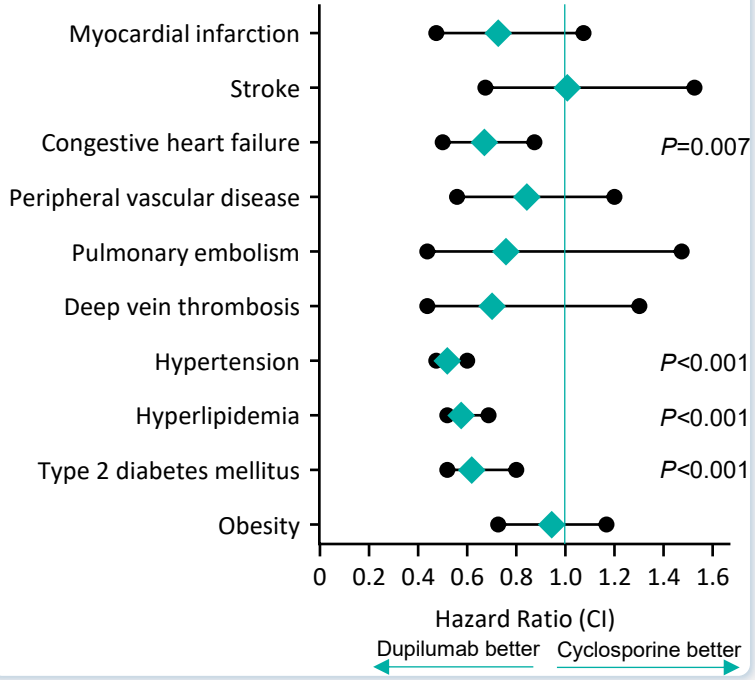
Adults

Risk of cardiovascular and metabolic outcomes among AD patients treated with systemic therapies

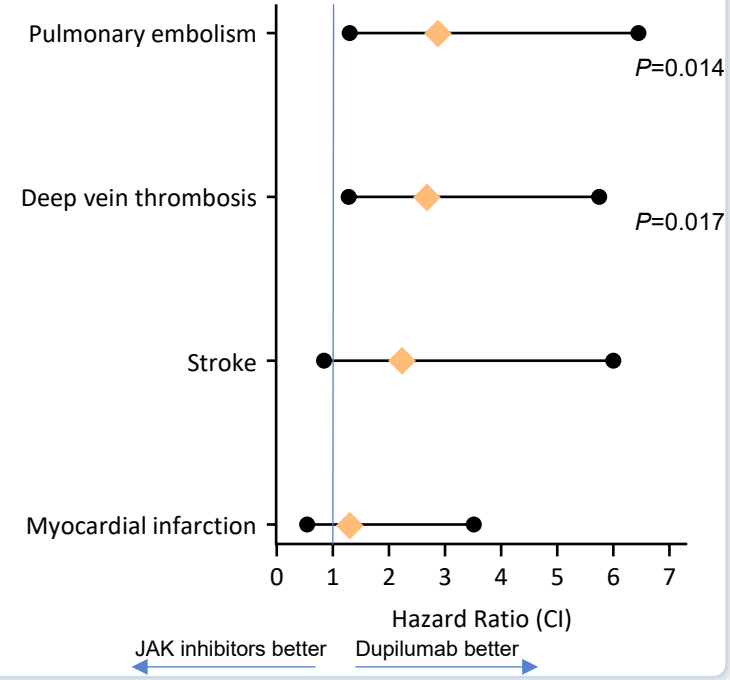
Dupilumab vs Methotrexate[1,a,*]



Dupilumab vs Cyclosporine[1,a]



JAK inhibitors vs Dupilumab[2,b]



[a]Global retrospective cohort study comprised two distinct analyses comparing patients with AD under different treatments: (i) initiators of dupilumab (n= 10,151) versus methotrexate (n= 10,151) and (ii) initiators of dupilumab (n = 6,629) versus TNFi (n = 6,629). Study groups were compared regarding the risk of 8 cardiovascular and 4 metabolic outcomes during the initial year following drug initiation
DM, diabetes mellitus; DVT, deep vein thrombosis; PVD, peripheral vascular disease.

Figures adapted from: 1. Kridin K, et al. *Archives of Dermatological Research*, 2025, 317(1): 296. 2. Kridin K, et al. *J Eur Acad Dermatol Venereol*. Published online July 21, 2025.

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- 2: Different approaches for childhood and adult AD
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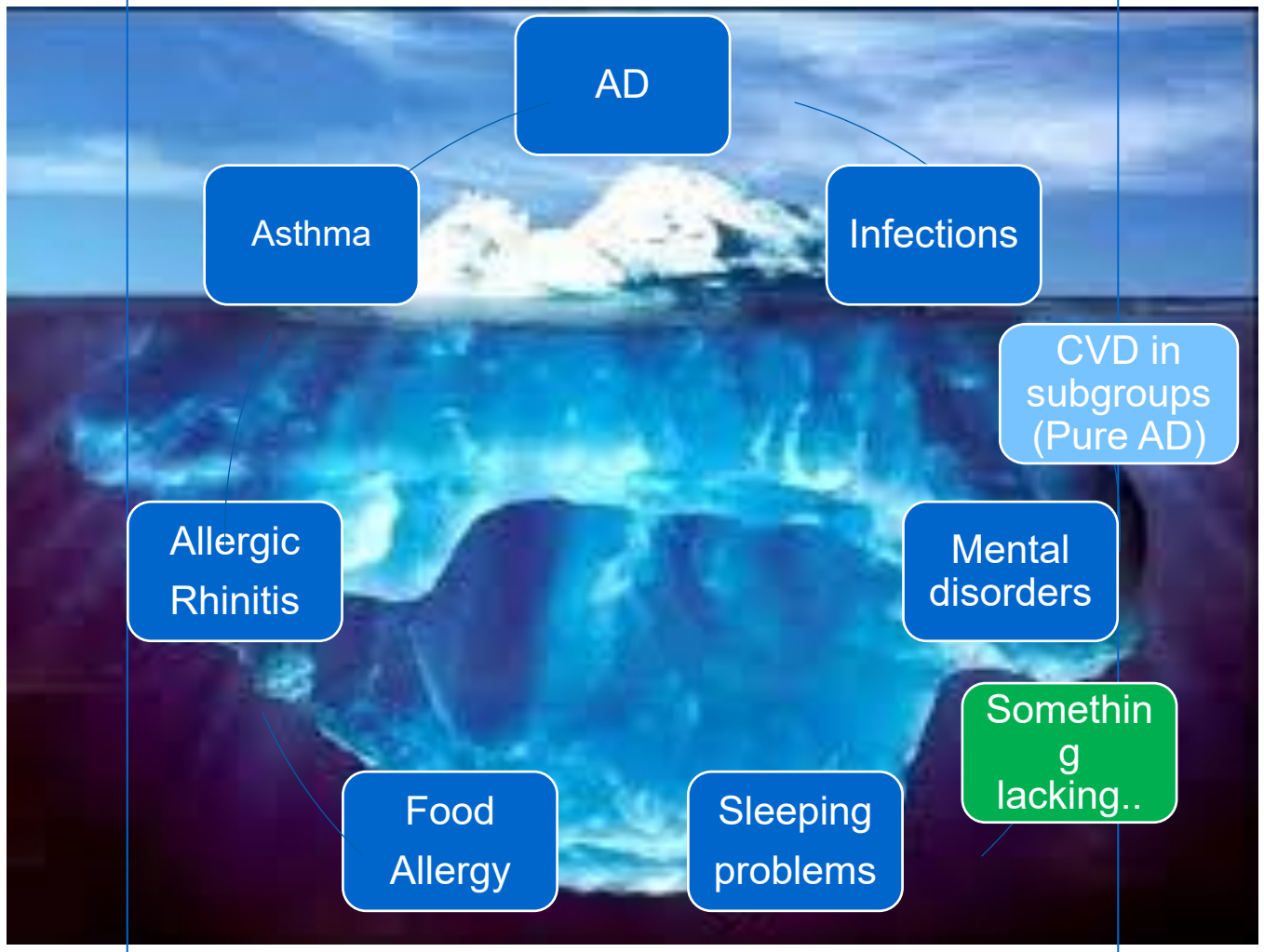
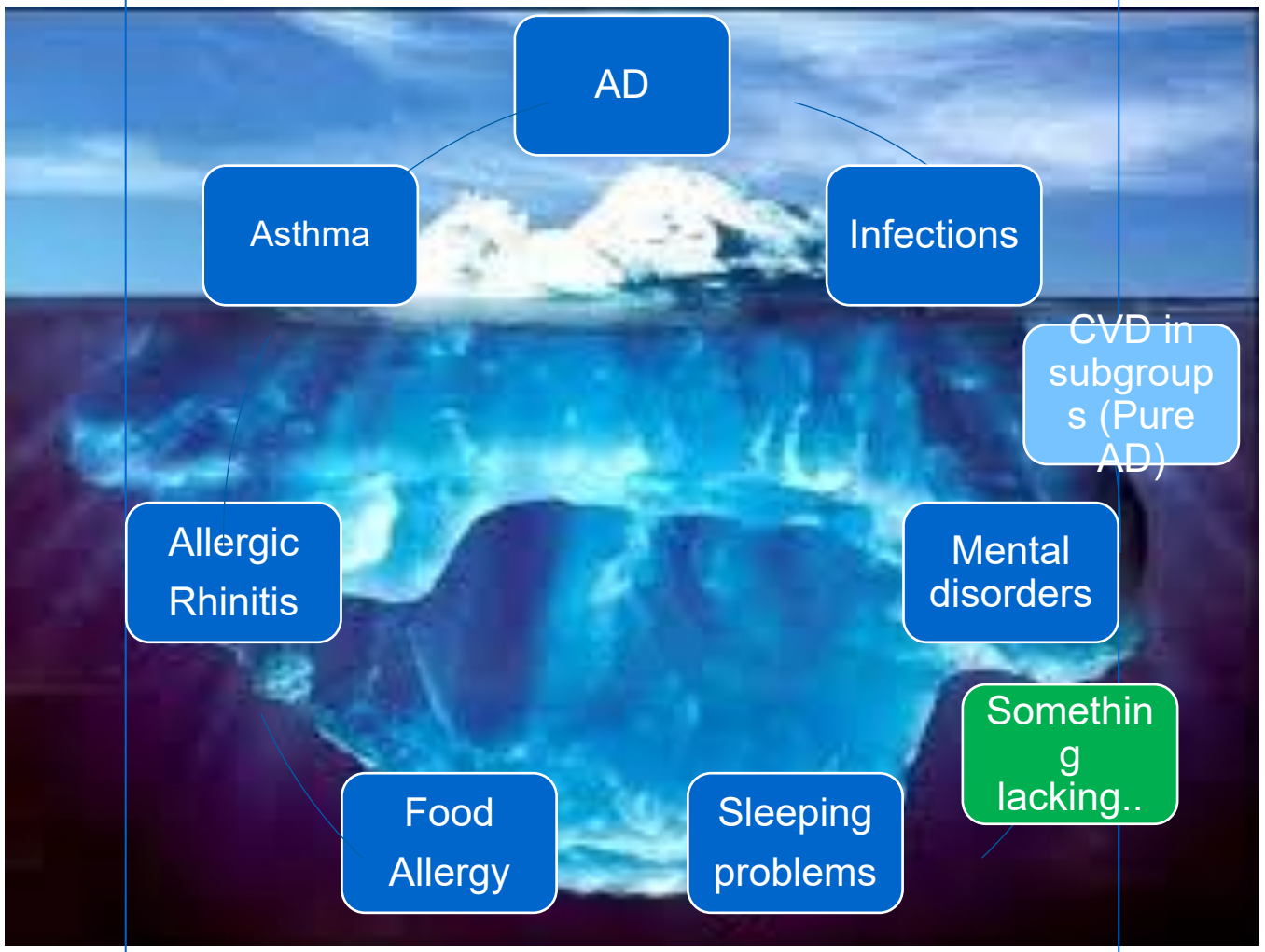
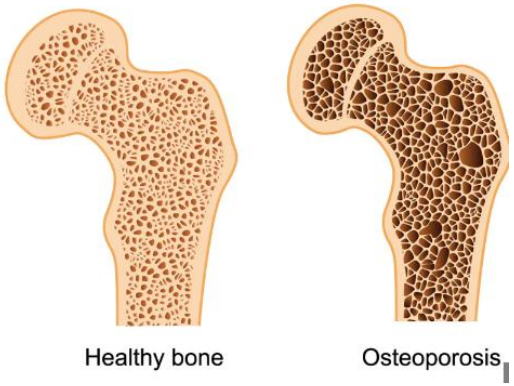
- 5: Adress not only SAD but also comorbidities

