

Il bambino con DA.

Cosa conta davvero nella prevenzione della marcia dell'allergico?



Diego Peroni
UO Pediatria AOUP
Università di Pisa

diego.peroni@unipi.it

La DA è la più frequente manifestazione iniziale di atopia

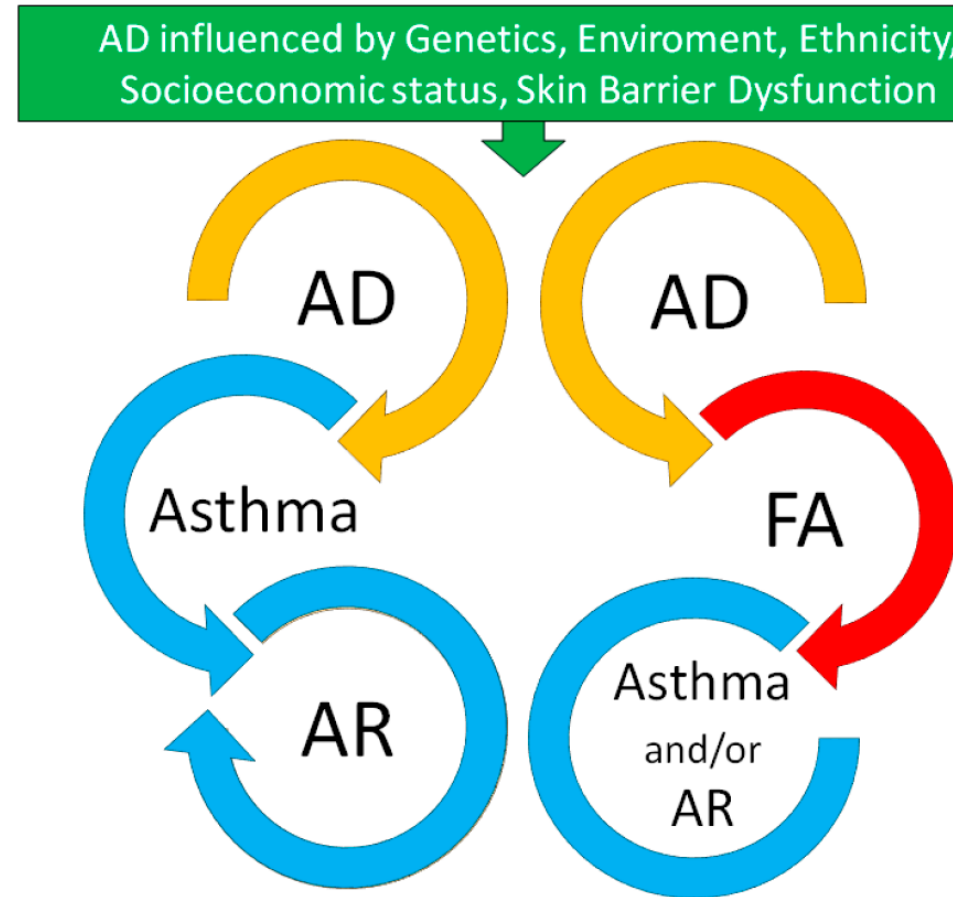


Figure 1. Allergic march trajectories starting from atopic dermatitis.

Real-World Onset of Atopic Comorbidities Relative to Atopic Dermatitis in Pediatric Patients. Leshem, Dermatol Ther, 2025

What was learned from this study?

Children diagnosed with AD at an early age mostly develop atopic comorbidities within 1 year following AD diagnosis, which is consistent with AD being the first clinical manifestation of the “atopic march” in the infant/toddler age group.

However, children diagnosed later have often already developed atopic comorbidities.

These real-world findings indicate the “atopic march” model may not accurately reflect comorbidity burden in all pediatric patients with AD.

Real-World Onset of Atopic Comorbidities Relative to Atopic Dermatitis in Pediatric Patients

Yael A. Leshem, Clara Weil, William W. Busse, Lisa A. Beck, Gabriel Chodick, Sonya L. Cyr, Kwinten Bosman, Robert Lubwama

OBJECTIVE

To describe the onset of atopic comorbidities among children newly diagnosed with **atopic dermatitis (AD)**



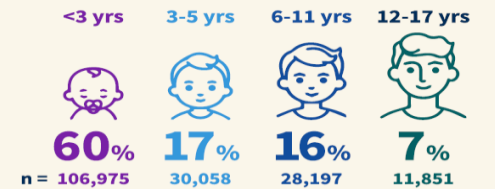
METHODS

Retrospective, observational cohort study using data from the **Israeli Maccabi Healthcare Services** including

Grouped by age at AD diagnosis

177,081

children with diagnosed AD

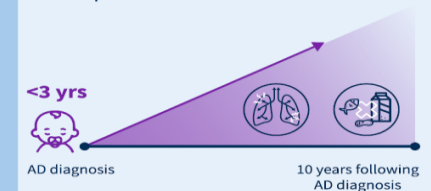


KEY MESSAGES

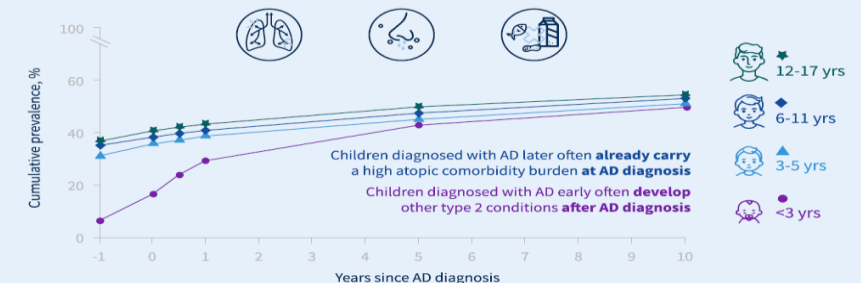
There is a **higher incidence of atopic comorbidities** at or within 1 year following AD diagnosis



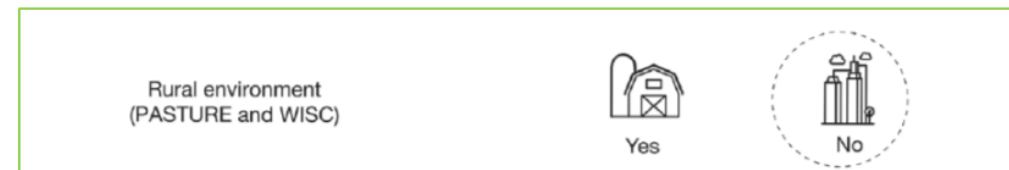
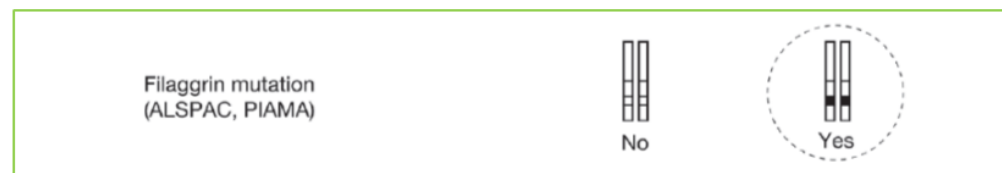
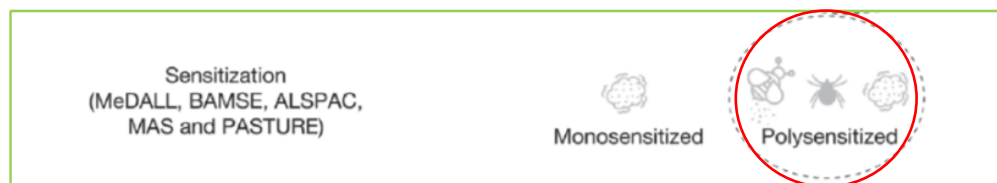
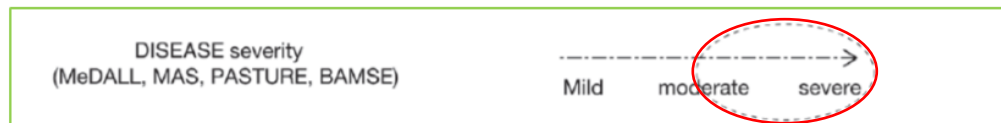
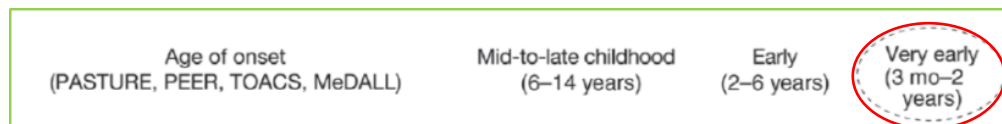
AD diagnosis at an early age coincides with a **sharper increase in comorbid asthma and food allergy** in the 10 years following diagnosis, compared to later onset AD



The **prevalence of atopic comorbidities increased** following AD diagnosis, to reach approximately 50% by 10 years after regardless of age at AD diagnosis



Fenotipi di rischio per Dermatite Atopica «in Marcia»



- Età di esordio (< 2 aa)
- Gravità della dermatite

fanno la differenza per:

- Persistenza
- Marcia atopica

QUANTE E QUALI SONO LE COMORBIDITÀ ATOPICHE NEL BAMBINO CON DA MODERATA-GRAVE

PEDISTAD

è un registro internazionale, longitudinale, di 10 anni che coinvolge bambini (<12 anni) con DA da moderata a grave

Popolazione

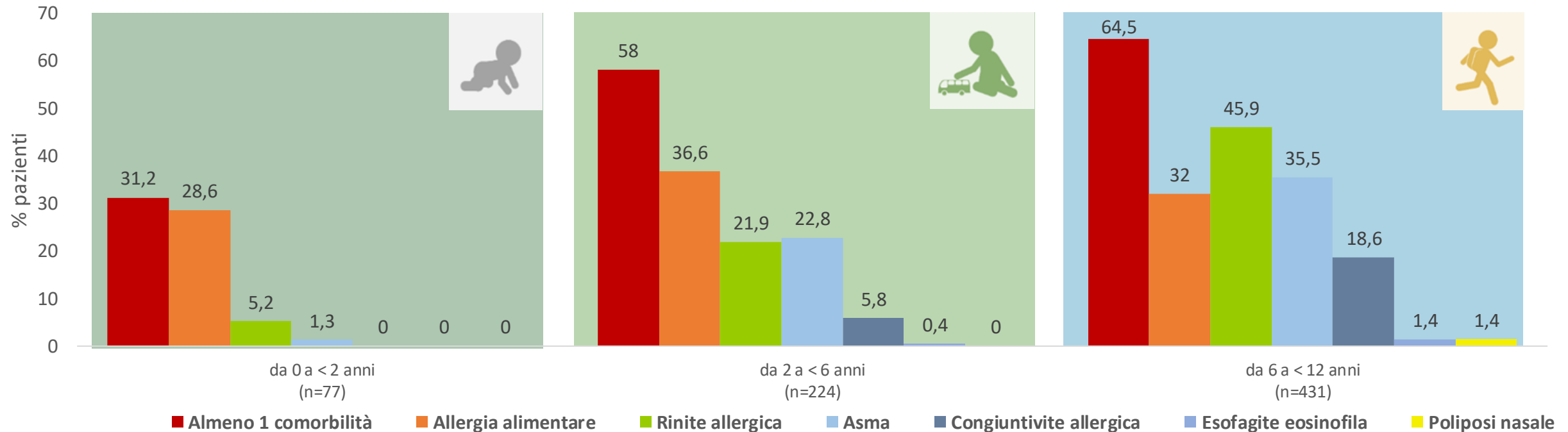


106 siti



n=732

COMORBIDITÀ ATOPICHE



DA: dermatite atopica

Adattato da Paller A, et al. JAAD 2022 novembre;87(5):1104-1108

Il bambino con DA.

