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Nutraceutica e Malattie Respiratorie

Nutrizione, allattamento al seno, vitamina D

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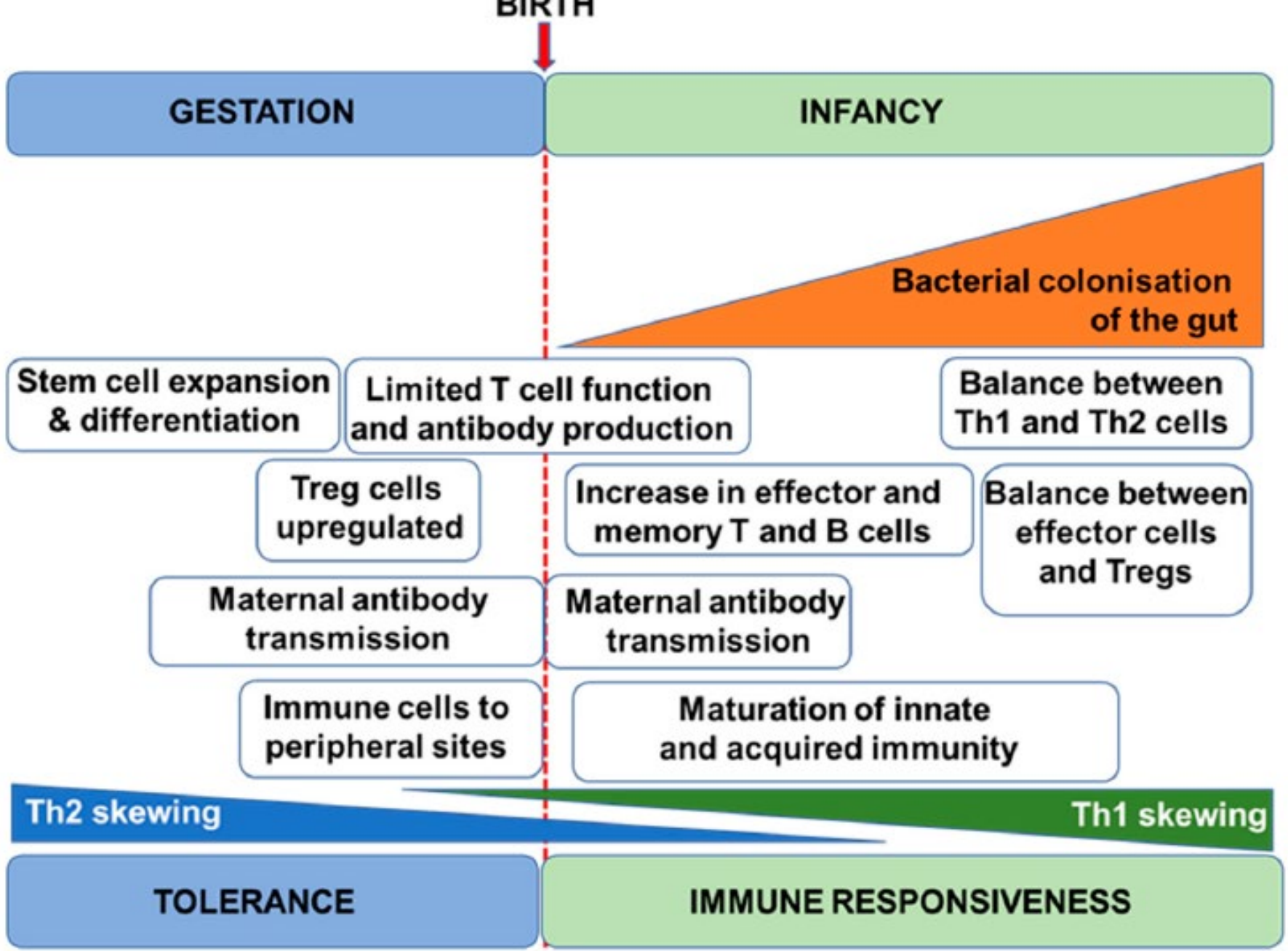


Miles, Nutrients 2021

Editorial: Role of early life nutrition in immunomodulation and microbiota development

Diego G. Peroni[1]*, Cristina Campoy[2,3,4] and Elvira Verduci[5]

frontiers | Frontiers in Nutrition

TYPE Editorial
PUBLISHED 16 October 2023
DOI 10.3389/fnut.2023.1266725

Early life nutrition

The concept of immune modulation is emerging and leads to fascinating prospective in order to prevent or treat, if already established, several disorders all comprised in the category of the non-communicable diseases.