Comorbidities in Atopic Dermatitis:



Comorbidities in Atopic Dermatitis:





ELSEVIER

Review

Current updates in the epide dermatitis

Shanthi Narla, MD*; Jonathan I. Silv

* Department of Dermatology, Medical College of Wisconsin, M
† Department of Dermatology, The George Washington Univer

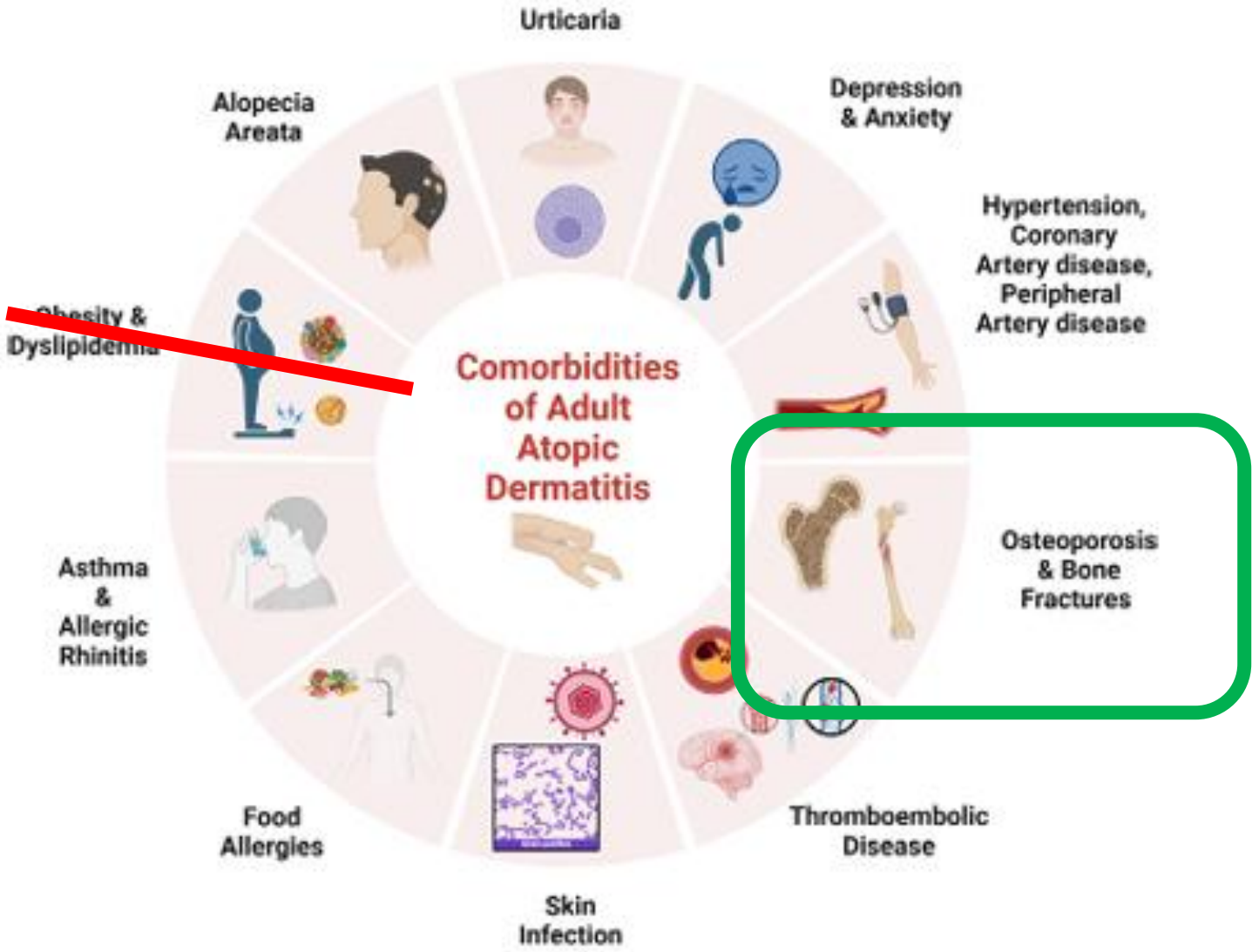


Figure 2. Comorbidities deemed moderately to highly probably associated with adult atopic dermatitis according to the American Academy of Dermatology guidelines on comorbidities. Created in BioRender.

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Bone mineral density, osteopenia osteoporosis, and fracture risk increased in patients with AD

Original Article

Page 1 of 11

Bone mineral density, osteopenia, osteoporosis, and fracture risk in patients with atopic dermatitis: a systematic review and meta-analysis

Di Wu[1#], Xiang-Dong Wu[1#], Xi Zhou[1], Wei Huang[2], Changqi Luo[3], Yong Liu[1]

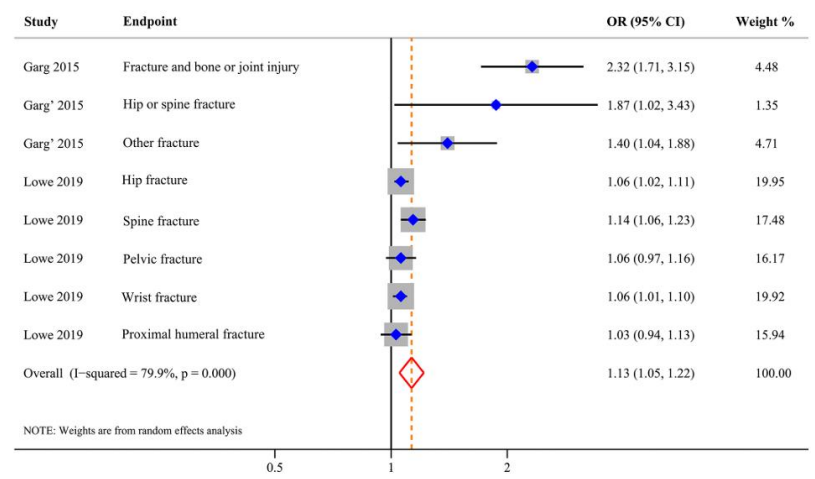

Figure 2 Forest plot showing the risk of fracture in patients with AD. CI, confidence interval; OR, odds ratio.