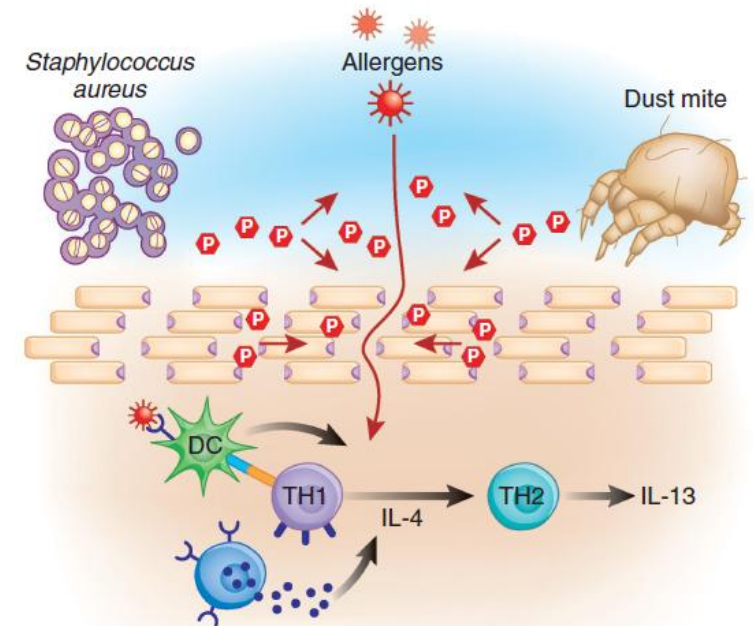
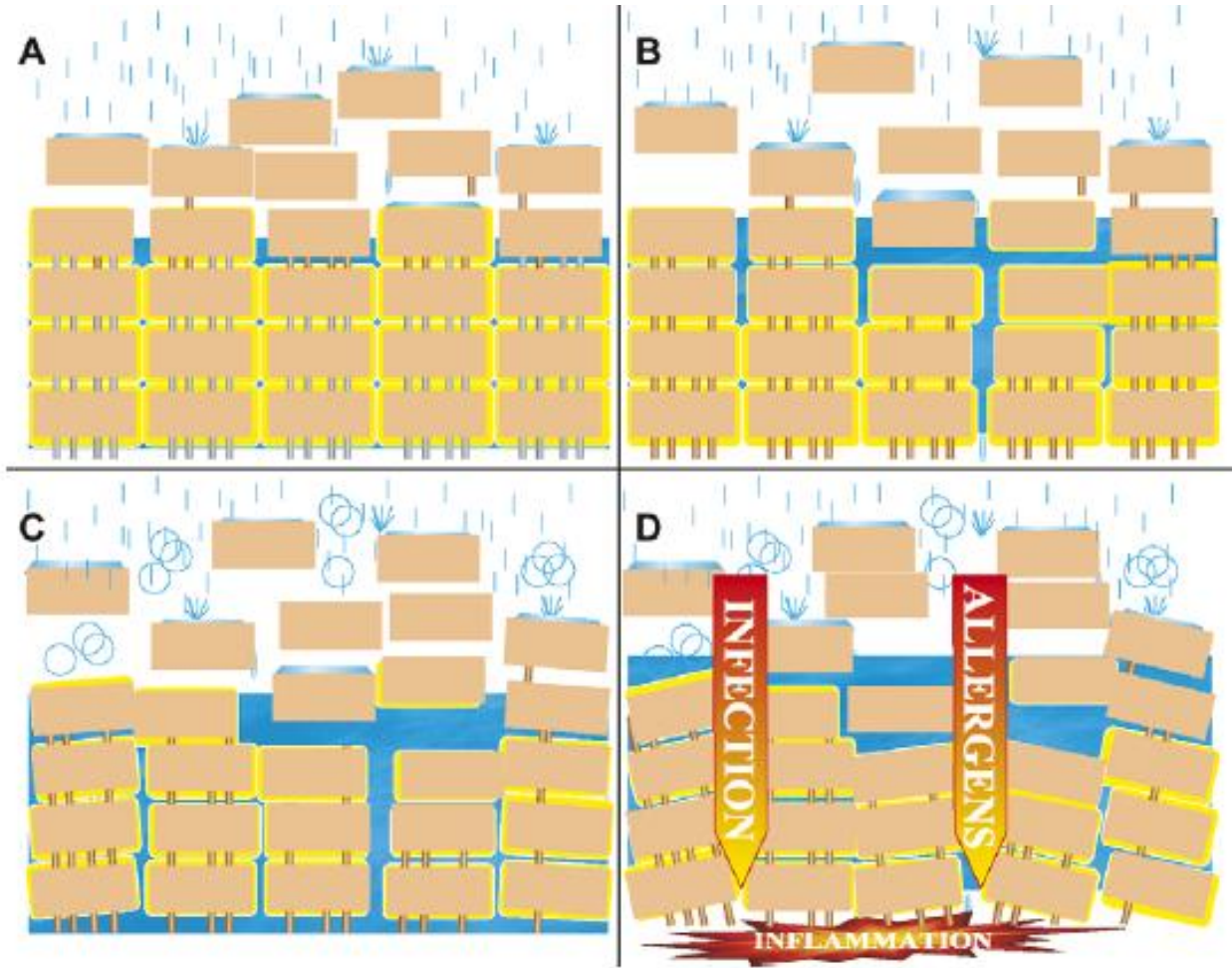
**Cosa conta davvero nella prevenzione
della marcia dell'allergico?**



Avendo cura della DA ?

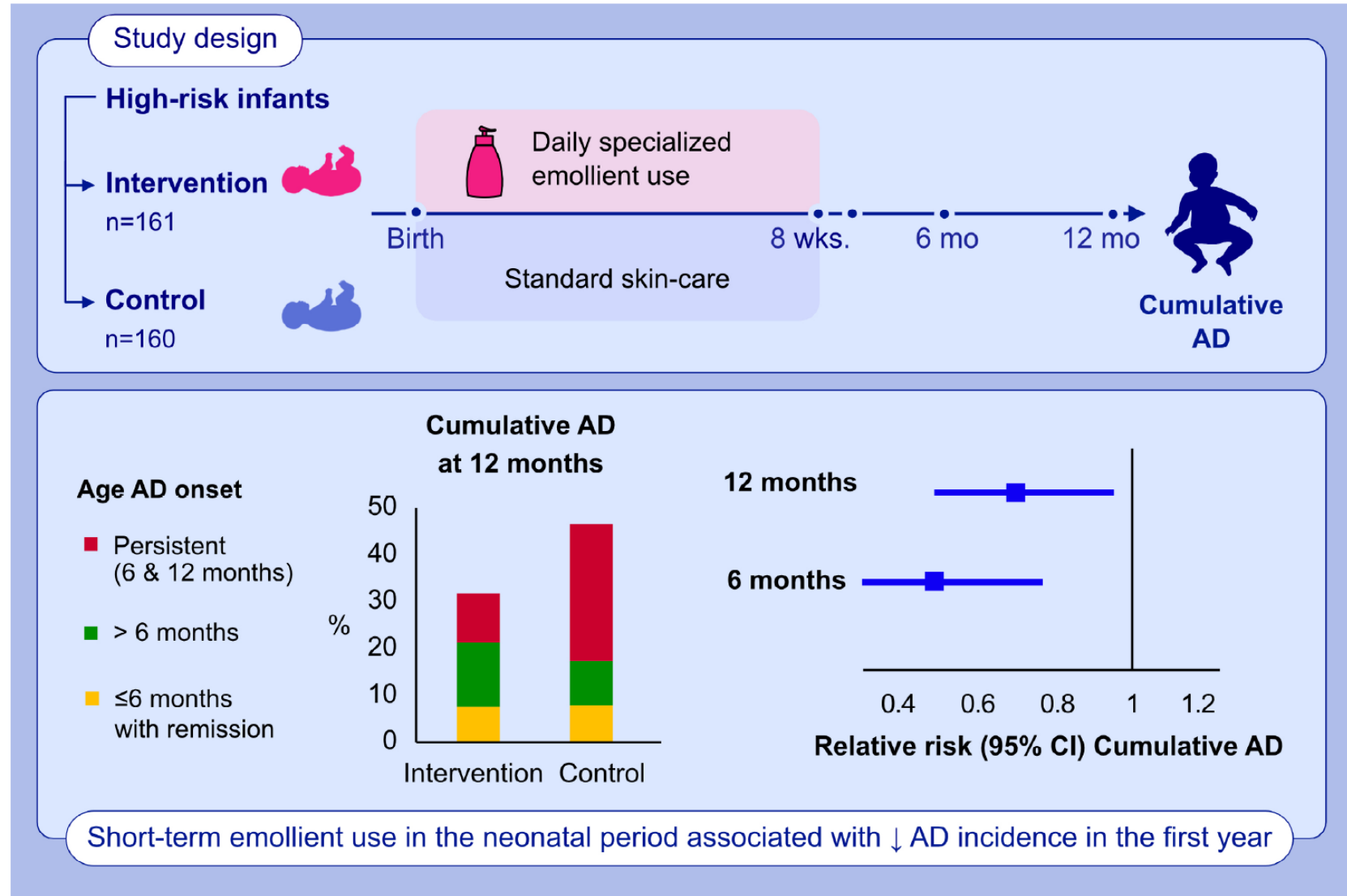
diego.peroni@unipi.it

Good care of the skin



Early initiation of short-term emollient use for the prevention of atopic dermatitis in high-risk infants-The STOP-AD randomised controlled trial.

Chaoimh CN. Allergy 2022

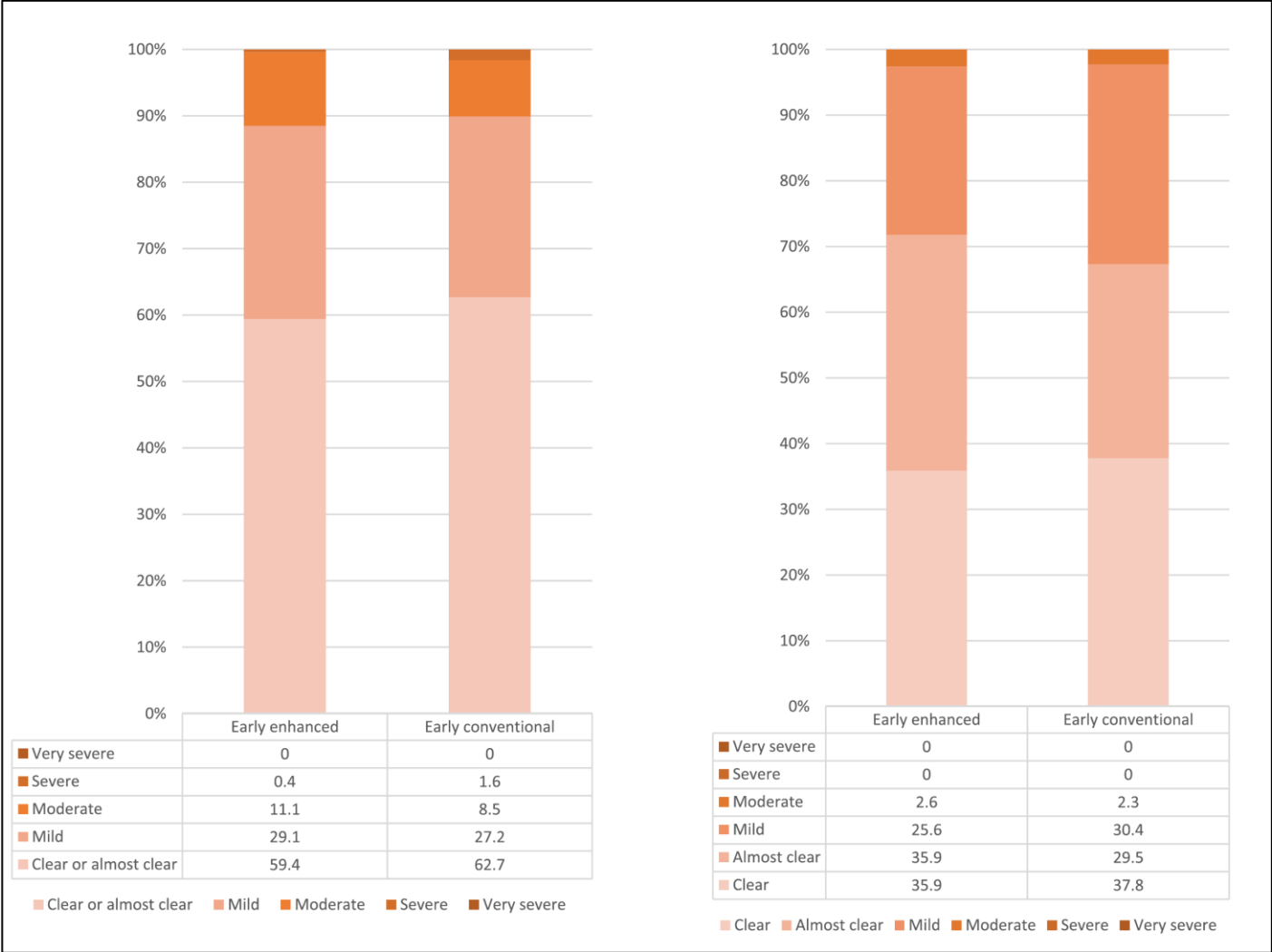


Three-Year Follow-Up of the PACI Randomized Controlled Trial (PACI-ON): Effects of Early Intervention for Atopic Dermatitis on Atopic March. Yamamoto, Allergy 2026

Good results in AD

Participants were randomized in infancy to early enhanced (proactive) or early conventional (reactive) TCS treatment (1:1) for atopic dermatitis (AD) until 28 weeks.

A total of 590 (91%) children who completed the PACI RCT were followed to age 3 years.



Three-Year Follow-Up of the PACI Randomized Controlled Trial (PACI-ON): Effects of Early Intervention for Atopic Dermatitis on Atopic March. Yamamoto, Allergy 2026

Some results in FA

Participants were randomized in infancy to early enhanced (proactive) or early conventional (reactive) TCS treatment (1:1) for atopic dermatitis (AD) until 28 weeks.

A total of 590 (91%) children who completed the PACI RCT were followed to age 3 years.

	PACI-ON All		Enhanced group		Conventional group		Enhanced vs. conventional
	(N= 590)		(N= 289)		(N= 301)		
	N ^a	n (%)	N ^a	n (%)	N ^a	n (%)	p
Hen's egg_Primary outcome							
Ever hen's egg raw	590	210 (35.6)	289	88 (30.4)	301	122 (40.5)	0.013
Ever hen's egg heated	590	108 (18.3)	289	57 (19.7)	301	51 (16.9)	0.396
Current hen's egg heated	590	24 (4.1)	289	13 (4.5)	301	11 (3.7)	0.679
Remission hen's egg heated	590	68 (11.5)	289	35 (12.1)	301	33 (11.0)	0.700
Hen's egg intake							
Free intake	487	445 (91.4)	237	214 (90.3)	250	231 (92.4)	0.413
Partial intake	487	40 (8.2)	237	22 (9.3)	250	18 (7.2)	
Complete elimination	487	1 (0.2)	237	1 (0.4)	250	0 (0.0)	
Not yet introduced	487	1 (0.2)	237	0 (0.0)	250	1 (0.4)	
Food allergy (FA)_Secondary outcomes							
Ever FA_milk	590	32 (5.4)	289	18 (6.2)	301	14 (4.7)	0.468
Ever FA_peanut	590	13 (2.2)	289	5 (1.7)	301	8 (2.7)	0.578
Ever FA_wheat	590	14 (2.4)	289	10 (3.5)	301	4 (1.3)	0.108
Ever FA_others	590	90 (15.3)	289	37 (12.8)	301	53 (17.6)	0.110
Ever FA_all	590	314 (53.2)	289	137 (47.4)	301	177 (58.8)	0.006

Three-Year Follow-Up of the PACI Randomized Controlled Trial (PACI-ON): Effects of Early Intervention for Atopic Dermatitis on Atopic March. Yamamoto, Allergy 2026

No results in RA

Participants were randomized in infancy to early enhanced (proactive) or early conventional (reactive) TCS treatment (1:1) for atopic dermatitis (AD) until 28 weeks.

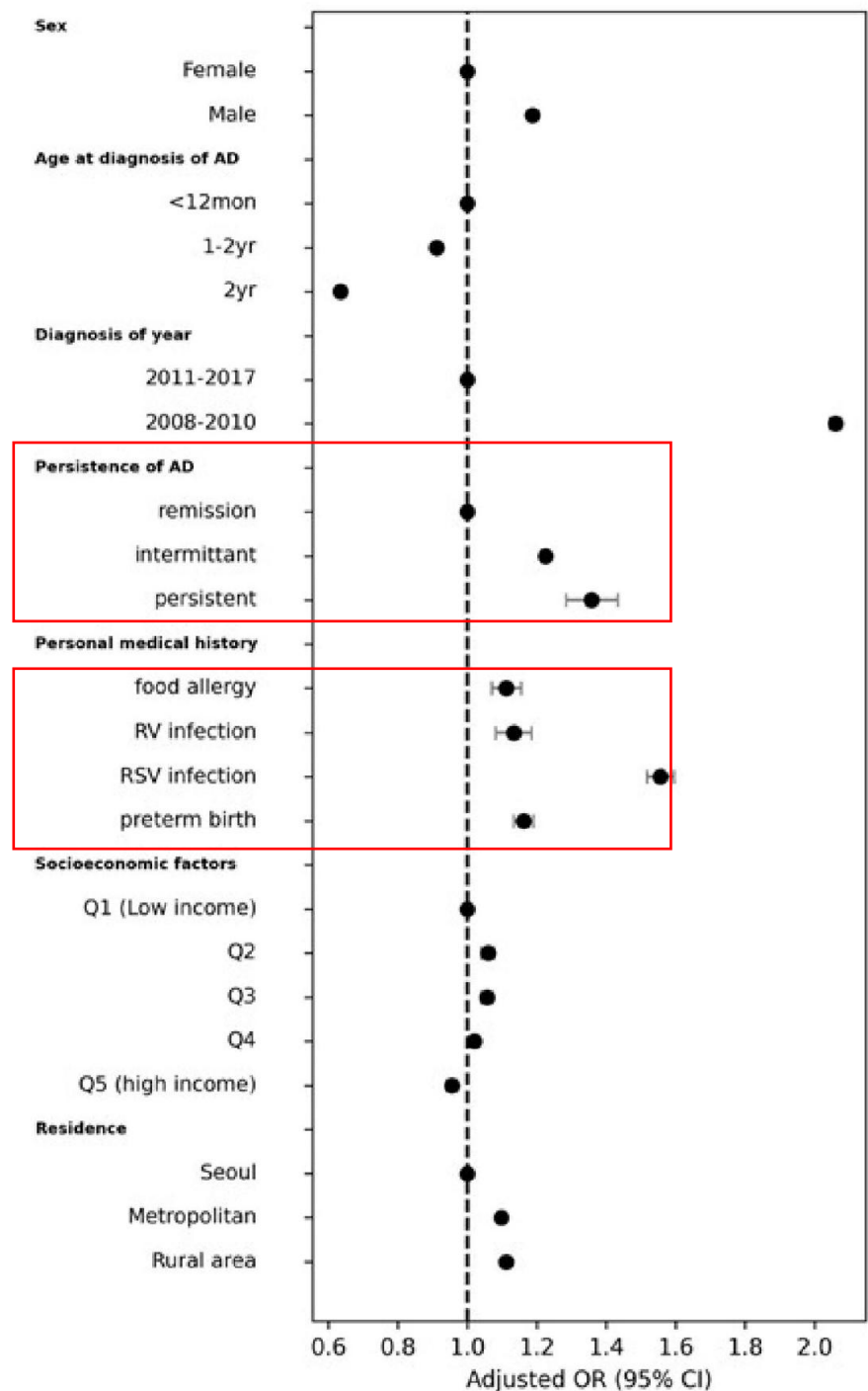
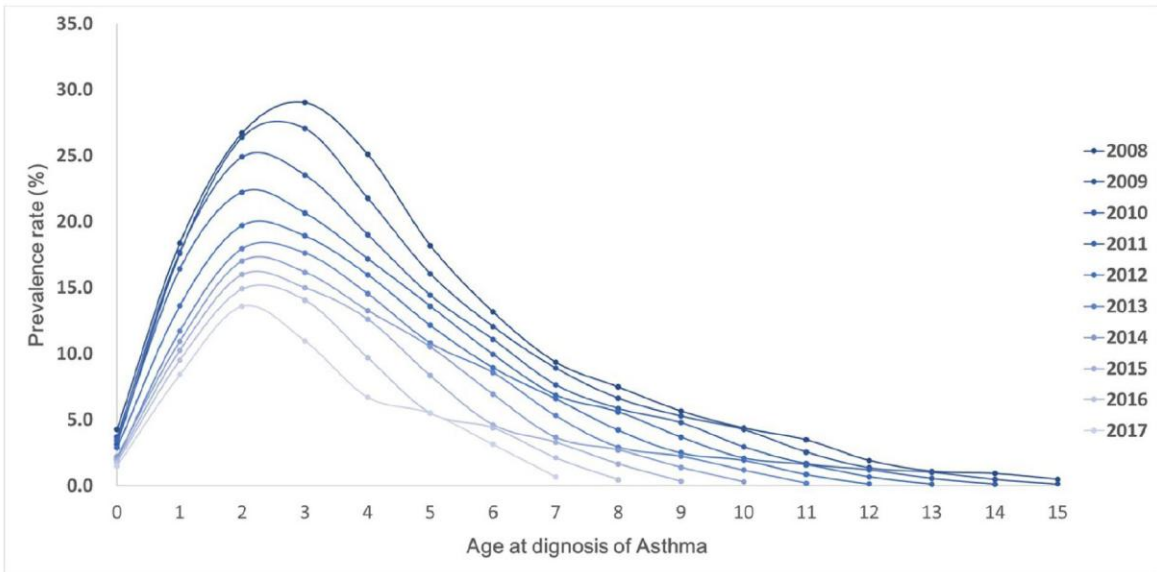
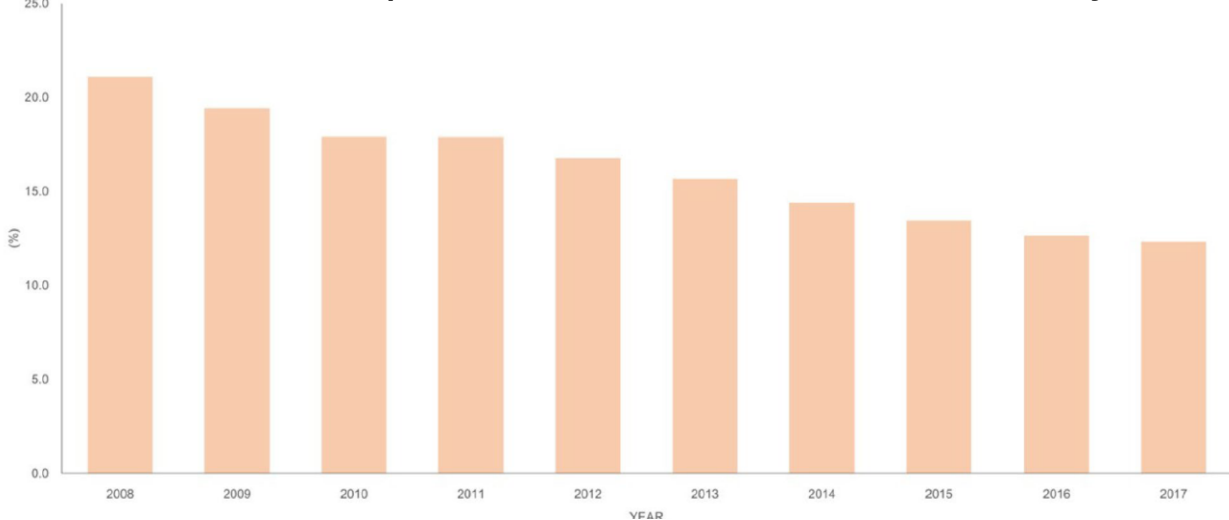
A total of 590 (91%) children who completed the PACI RCT were followed to age 3 years.

TABLE 4 | Wheeze, asthma, and rhinitis at 3 years old.

	PACI-ON All		Enhanced group		Conventional group		Enhanced vs. conventional <i>p</i>
	(N = 590)		(N = 289)		(N = 301)		
	N ^a	<i>n</i> (%)	N ^a	<i>n</i> (%)	N ^a	<i>n</i> (%)	
Respiratory							
Current wheeze	487	78 (16.0)	237	33 (14.0)	250	45 (18.0)	0.320
Ever asthma	487	54 (11.1)	237	29 (12.2)	250	25 (10.0)	0.472
Asthma_controler	395	39 (9.9)	195	20 (10.3)	200	19 (9.5)	0.867
Asthma ED visit	393	8 (2.0)	194	4 (2.1)	199	4 (2.0)	1.000
Asthma admission	395	7 (1.8)	194	4 (2.1)	201	3 (1.5)	0.720
Nose							
Current rhinitis	487	198 (40.7)	237	91 (38.4)	250	107 (42.8)	0.320
Ever rhinitis	487	205 (42.1)	237	94 (39.7)	250	111 (44.4)	0.313
Ever hay fever	485	43 (8.9)	236	18 (7.6)	249	25 (10.0)	0.425