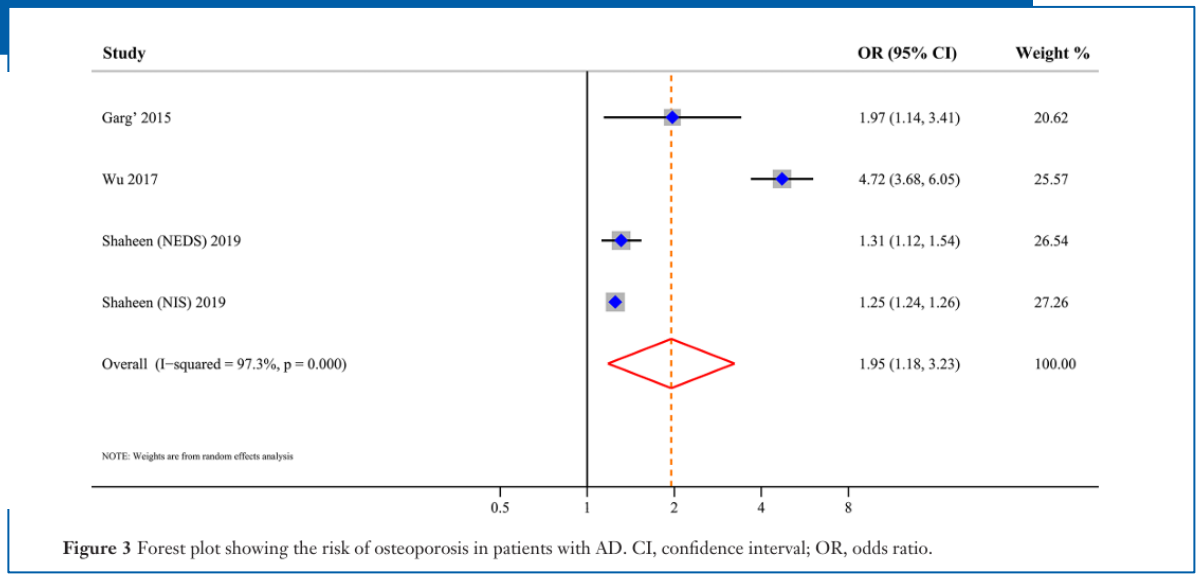

Figure 3 Forest plot showing the risk of osteoporosis in patients with AD. CI, confidence interval; OR, odds ratio.

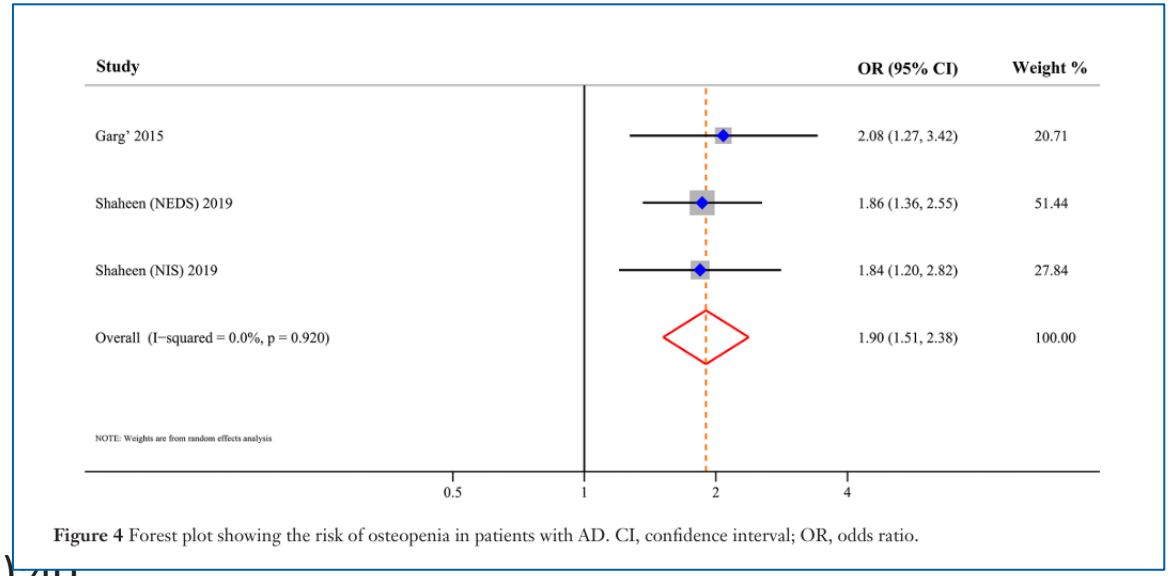

Figure 4 Forest plot showing the risk of osteopenia in patients with AD. CI, confidence interval; OR, odds ratio.

Wu D et al.Ann Transl Med. 2021 Jan;9(1):40

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Fracture incidence in children after developing atopic dermatitis

Allergy EAACI WILEY

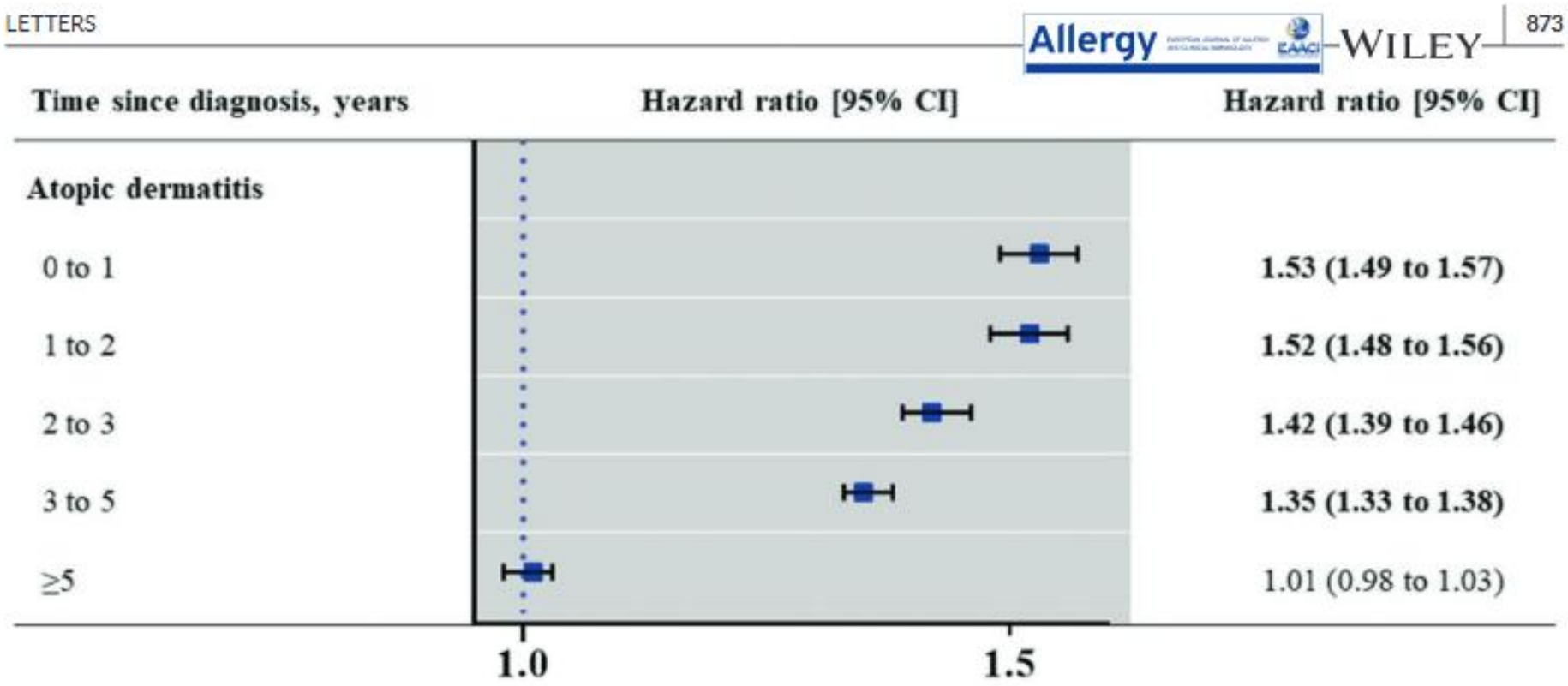

FIGURE 1 Adjusted HR for the likelihood of incident fracture at different time points after AD diagnosis. Blue dots indicate adjusted HR for AD; Whiskers represent 95% CIs. AD, atopic dermatitis; CI, confidence interval; HR, hazard ratio

Lee SW et al. Fracture incidence in children after developing atopic dermatitis: A Korean nationwide birth cohort study. Allergy. 2023 Mar;78(3):871-875