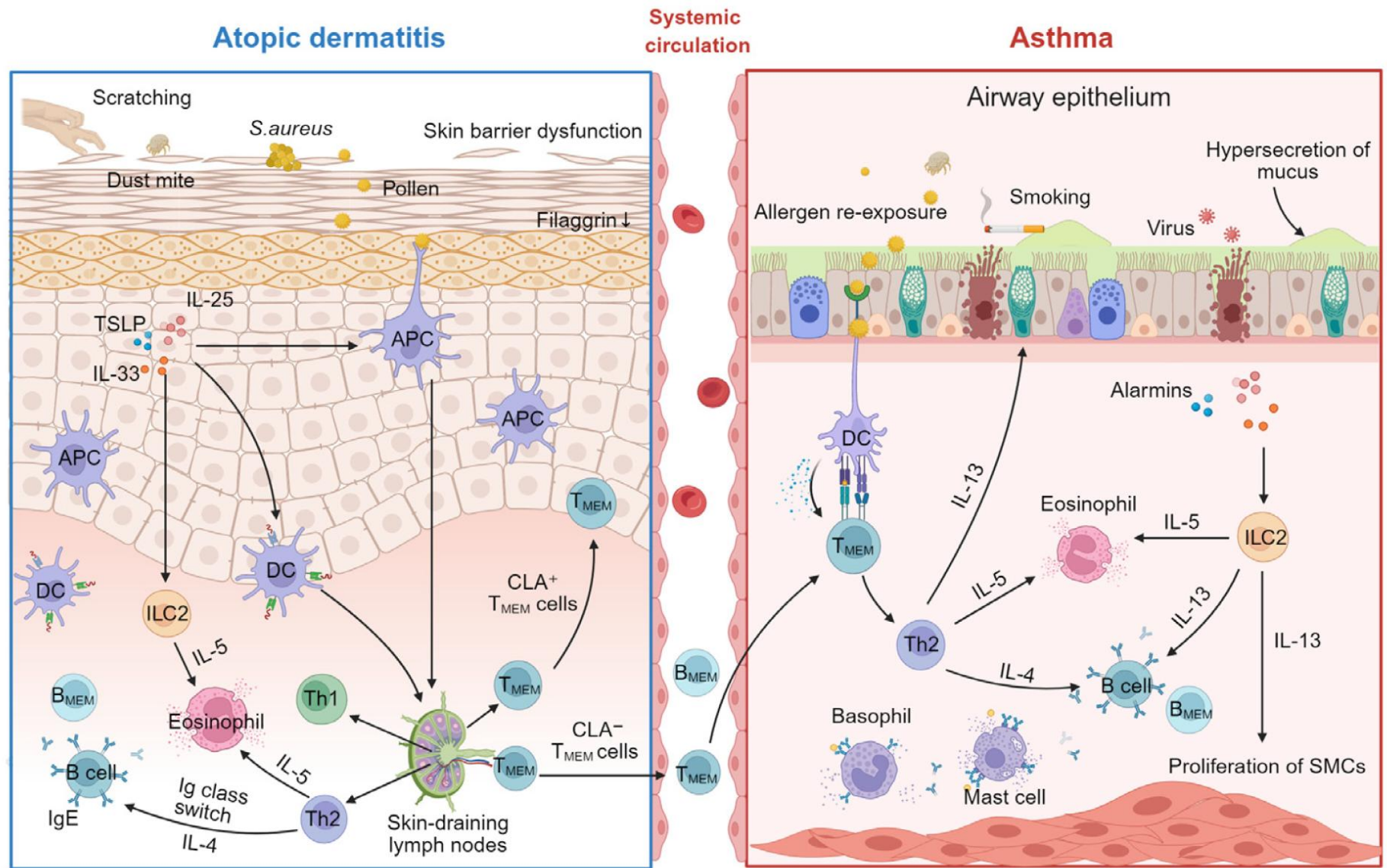
Asthma prevalence and risk factors in early-onset atopic dermatitis using Korean National Health Insurance Service data. Kim, Scient Rep 2025

Prevalence of atopic dermatitis in children under 2 years of age



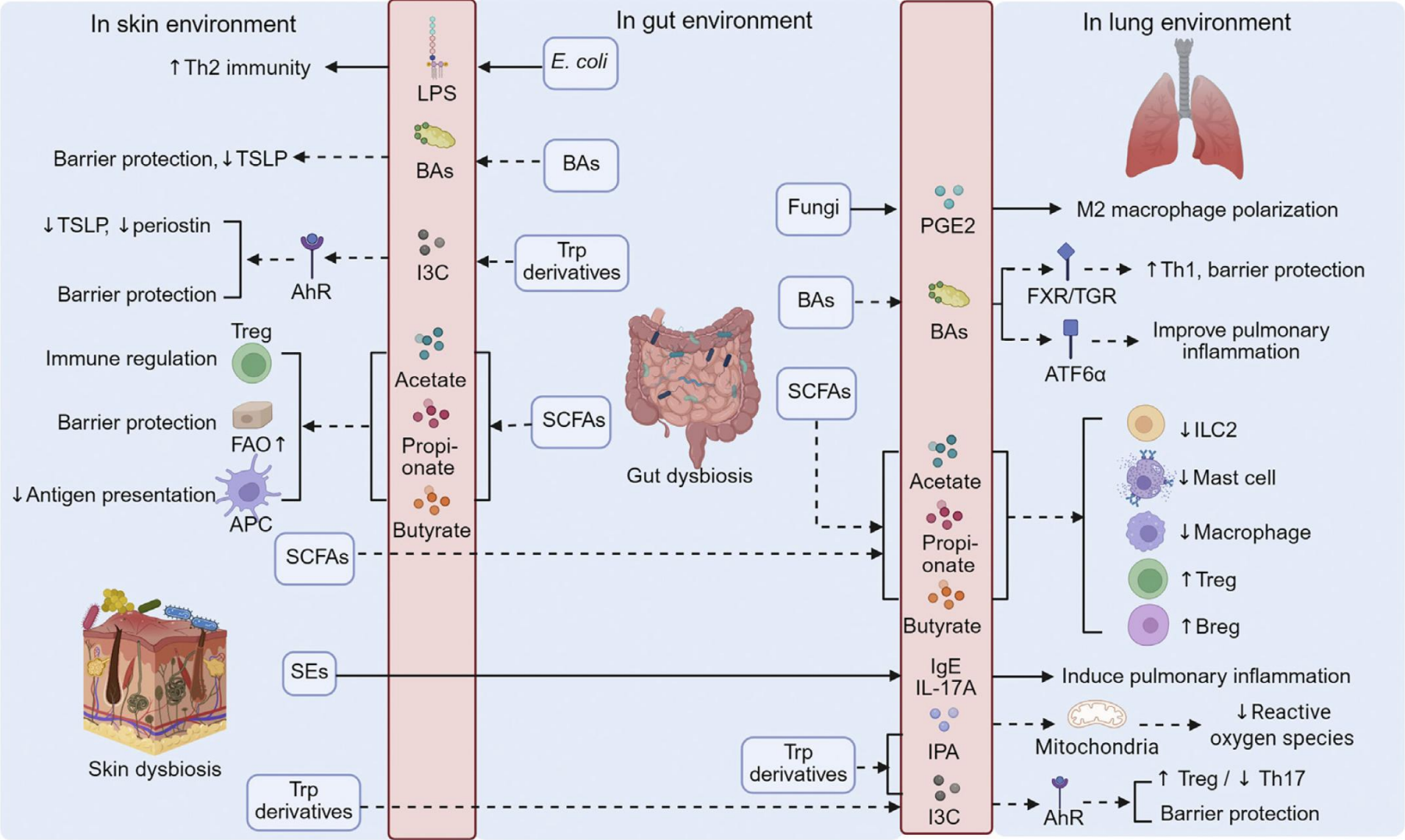
Skin-lung axis in the atopic march: The immune link from skin to lungs. Zhu CMJ 2025

Skin barrier dysfunction in AD facilitates allergen penetration and induces epithelial alarmin release, promoting the activation of ILC2s and DCs. Activated DCs migrate to skin-draining lymph nodes to prime naive CD4+ T cells toward Th2 differentiation



Skin-lung axis in the atopic march: The immune link from skin to lungs. Zhu CMJ 2025

Metabolic-immune crosstalk across the skin–gut–lung axis in AM.
 Microbial dysbiosis alters the profiles of microbial-derived metabolites. These dysregulated metabolite patterns modulate epithelial and immune regulatory pathways, reshaping systemic immune homeostasis and compromising barrier integrity in distant organs



Il bambino con DA.