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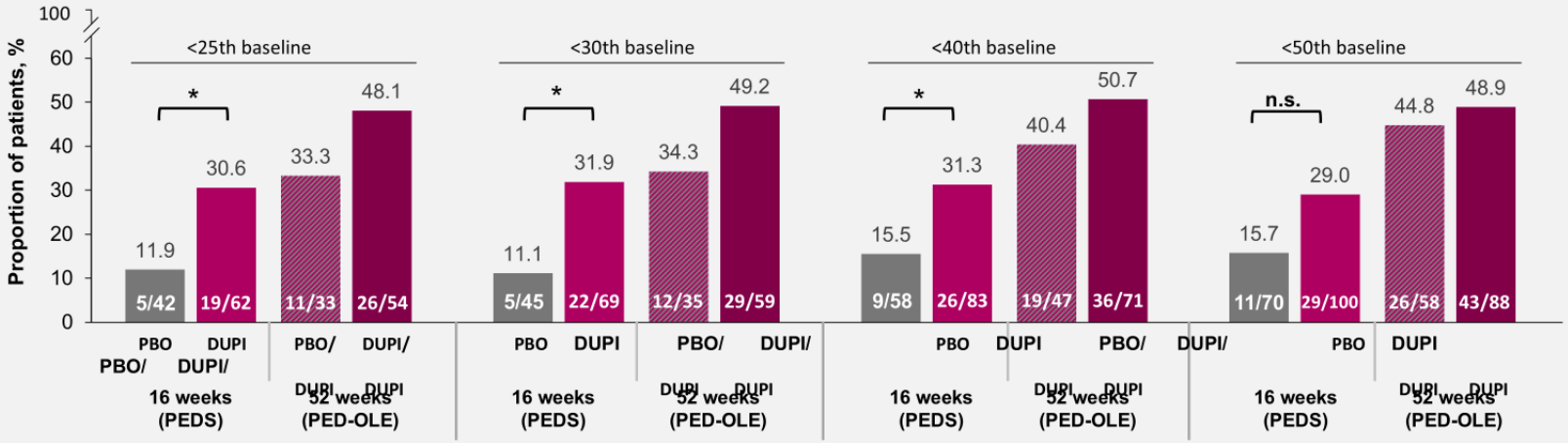
Treatment with Dupilumab Significantly Improved Vertical Growth in Children of Lower Stature with AD[1]

6-11 years

LIBERTY AD PEDS & PED-OLE

PEDS: 16 weeks on PBO/DUPI +TCS
PED-OLE: 36 weeks on DUPI (no TCS)



Catch-up growth observed with dupilumab treatment in the 16-week PEDS trial was reproducible in placebo patients that switched to dupilumab at week 16, with ~33-44% achieving ≥5 percentile height improvement at week 52[1]

*$p<0.05$, n.s., not significant. White numbers inside bars denote number of patients achieving ≥5 percentile improvement over total patients per group.
BL, baseline; PBO, placebo; DUPI, dupilumab; PBO/DUPI, placebo group in PEDS that transitioned to dupilumab treatment in PED-OLE at Week 52; DUPI/DUPI, dupilumab treatment group in PEDS that remained on dupilumab treatment in PED-OLE at Week 52.
Figure adapted from: 1. Irvine A, et al. Growth Analysis in Children Aged 6 to 11 Years With Severe AtopicDermatitis and Impact of Dupilumab Treatment on Height. Poster Presented at the *Relevant Advanced Practice Immuno-Dermatology Symposium (RAPIDS);* Rio Grande, Puerto Rico; April 9 - 13, 2025.

Treatment with Dupilumab Significantly Improved Vertical Growth in Children of Lower Stature with AD[1]

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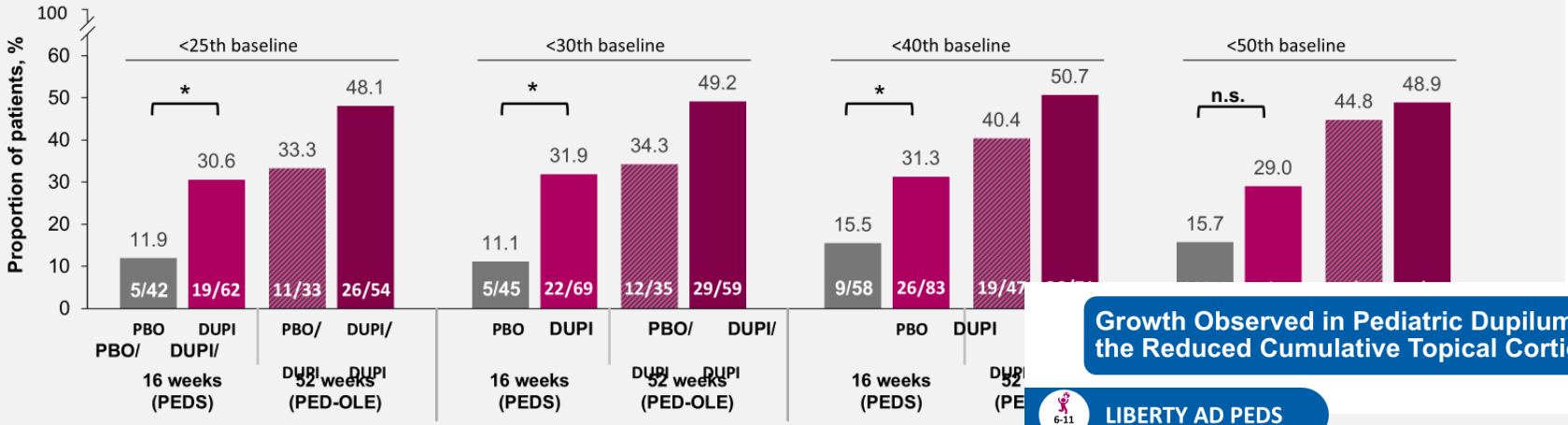


Catch-up growth observed with dupilumab treatment in the 16-week PEDS tria that switched to dupilumab at week 16, with ~33-44% achieving ≥5 percent

*$p<0.05$, n.s., not significant. White numbers inside bars denote number of patients achieving ≥5 percentile improvement over total patients per group. BL, baseline; PBO, placebo; DUPI, dupilumab; PBO/DUPI, placebo group in PEDS that transitioned to dupilumab treatment in PED-OLE at Week 52; dupilumab treatment in PED-OLE at Week 52.
Figure adapted from: 1. Irvine A, et al. Growth Analysis in Children Aged 6 to 11 Years With Severe AtopicDermatitis and Impact of Dupilumab Treatm *Immuno-Dermatology Symposium (RAPIDS);* Rio Grande, Puerto Rico; April 9 - 13, 2025.

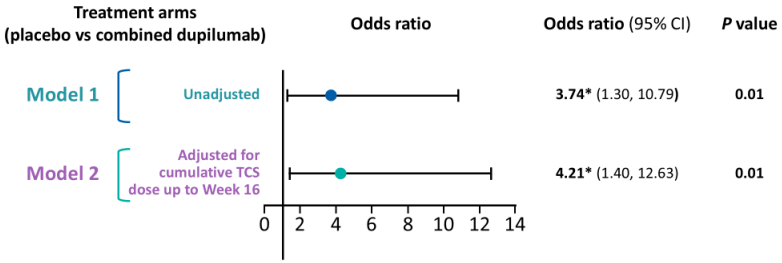
Growth Observed in Pediatric Dupilumab Patients Appears to Be Irrespective of the Reduced Cumulative Topical Corticosteroid Usage[1]

6-11 years

LIBERTY AD PEDS

Cumulative doses of low- and medium-potency topical corticosteroids used in the 16-week placebo-controlled PEDS trial were significantly lower in patients treated with dupilumab compared to placebo (*P*=0.034)[1]
(data not shown)

Odds ratio for growth attainment in the shorter stature population at baseline[1]



These data suggest that topical corticosteroids may not impact growth in 16 weeks, or that a potential negative effect of TCS use on growth during that period could be counteracted by treatment with dupilumab

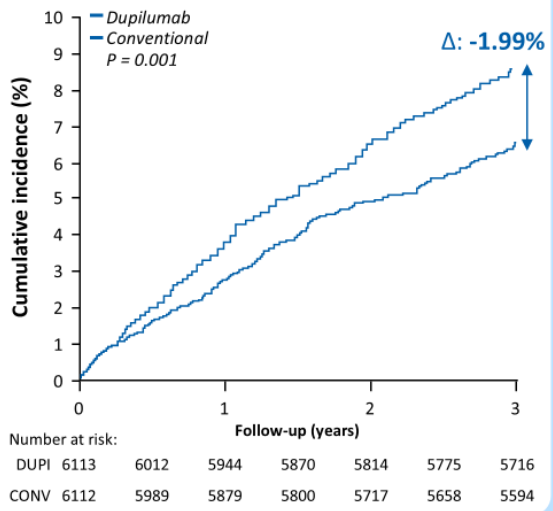
Children aged 6 to 11 years with severe AD received dupilumab (300 mg q4w or 200 mg q2w) or placebo plus a standardized low- and medium-potency TCS treatment regimen for 16 weeks in LIBERTY AD PEDS trial. Cumulative TCS dose was recorded over the 16-week treatment period. A logistic regression model was conducted, with the response variable defined as achieving a ≥5-percentile increase in height from baseline to Week 16 in a subset of patients below the 30th baseline height percentile (n = 114); the covariate was the cumulative TCS dose. P values for summary statistics were calculated using Welch's unpaired t-test.
TCS, topical corticosteroid.
Figure adapted from: 1. Irvine A, et al. Growth Improvement in Children 6 to 11 Years With Severe Atopic Dermatitis Treated With Dupilumab Irrespective of Cumulative TCS Use. Poster presented at *RAD*, June 6-7, 2025, Nashville, USA.

Lower Incidence of Neuropsychiatric Disorders Was Seen in Adults with AD Treated with Dupilumab vs. Conventional Therapy in TriNetX[1]

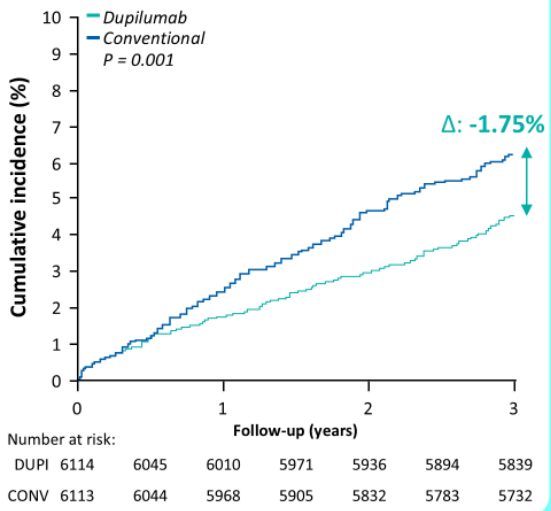
TriNetX

Adults

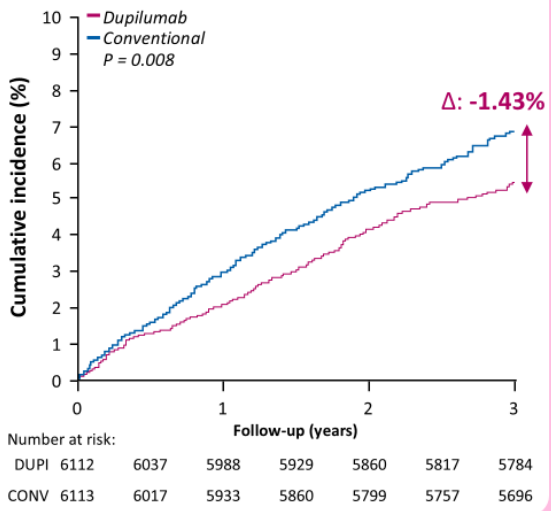
Anxiety[1]



Depressive disorders[1]



Sleep disorders[1]



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85

Figures adapted from: 1. Lin TL, et al. *Ann Allergy Asthma Immunol*. 2025;134(3):333-340.e6.

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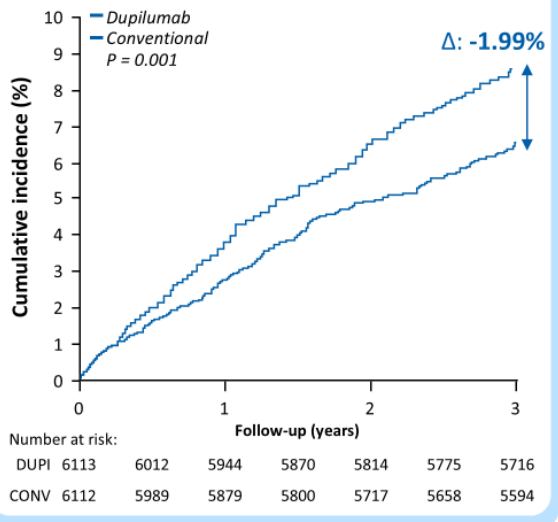
Lower Incidence of Neuropsychiatric Disorders Was Seen in Adults with AD Treated with Dupilumab vs. Conventional Therapy in TriNetX[1]

TriNetX

Adults

Anxiety[1]



Depressive disorders[1]

Sleep disorders[1]

There Is Growing Evidence for the Association of Various Systemic Diseases With AD including bone health

Mental health

Adult patients with AD have a higher likelihood of depression than patients with other chronic diseases[1,2]

Pediatric patients with AD **are 2–6 times more likely to have anxiety, depression, and ADHD** than those without AD[2,3]

Cardiovascular health

Adult and pediatric patients with AD are at higher risk for various cardiovascular events than those without AD[4,a]

- Pulmonary embolism
- Myocardial infarction
- Deep vein thrombosis
- Stroke

Bone health

Evidence suggests that AD is associated with:

- Decreased bone mineral density[5,6]
- Increased risk of fractures[7,8]
- Growth impairment in children and adolescents[9]

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Figures adapted from: 1. Lin TL, et al. *Ann Allergy Asthma Immunol*. 2025;134(3):

1. Thyssen JP, et al. *J Allergy Clin Immunol*. 2023;151:1155–1162. 2. Johnson JK, et al. *Dermatitis*. 2024;35:386–391. 3. Hou A, Silverberg JI. *Pediatr Dermatol*. 2021;38:606–612. 4. Wan J, et al. *J Allergy Clin Immunol Pract*. 2023;11:3123–3132. 5. Wu D, et al. *Ann Transl Med*. 2021;9:40. 6. Silverberg JI. *Pediatr Allergy Immunol*. 2015;26:54–61. 7. Lee AW, et al. *Allergy*. 2023;78:871–875. 8. Arkwright PD, Mughal MZ. *J Allergy Clin Immunol*. 2020;145:487–488. 9. Silverberg JI, et al. *JAMA Dermatology*. 2015;151:401–409.

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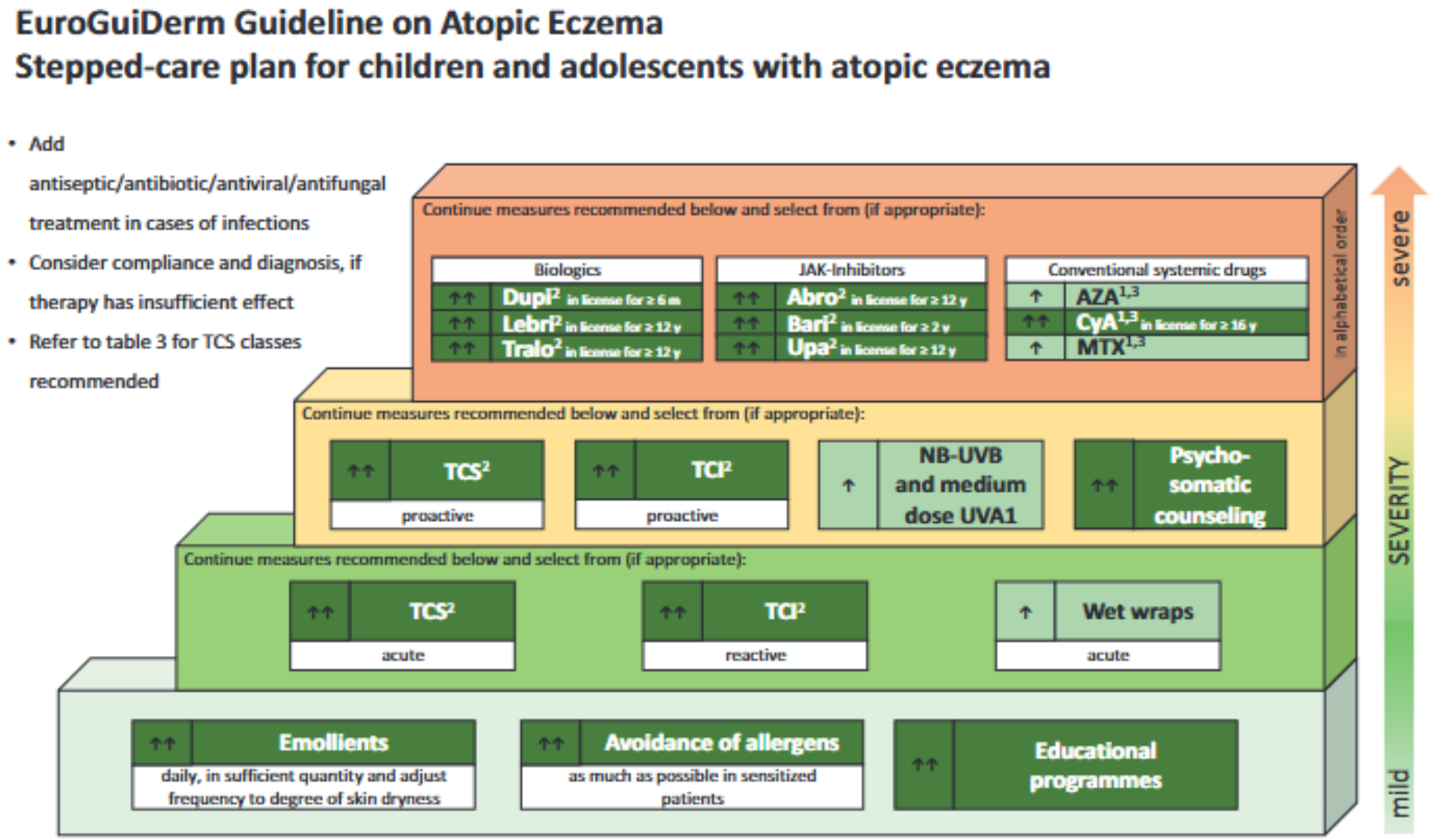
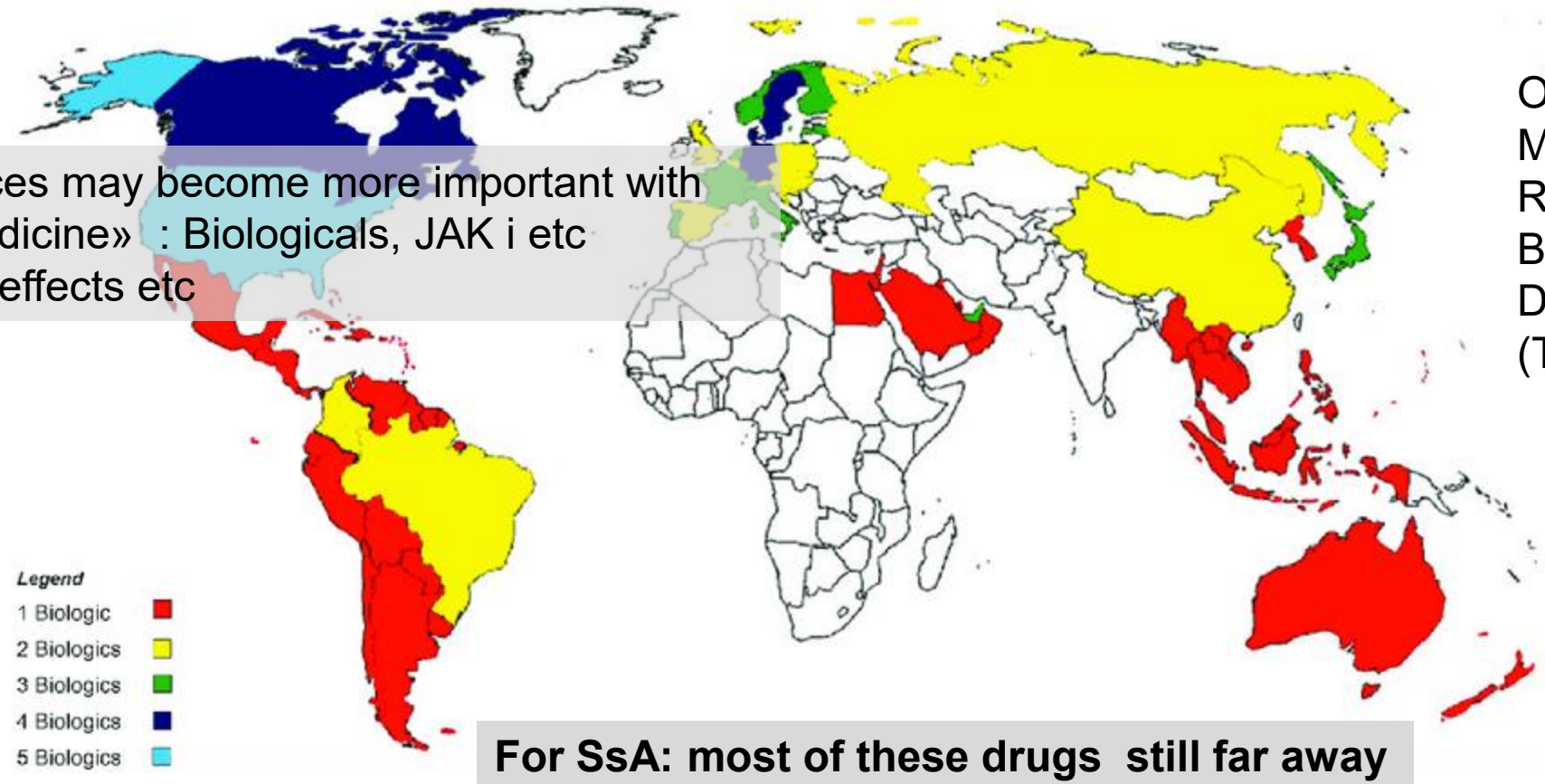
Wollenberg A et al. European Guideline (EuroGuiDerm) on atopic eczema: Living update. J Eur Acad Dermatol Venereol. 2025 May 2. doi: 10.1111