**Cosa conta davvero nella prevenzione
della marcia dell'allergico?**

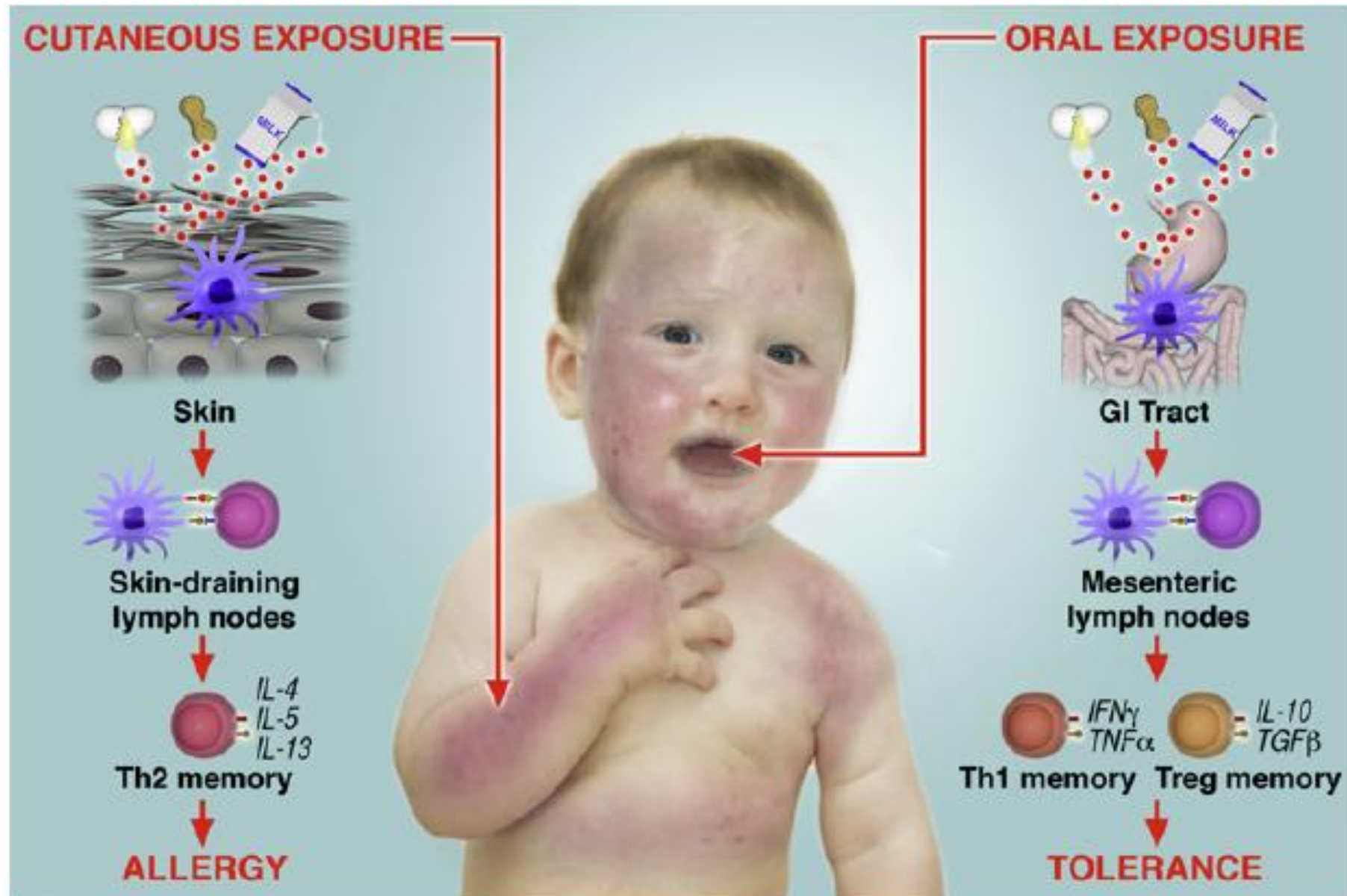


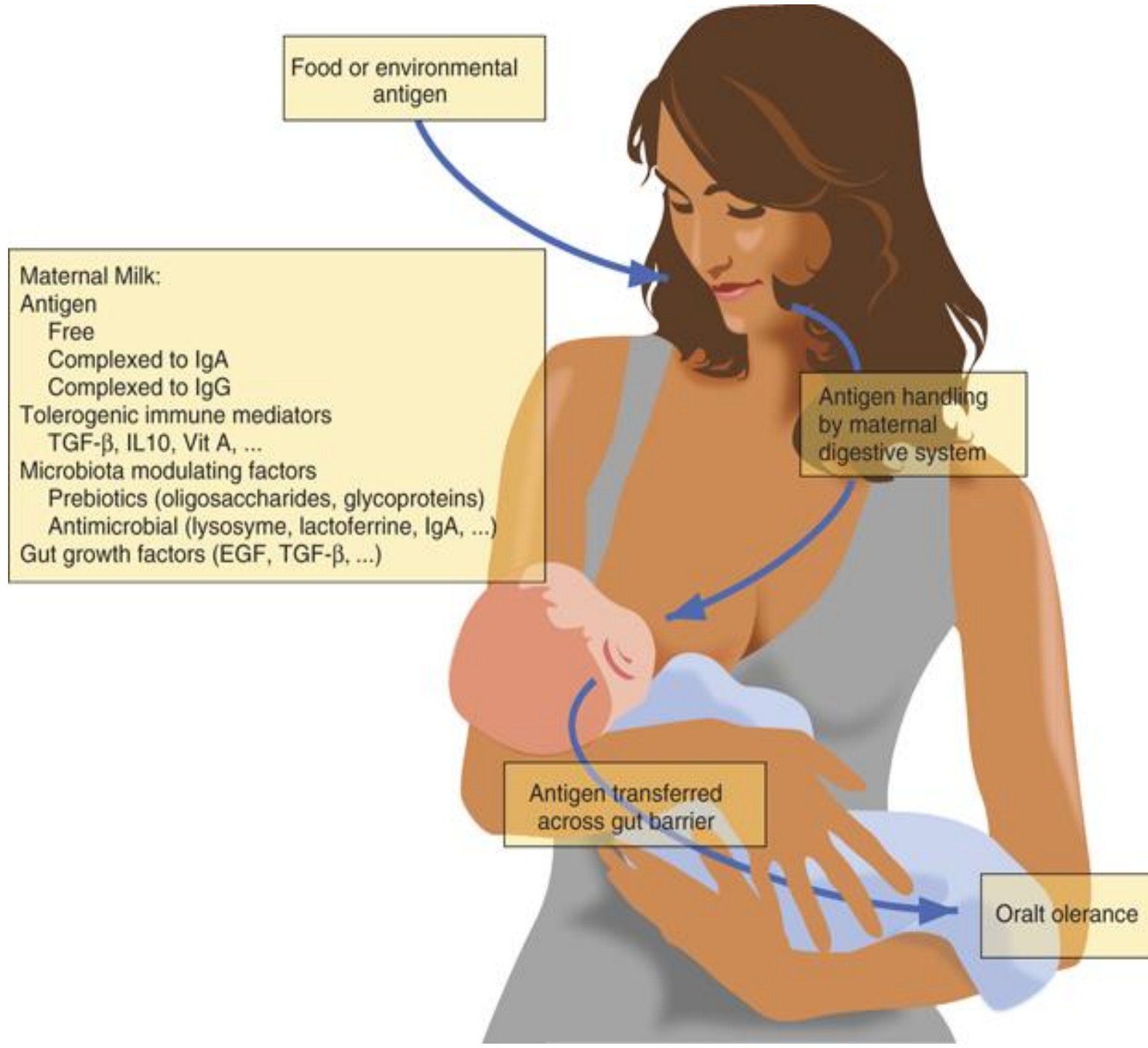
La dieta e/o supplementazioni?

diego.peroni@unipi.it

Epidemiologic risks for food allergy

Lack, JACI 2008;121:1331-6



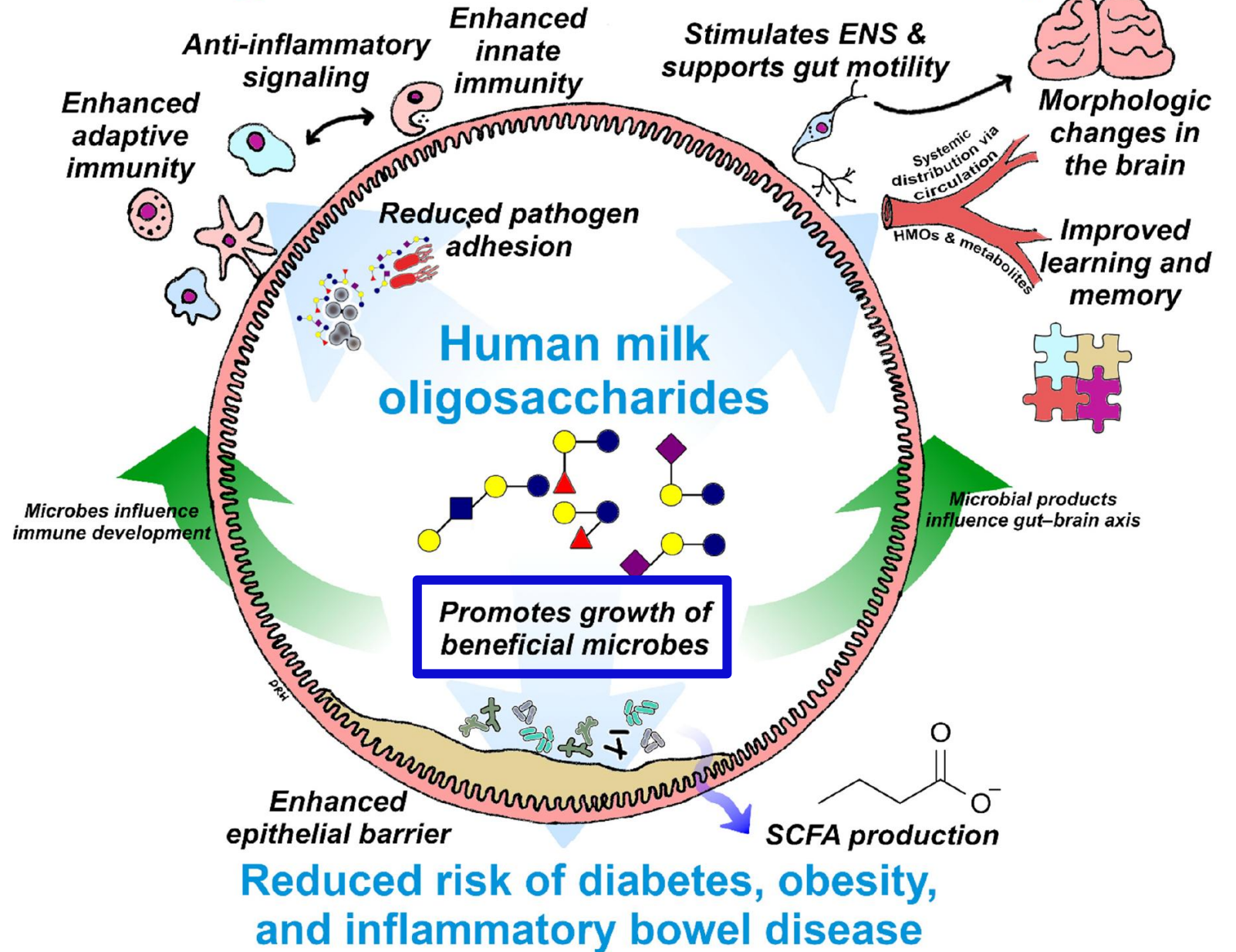


**Multifunctional Benefits
of Prevalent HMOs:
Implications for Infant
Health.**

Hill, Nutrients 2021

**Reduced risk of infection,
NEC, allergy, and asthma**

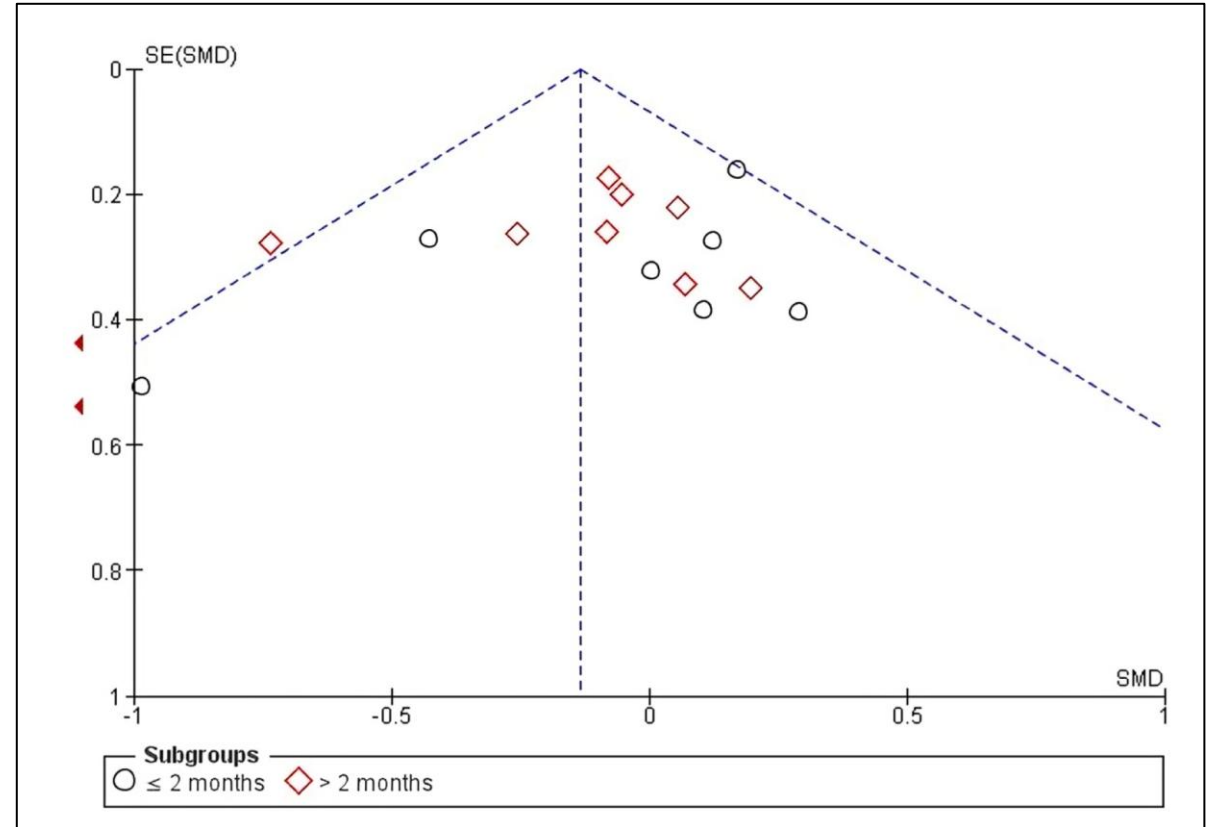
**Supports cognitive
development**



Probiotics for pediatric atopic dermatitis: A systematic review and meta-analysis of randomized controlled trials. Arif, JACIlg 2026

Analysis found that **probiotics can improve patient-reported quality of life** in the short-term but not clinical results.

SCORAD varies considerably over time and **paucity of long-term follow-up data** makes it difficult to determine the long-term clinical value of probiotics



Forest plot comparing probiotics and placebo for SCORAD score.

Effect of Synbiotic on the Gut Microbiota of Cesarean Delivered Infants: A Randomized, Double-blind, Multicenter Study.

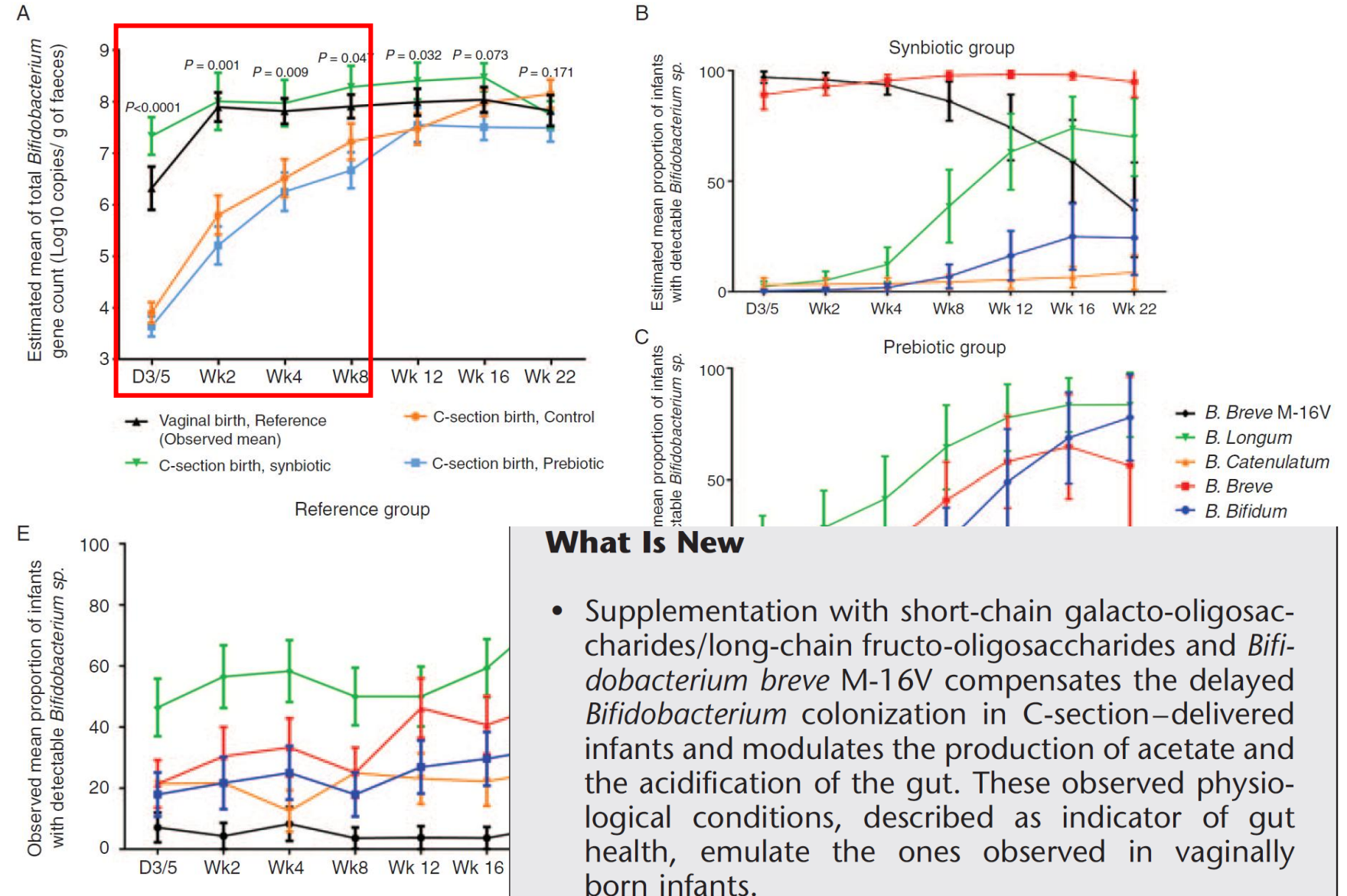
Chua, JPGN 2017;65: 102

Cesarean-born infants.