Availability of biologics in asthma worldwide

Such differences may become more important with «precision medicine» : Biologicals, JAK i etc
Efficacy, Side effects etc



Omalizumab
Mepolizumab
Reslizumab
Benralizumab
Dupilumab
(Tezepelumab)

For SsA: most of these drugs still far away

Caminati, M. & Morais-Almeida, Mario & Bleecker, E. & Ansotegui, I. & Canonica, G.W. & Bovo, C. & Senna, Gianenrico. (2021). Biologics and global burden of asthma: A worldwide portrait and a call for action. World Allergy Organization Journal. 14. 100502. 10.1016/j.waojou.2020.100502.

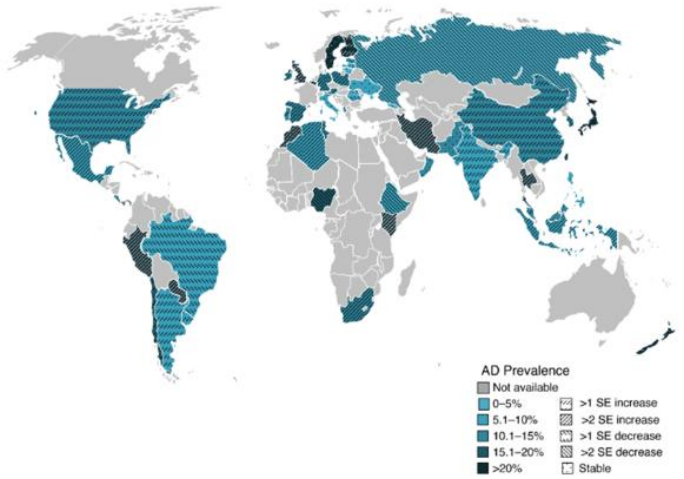
Received: 7 September 2023 | Accepted: 17 November 2023

DOI: 10.1111/jdv.19723

POSITION STATEMENT

Atopic dermatitis: A global health perspective

Ousmane Faye[1] | Carsten Flohr[2,3] | Kenji Kabashima[4,5] | Lin Ma[6] | Amy S. Paller[7] | Fahafahantsoa Rabenja Rapelanoro[8] | Martin Steinhoff[9,10,11,12,13,14,15] | John C. Su[16,17] | Roberto Takaoka[18,19] | Andreas Wollenberg[18,19,20,21] | Yik Weng Yew[22] | Jose A. Ruiz Postigo[23] | Peter Schmid-Grendelmeier[18,24,25,26] | Alain Taïeb[18,27]



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POSITION STATEMENT

JEADV

Atopic dermatitis: A global health perspective

GADA Director

Professor Carsten Flohr
UK

GADA Core Team

Dr. Suzanne Keddie
UK

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artin
erg[18]
ende

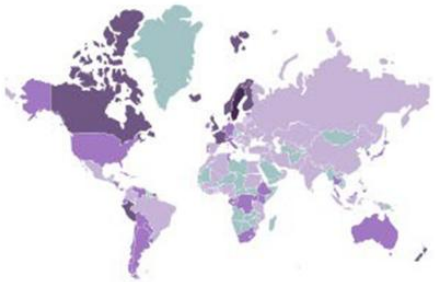
How common is atopic dermatitis?

GADA GLOBAL ATOPIC DERMATITIS ATLAS

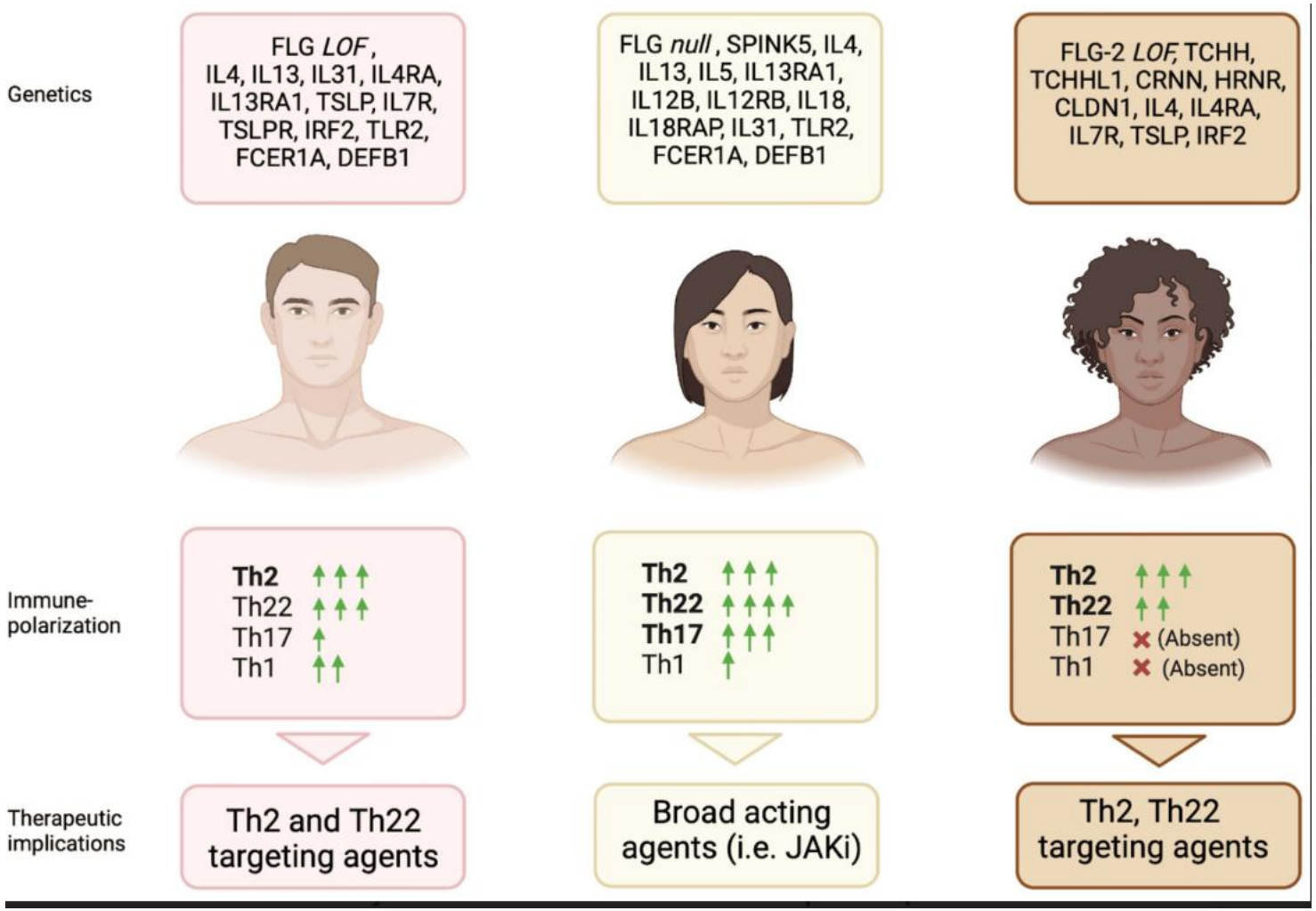
> Atopic dermatitis affects around 20% of children and up to 10% of adults. Yet, the prevalence and disease burden of atopic dermatitis varies considerably between countries. The reasons for these variations are still poorly understood.