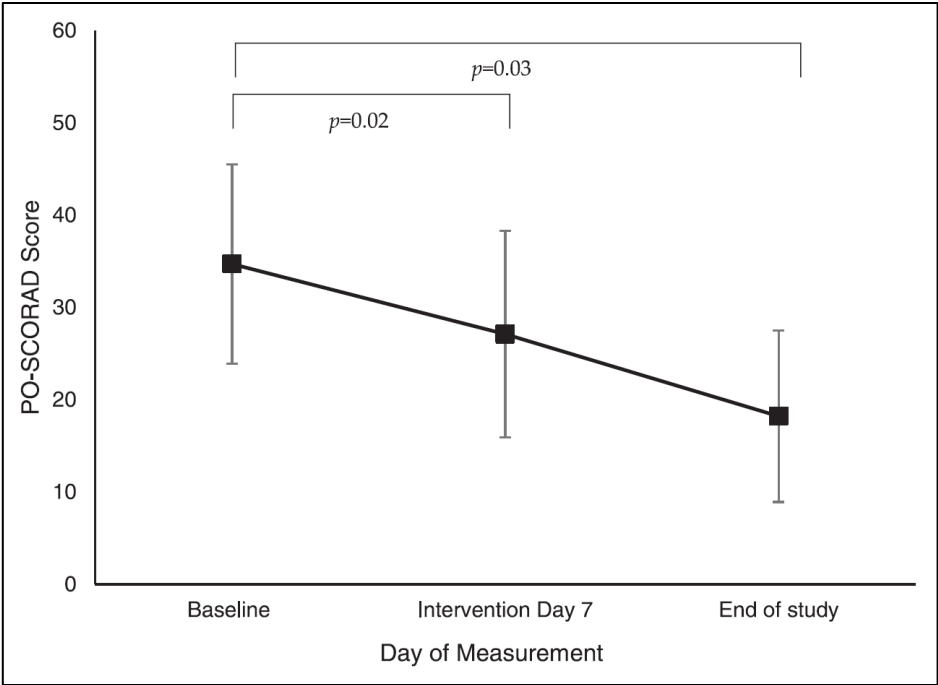
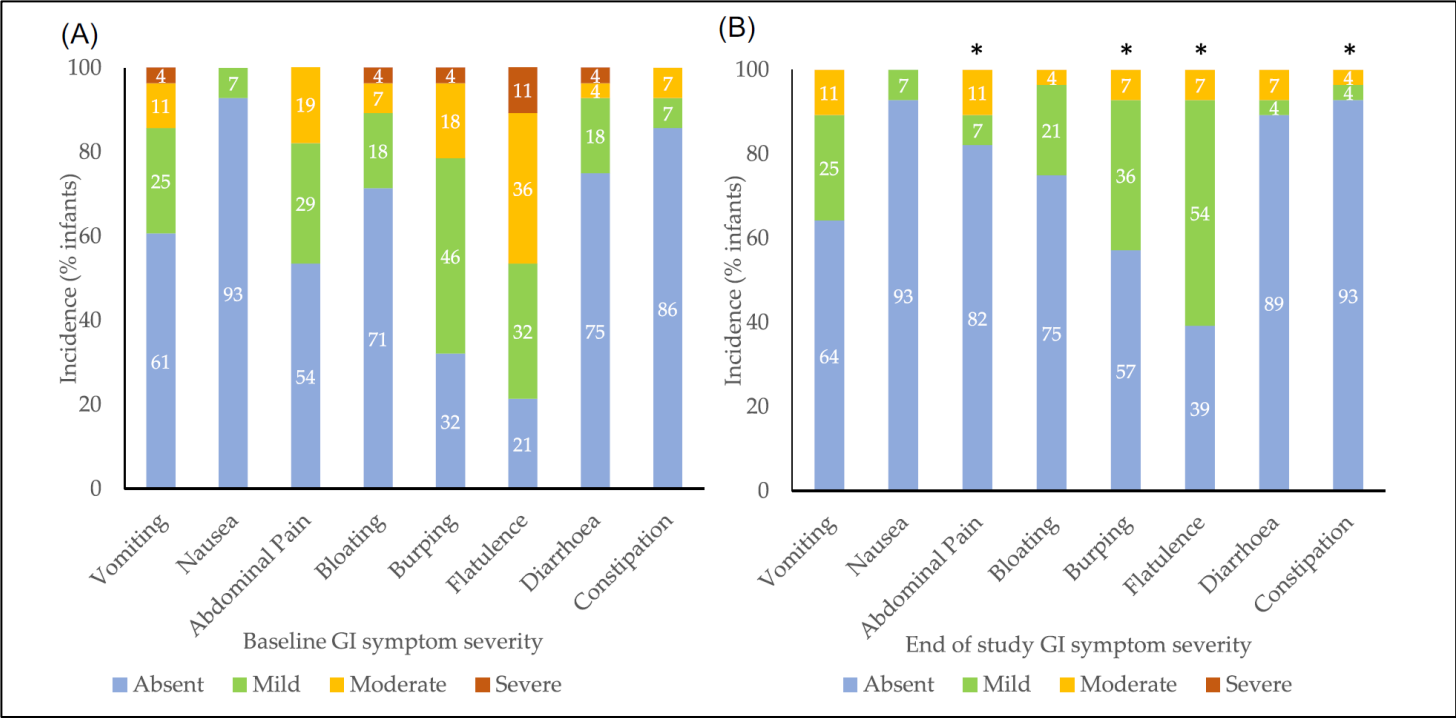
Infants were randomized to receive

- a standard formula (control),
- the same with scGOS/lcFOS and *B. breve* M-16V (synbiotic),
- or with scGOS/lcFOS (prebiotic)

from birth until week 16.



Synbiotic containing extensively hydrolyzed formula improves gastrointestinal and atopic symptom severity, growth, caregiver quality of life, and hospital-related healthcare use in infants with cow's milk allergy. Hubbard, Immun Inflamm Dis. 2022



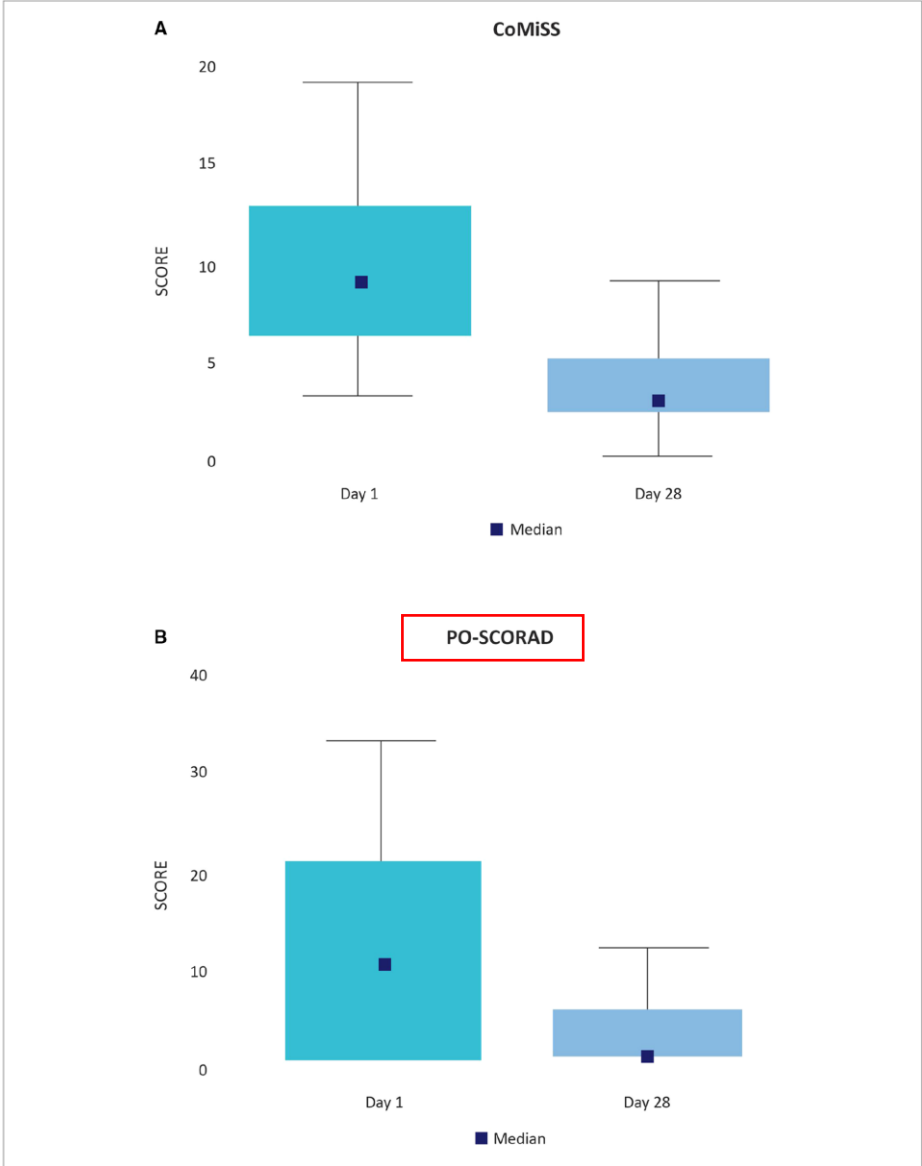
To evaluate a synbiotic-containing, whey-based eHF (SeHF) with GOS, FOS, and bifidobacterium breve M-16V in infants with CMA.

A 31-day one-arm pilot study in 29 infants with CMA

Efficacy of an extensively hydrolyzed formula with the addition of synbiotics in infants with cow’s milk protein allergy: a real-world evidence study. Soria, Front Allergy 2023

	Disappeared or improved <i>n</i> (%)	Stayed the same or got worse <i>n</i> (%)	<i>P</i>
Gastrointestinal symptoms	58 (92%)	5 (8%)	<i>p</i> < 0.05
	CI 95% 85–98	CI 95% 1.4–14.5	
Dermatological symptoms	41 (87.5%)	6 (12.5%)	<i>p</i> < 0.05
	CI 95% 77–96	CI 95% 2.8–21.1	
Respiratory symptoms	12 (63%)	7 (37%)	<i>p</i> = 0.1
	CI 95% 41–85	CI 95% 15–59	
Overall symptoms	62 (95.4%)	3 (4.6%)	<i>p</i> < 0.05
	CI 95% 89–100	CI 95% 0.2–10.2	

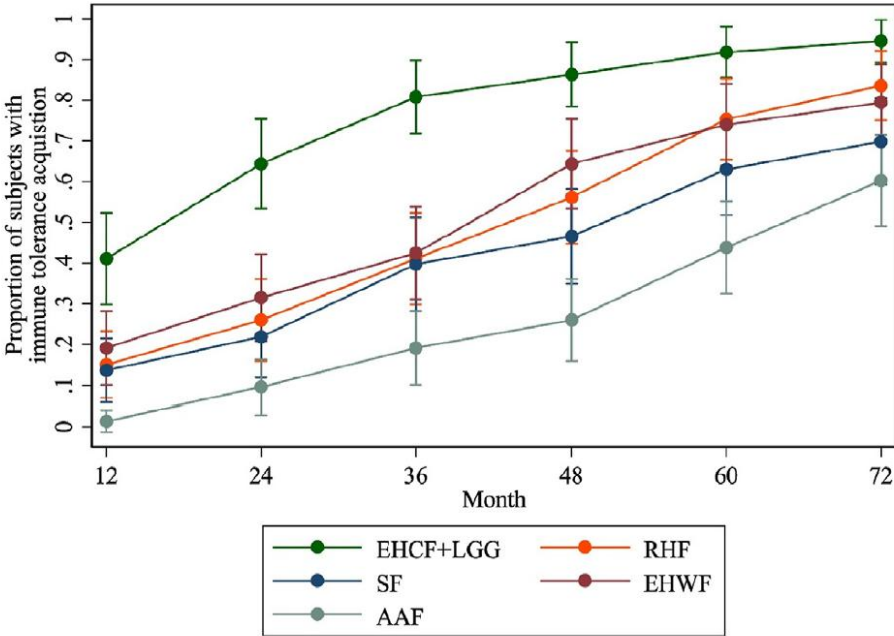
observational, longitudinal, prospective, and multicentric real-world evidence study. The intervention phase (EHF with synbiotics) lasted 28 days and was completed by 65 patients



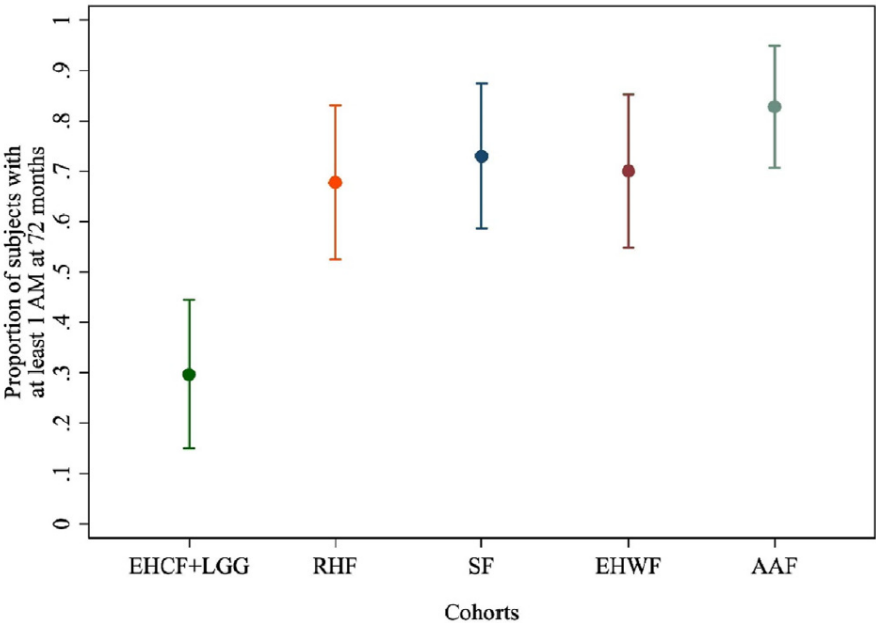
Long term impact of formula choice in children with cow milk protein allergy: 6-year follow-up of the Atopic March Cohort Study.

Nocerino R, Clin Nutr 2025

Cumulative incidence of immune tolerance acquisition in the five treatment cohorts at 72 months



Incidence of at least 1 AM at 72 months in the five treatment cohorts



The dietary treatment with EHCF þ LGG is associated with lower incidence of AMs and higher rate of immune tolerance acquisition in children with CMPA

Il bambino con DA.

Cosa conta davvero nella prevenzione
della marcia dell'allergico?



I farmaci ?

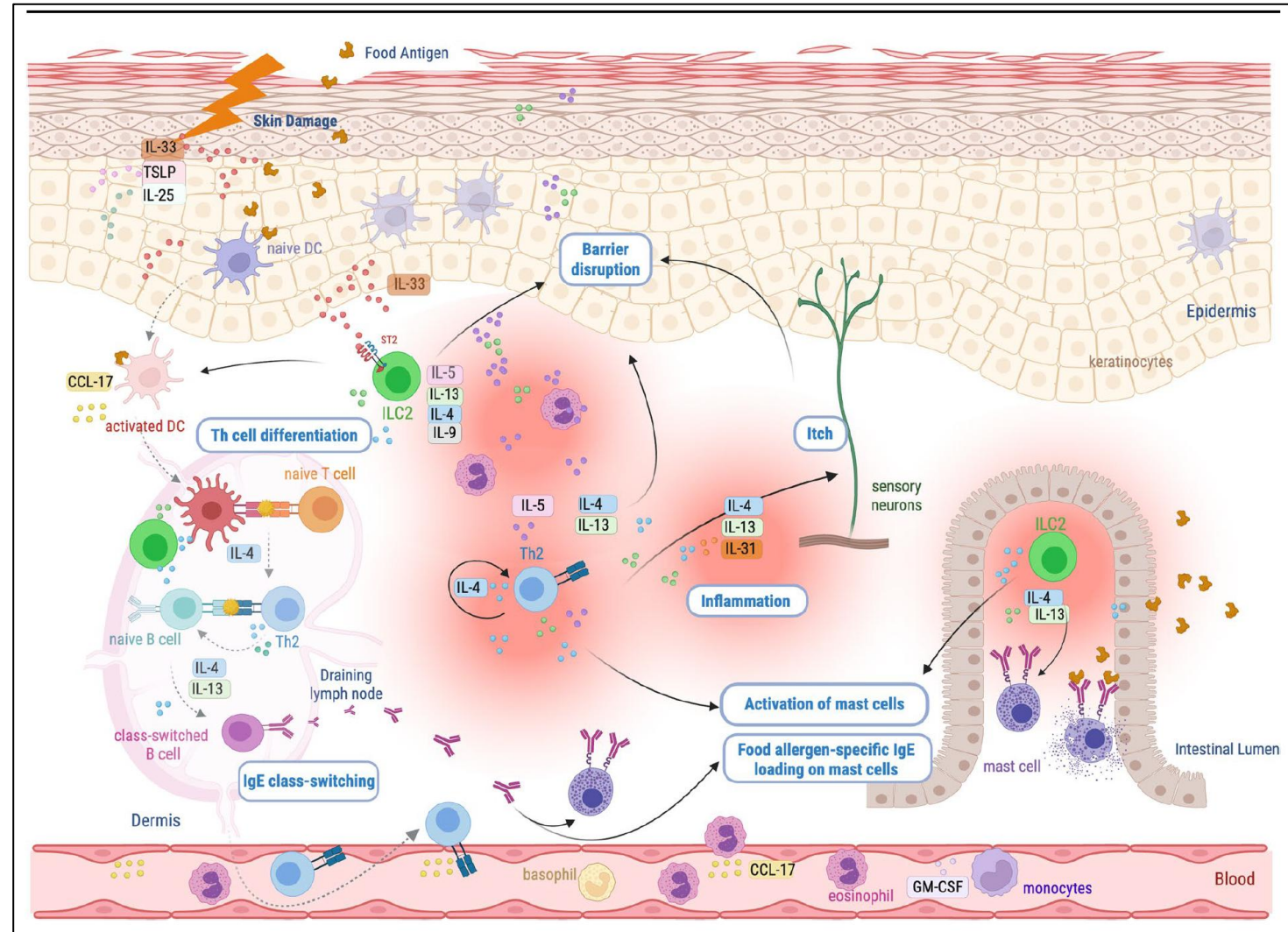
diego.peroni@unipi.it

Atopic Comorbidities and Topical Steroids in Early Childhood Atopic Dermatitis: Are We Missing a Piece of the Puzzle? Chau, Clinical Reviews in Allergy & Immunology

Although TCS remain a valuable tool, the findings suggest that they only partially address **type 2 inflammation**.

In contrast, **biologics, such as dupilumab**, demonstrate the potential for more targeted and comprehensive treatment strategies.

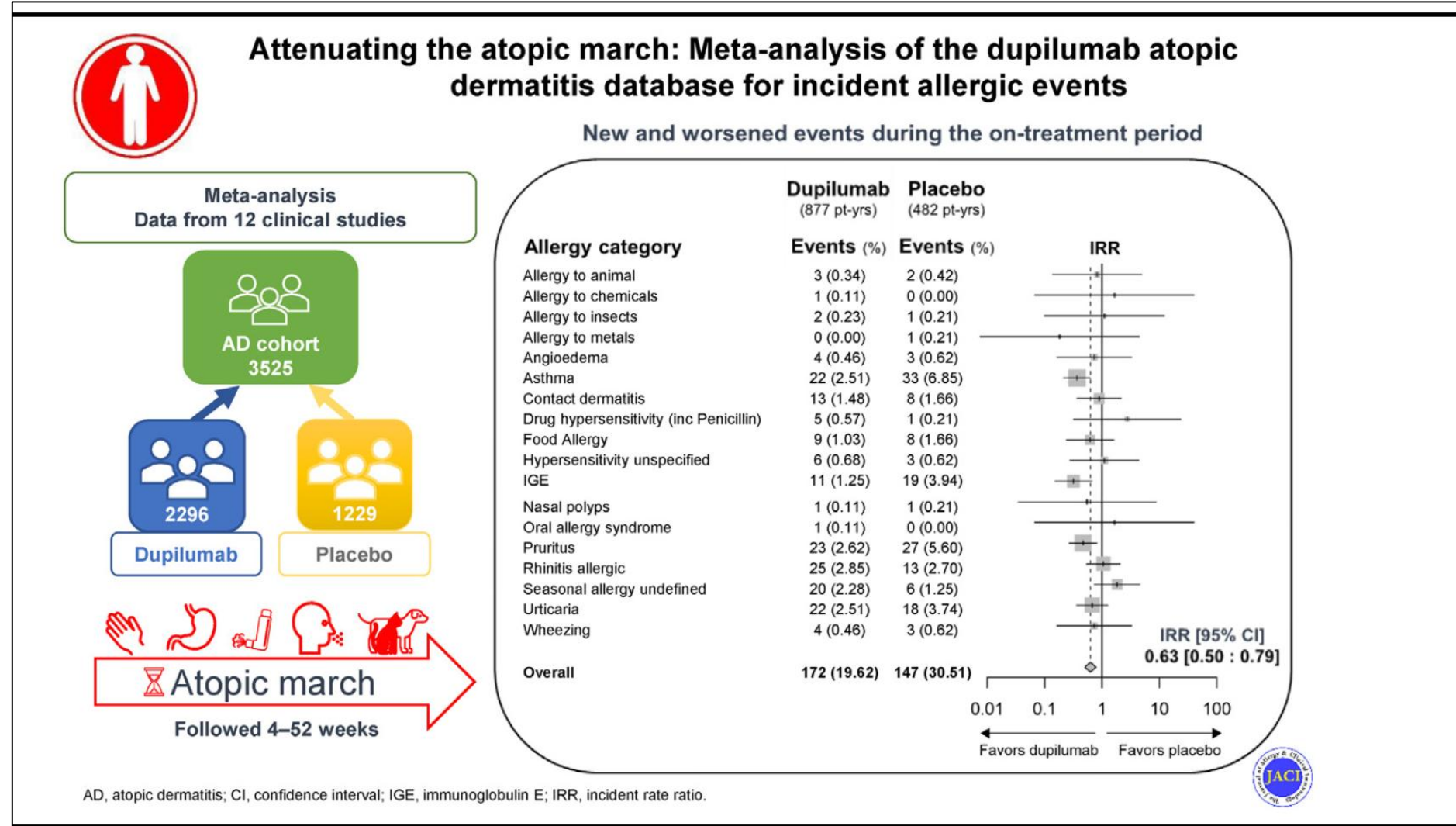
These approaches encompass both **innate and adaptive immune** components, while also providing **downstream regulation of IgE-mediated allergen sensitization**



Attenuating the atopic march: Meta-analysis of the dupilumab atopic dermatitis database for incident allergic events. Geba G, JACI 2023