- **Prevalence and incidence** +
- **Prevalence per age group** +
- **Prevalence per country** +
- **Global burden of disease from atopic dermatitis** +

View the data in the map



Overview of Atopic Dermatitis in 3 Different Ethnic Groups

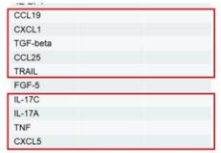


Chiricozzi A et al….. Girolomoni G. Overview of Atopic Dermatitis in Different Ethnic Groups. J Clin Med. 2023 Apr 4;12(7):2701

Overview of Atopic Dermatitis in 3 Different Ethnic Groups

Evidence for different immune signatures and sensitization patterns in sub-Saharan African vs. Central European atopic dermatitis patients

- IL-17 –dominated signature in SsA patients



Pro-inflammatory, Th17-related mediators

dominate in the serum of TZ AD patients compared to CH AD patients

- exhibiting dominant T_H2 and T_H22 skewing
- attenuation of lipid metabolism-related products

Lang CCV et al. Ann Allergy Asthma Immunol. 2021 Sep;127(3):334-341
Lang CCV et al. J Eur Acad Dermatol Venereol. 2021 Feb;35(2):e140-e142

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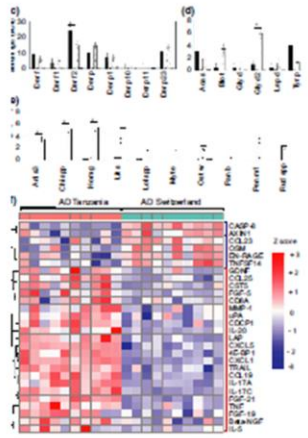

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Improved acces to treatment in AD on a global scale

Meeting WHO- ISAD

Patients, experts and Industry 23.10.2025

Accepted in Aug 2025

EML application « Moisturizers for AD » submitted Nov 1st 2024

Inclusion of urea- and glycerol-based topical moisturizers on the EML and EMLc for the treatment of atopic dermatitis in adults and children

Applicants:
International Society of Atopic Dermatitis
Co-Applicant:
WHO Department of control of Neglected Tropical Diseases
Persons to contact: Prof Alain Taieb, ISAD
Email: alain.taieb@u-bordeaux.fr
Phone: + 33 647679795
Dr Jose Ruiz Postigo, WHO NTDs
Email: postigoj@who.int
Phone : + 41 795163882

Writing group: dermatologists, pharmacists, from academia or industry,

Support: GlobalSkin (Patient advocacy)
ILDS (Int League Derm Soc)
ASDV (African Soc Derm Vener)

223 | WHO Expert Committee on the Selection and Use of Essential Medicines 2023
World Health Organization

ISAD
INTERNATIONAL SOCIETY OF ATOPIC DERMATITIS

- 1: We have to define/consider subtypes
- 2: Different approaches for childhood and adult AD
- 3. We have to define (and exclude/avoid) Trigger factors
- 4. We have to integrate tne needs and expections of our patients
- 5: Adress not only SAD but also comorbidities
- 6: Adapted T2T and treatment approaches for different cultural and socioecconomic settings

AMCC


AMCC
Anterior
Mid
Cingulate
Cortex

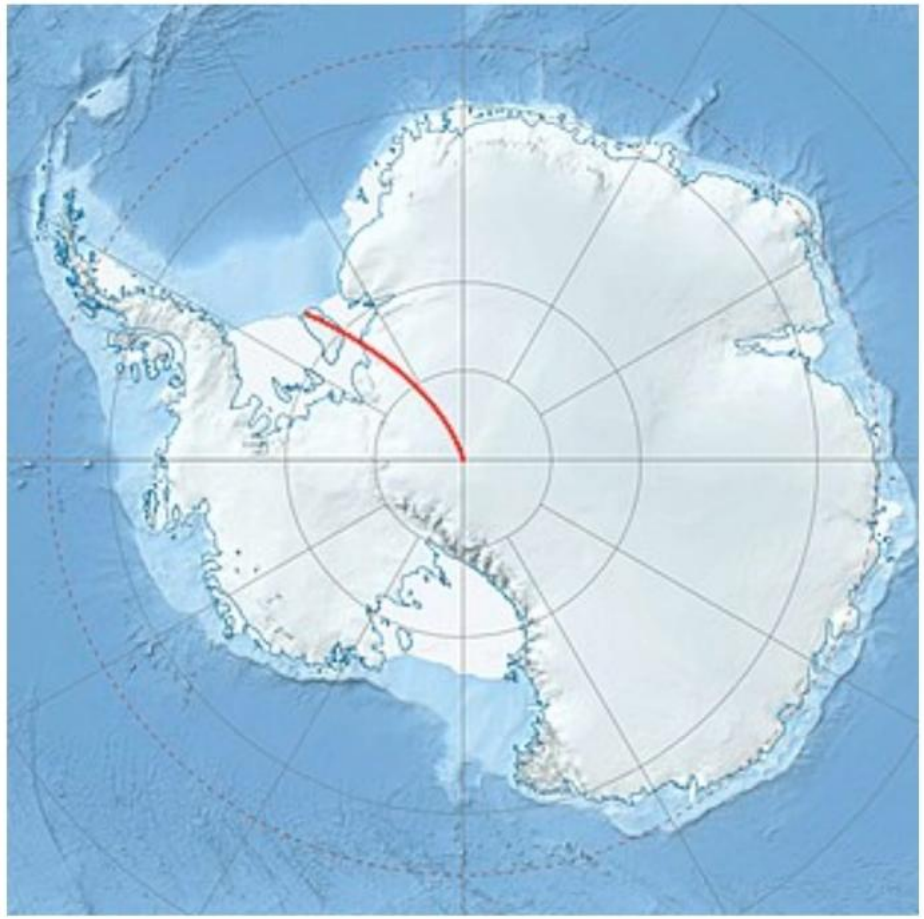

AMCC
Anterior
Mid
Cingulate
Cortex
The place in
your brain
to enhance
your will power
and endurance:

AMCC
Anterior
Mid
Cingulate
Cortex

The place in
your brain
to enhance
your will power
and endurance:
Can be rehearsed

AMCC
Anterior
Mid
Cingulate
Cortex

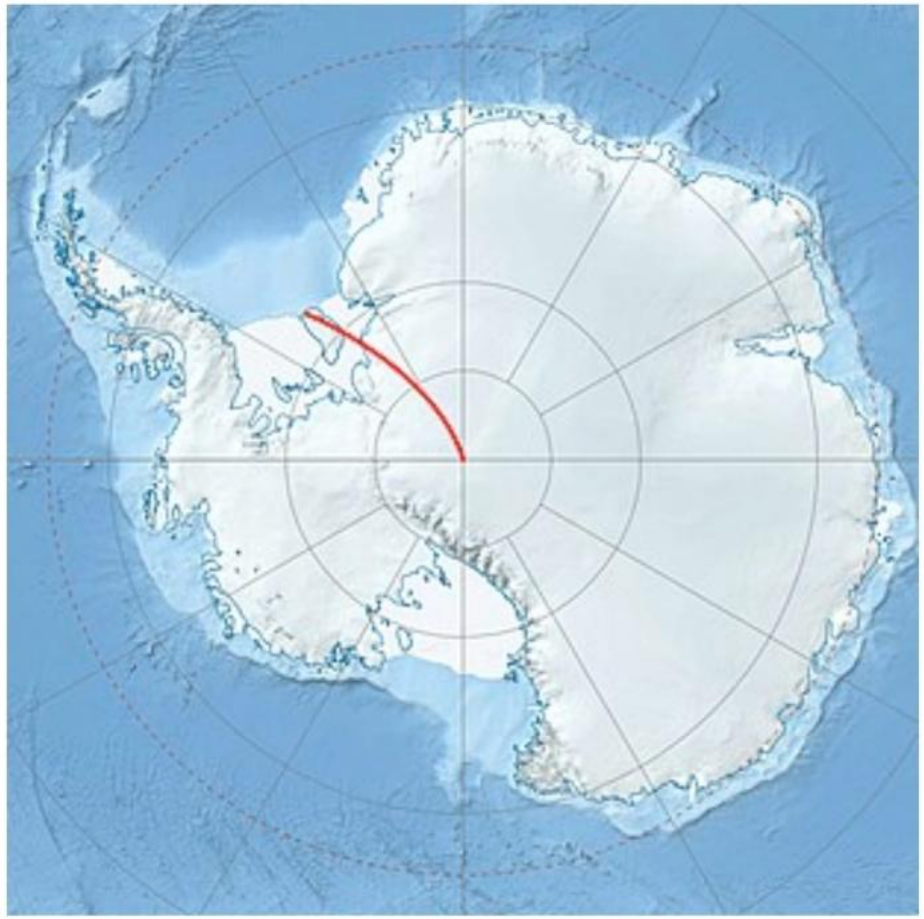
Soloexpedition zum Südpol



Die 1381 Kilometer lange Route der Expedition Anja Blachas von der Gould Bay auf der Berkner-Insel bis zum Südpol

AMCC
Anterior
Mid
Cingulate
Cortex

Soloexpedition zum Südpol



Die 1381 Kilometer lange Route der Expedition Anja Blachas von der Gould Bay auf der Berkner-Insel bis zum Südpol

Her motto:
Not bad for a girl

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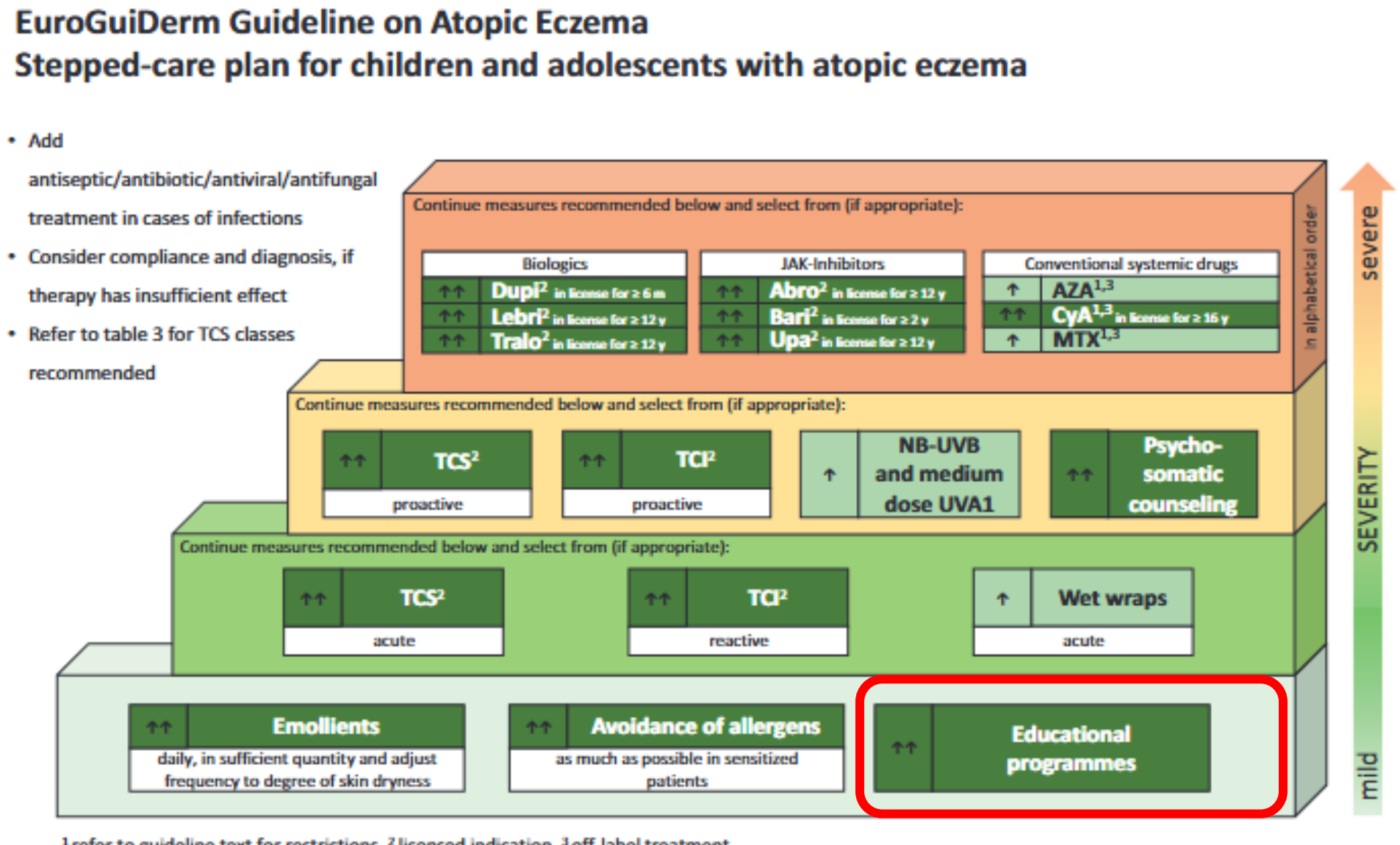

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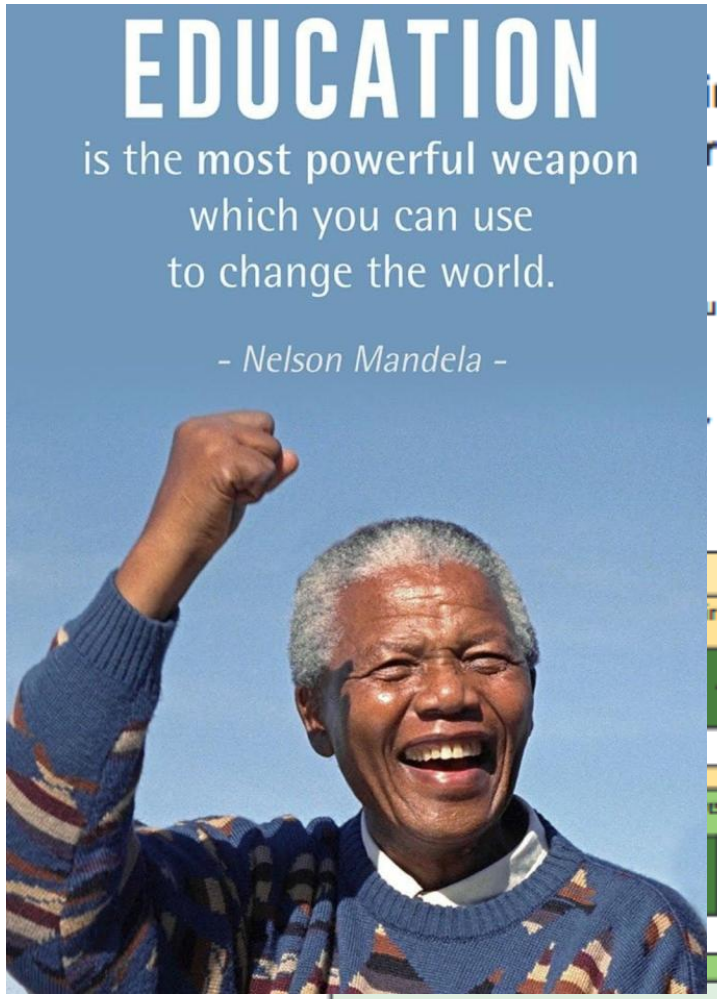

Eczema school - through training from patient management to self-management!

- ✓Six weekly meetings of 2 h each (eg Wednesday evening 19.00 – 21.00)
- ✓trainer is gathering information from participants, putting them into perspective
- ✓each session focusses on certain aspects, always starting from subjective experiences of patients/parents
- ✓only short blocks of lectures
- ✓"homework" and round-table discussions to improve sustainability of learned concepts

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<www.neurodermitisschulung.de>

- 1: We have to define/consider subtypes
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- 4. We have to integrate tne needs and expections of our patients
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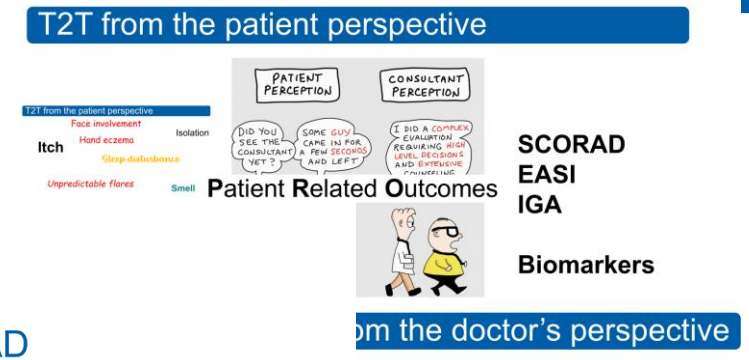
- 6: Adapted T2T and treatment approaches for different cultural and socioecconomic settings
- 7: Integrate educational and behaviroul approaches

Towards personalized therapy and potential disease modification in AD: We are closer than ever



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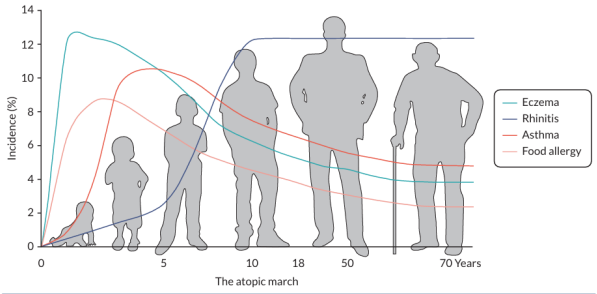

FIGURE 1 Illustration of the typical onset of symptoms of allergic diseases during childhood. Reprinted from Davidson*et al.* (2019),[15] Copyright (2023), with permission from Elsevier.

T2T in Atopic Dermatitis (Treat to target)

Better Access to Treatments for AD on a global scale

USZ Universitäts Spital Zürich


Thanks for your attention
Peter.schmid@usz.ch
CK-CARE
DAVOS