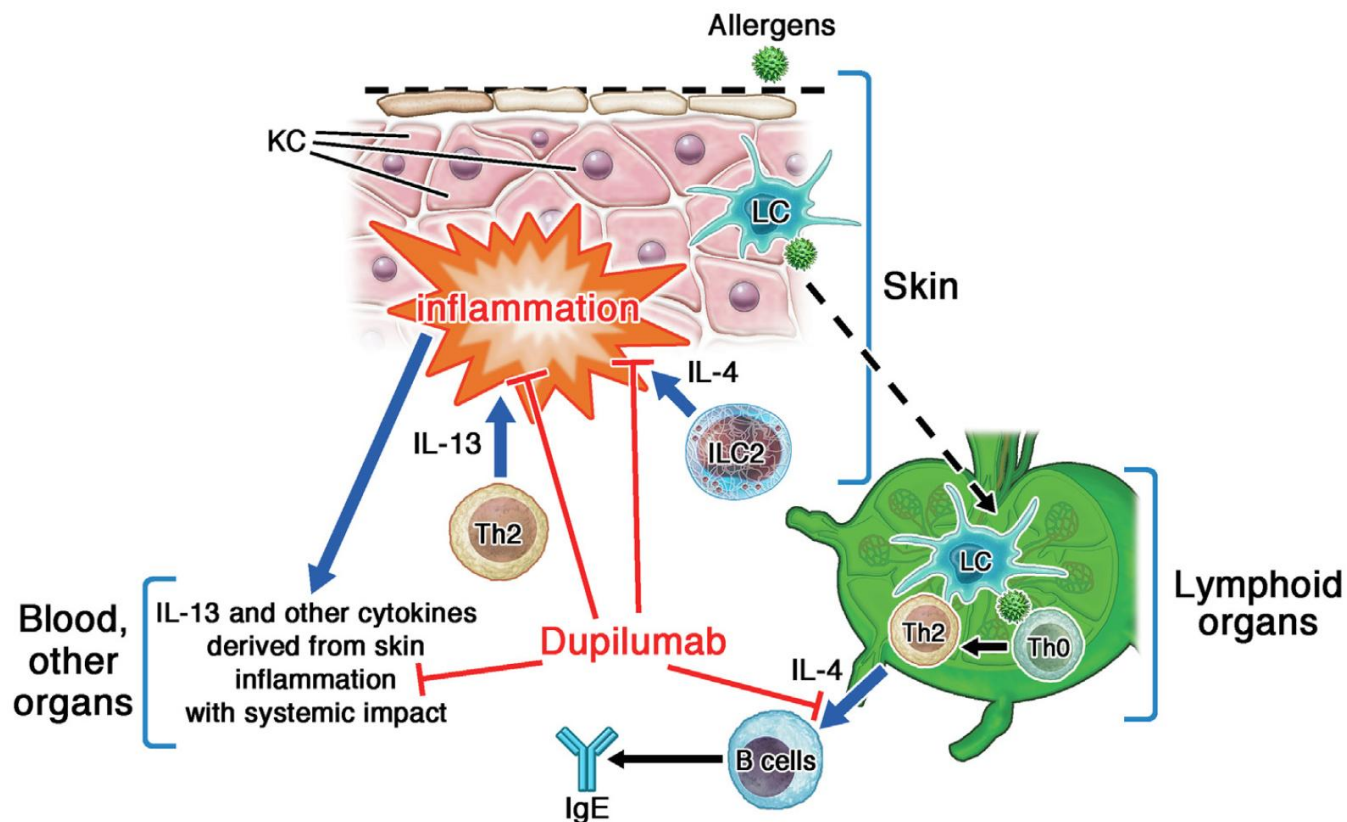
Atopic march is associated with progressive allergic disease burden, and there are no disease-modifying treatments.

Dupilumab was associated with fewer new/worsening allergies in AD and may attenuate atopic march



In search of the Holy Grail in atopic dermatitis: Will dupilumab become the first disease-modifying atopic dermatitis drug?

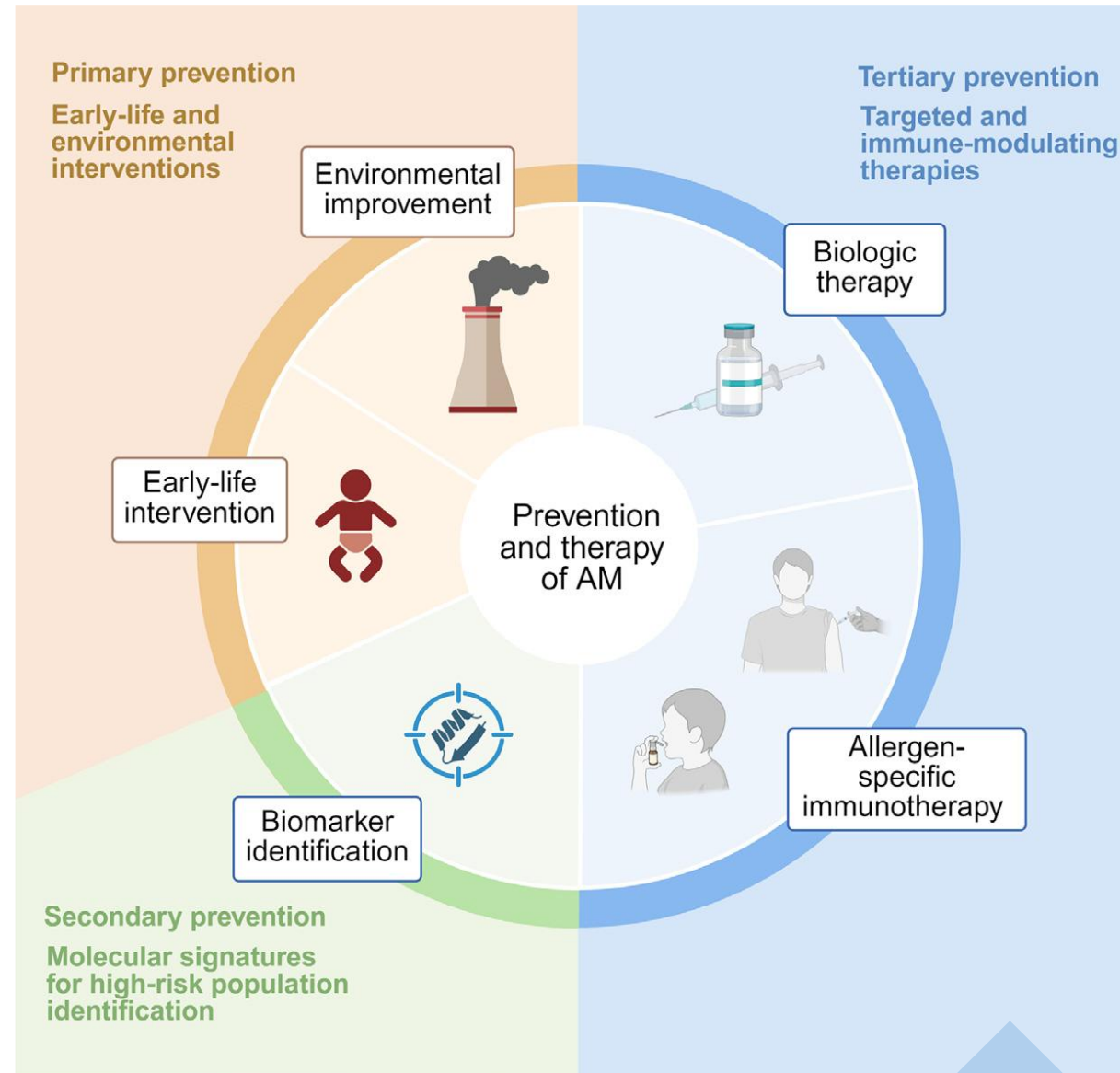
T Bieber, JACI 2023



Reduced skin inflammation will also **hamper the skin-derived sensitization** mechanisms initiated by epidermal Langerhans cells (LCs) that have captured allergens, ultimately leading to increased allergen-specific IgE contributing to new allergies as described in the atopic march.

By blocking the biologic activity of IL-4, dupilumab should also **directly hamper the widening of the IgE synthesis** generated by the skin-derived sensitization.

La prevenzione è una bella sfida



Mark, 7 anni

Motivo della visita:

Da tre anni riferita comparsa di dermatite atopica, prevalentemente a livello delle estremità (dorso delle mani, pieghe interdigitali e dorso dei piedi).

Per tale sintomatologia è stata effettuata terapia con Antistaminico orale a cicli di 2 settimane, associata a regolare applicazione di creme emollienti e utilizzo di saponi oleosi.

Nel 2022 effettuati esami ematici in Russia con riscontro di IgE specifiche per albume (0.43 kUA/L) e IgE specifiche per il latte (0.48 kUA/L) lievemente al di sopra del limite .

Nega reazioni immediate dopo l'assunzione di latte e uova, ma per tali risultati indicata dallo specialista dermatologo dieta priva di uova, latte e derivati.

Mark, 7 anni

- **Prick Test per latte e uova** (albume, tuorlo, lattealbumina, betalattoglobulina, caseina): negativi
- **Prick by prick latte:** negativo

Mark, 7 anni

Consigli:

- In considerazione della clinica e della negatività alle prove cutanee, si consiglia reintroduzione graduale di uova e latte nella dieta.
- Docce con acqua tiepida (non troppo calda) per non più di 10 minuti
- Utilizzare **saponi oleosi** per il bagno, da eseguire 2-3 volte a settimana; asciugare la cute tamponando, senza frizionare. Utilizzare biancheria in cotone ed evitare il contatto con la lana.
- Applicare una **crema emolliente per dermatite atopica** 2 volte al giorno sulle aree di cute xerotica e sempre dopo il bagno.
- Nelle fasi acute (lesioni rosso vivo con ragadi ed essudato) applicare **crema a base di cortisone** esclusivamente sulle lesioni attive: dopo almeno un'ora dall'applicazione delle altre creme, 1 applicazione 2 volte al giorno per 5-7 giorni.
- In caso di spiccato prurito (soprattutto la notte) o arrossamento cutaneo assumere **antistaminico orale** una volta al giorno per 3-5 giorni.

Rajan, 4 anni

Motivo della visita:

Da circa un anno Dermatite Atopica localizzata prevalentemente a livello del volto e regione periauricolare.

Effettuata per tale motivo visita dermatologica con indicazione a effettuare terapia antistaminica orale e applicazione di creme emollienti, e a limitare l'assunzione di latte vaccino e derivati.

I genitori riferiscono che il bambino ha sempre assunto latticini, senza alcuna reazione associata.

Rajan, 4 anni

- **Prick test Proteine del latte** (lattoalbumina, beta lattoglobulina, caseina) → Positività per betalattoglobulina (Pomfo 5 mm, Eritema 13 mm)
- **Prick by Prick Latte fresco** → Positivo (Pomfo 4 mm, Eritema 16 mm)

Rajan, 4 anni

Esame	Esito	Unità di misura	Valori di riferimento
Esame Emocromocitometrico			
Leucociti	14,73	10 ³ /μL	5,0 - 15,0
Eritrociti	4,88	10 ⁶ /μL	4,0 - 5,4
Emoglobina	13,4	g/dL	12,0 - 14,0
Ematocrito	39,5	%	33 - 42
Vol. Corpuscolare Medio	80,9	fL	75,0 - 90,0
Cont. Emogl. Corp. Medio	27,5	pg	26 - 33
Conc. Emogl. Corp. Media	33,9	g/dL	31 - 36
Anisocitosi Eritrocitaria	12,4	%	11,5 - 15,0
Piastrine	313	10 ³ /μL	140 - 450
Vol. Piastrinico Medio	9,5	fL	8,0 - 11,9
G.neutrofili %	44,7	%	35,0 - 65,0
Linfociti %	26,5 *	%	30,0 - 70,0
Monociti %	8,2	%	2,0 - 13,0
G.eosinofili %	19,6 *	%	fino a 5,0
G.basofili %	1,0 *	%	fino a 0,5
G.neutrofili	6,60	10 ³ /μL	1,25 - 9,75
Linfociti	3,90	10 ³ /μL	1,50 - 10,50
Monociti	1,21 *	10 ³ /μL	fino a 0,9
G.eosinofili	2,88 *	10 ³ /μL	fino a 0,7
G.basofili	0,14	10 ³ /μL	fino a 0,2
Immunoglobuline IgE	3.483 *	U/mL	50 - 120

Esame	Metodo	Esito	Unità di misura	Valori di riferimento
Ricerca IgE specifiche				
IgE specifiche Alim. pediatria				
f1-Albume		1,19 *	kUA/L	> 0,1 Pres. Sensibilizzaz.
f2-Latte		2,16 *	kUA/L	> 0,1 Pres. Sensibilizzaz.
f3-Pesce (merluzzo)		0,01	kUA/L	> 0,1 Pres. Sensibilizzaz.
f4-Grano		0,22 *	kUA/L	> 0,1 Pres. Sensibilizzaz.
f13-Arachide		0,08	kUA/L	> 0,1 Pres. Sensibilizzaz.
f24-Gambero		0,08	kUA/L	> 0,1 Pres. Sensibilizzaz.
f25-Pomodoro		0,45 *	kUA/L	> 0,1 Pres. Sensibilizzaz.
f49-Mela		0,06	kUA/L	> 0,1 Pres. Sensibilizzaz.

Il Dirigente

Rajan, 4 anni

Consigli:

- In considerazione della debole reazione alle prove allergologiche cutanee, a domicilio **reintrodurre latte vaccino e derivati**
- Utilizzare **saponi oleosi** per dermatite atopica per il bagnetto, da eseguire 2-3 volte a settimana; asciugare tamponando la cute, senza frizionare. Utilizzare biancheria in cotone ed evitare il contatto con la lana.
- Applicare una **crema emolliente per dermatite atopica** almeno 1 volta al giorno sulle aree di cute xerotica e sempre dopo il bagno.
- Nelle fasi acute (lesioni rosso vivo con ragadi ed essudato) applicare **crema a base di cortisone** esclusivamente sulle lesioni attive: 1 applicazione 2 volte al giorno per 3-4 giorni