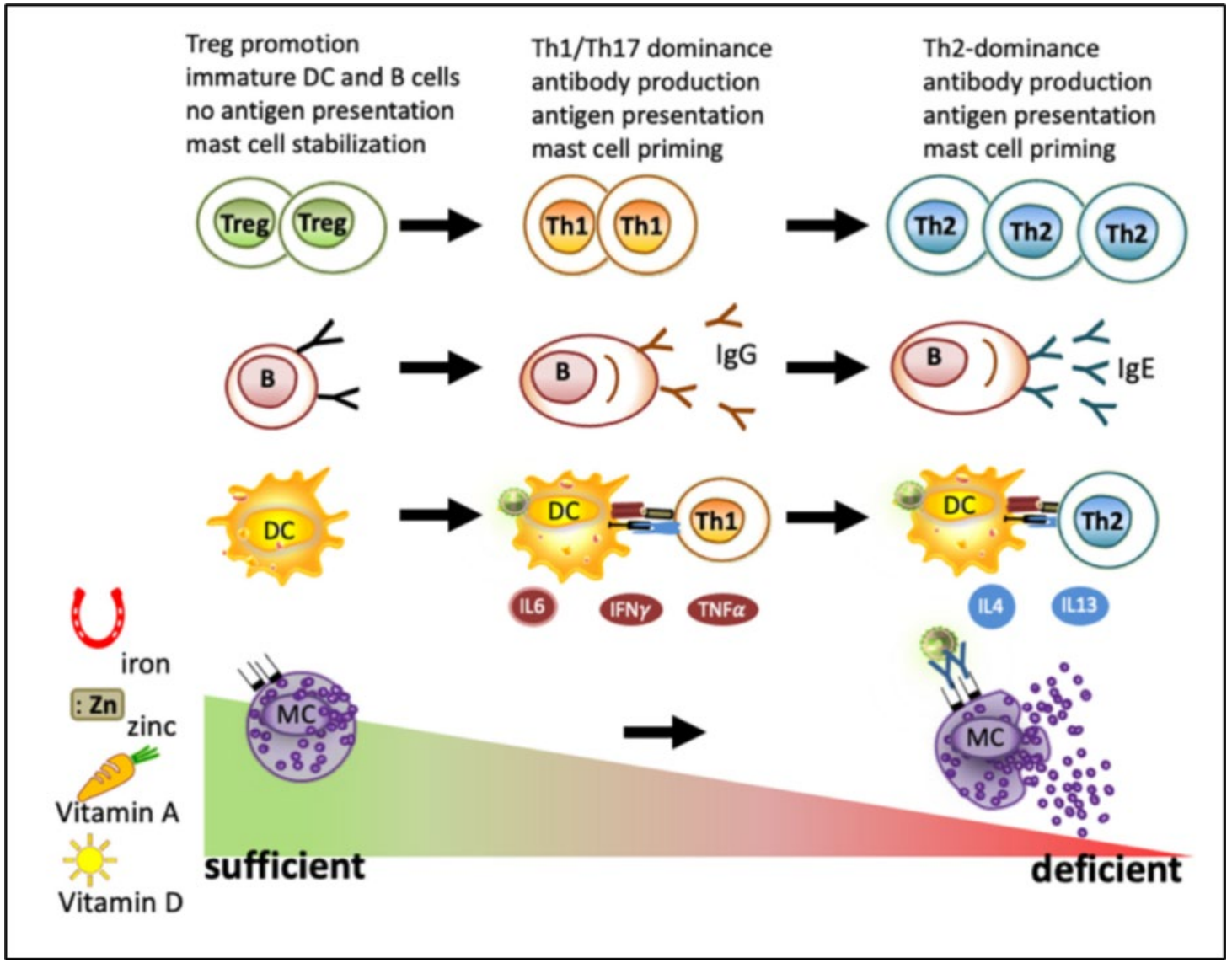
All this evidence highlights the importance of a balanced diet from the pregnancy, early life, thought adulthood to minimize and/or prevent health problems.

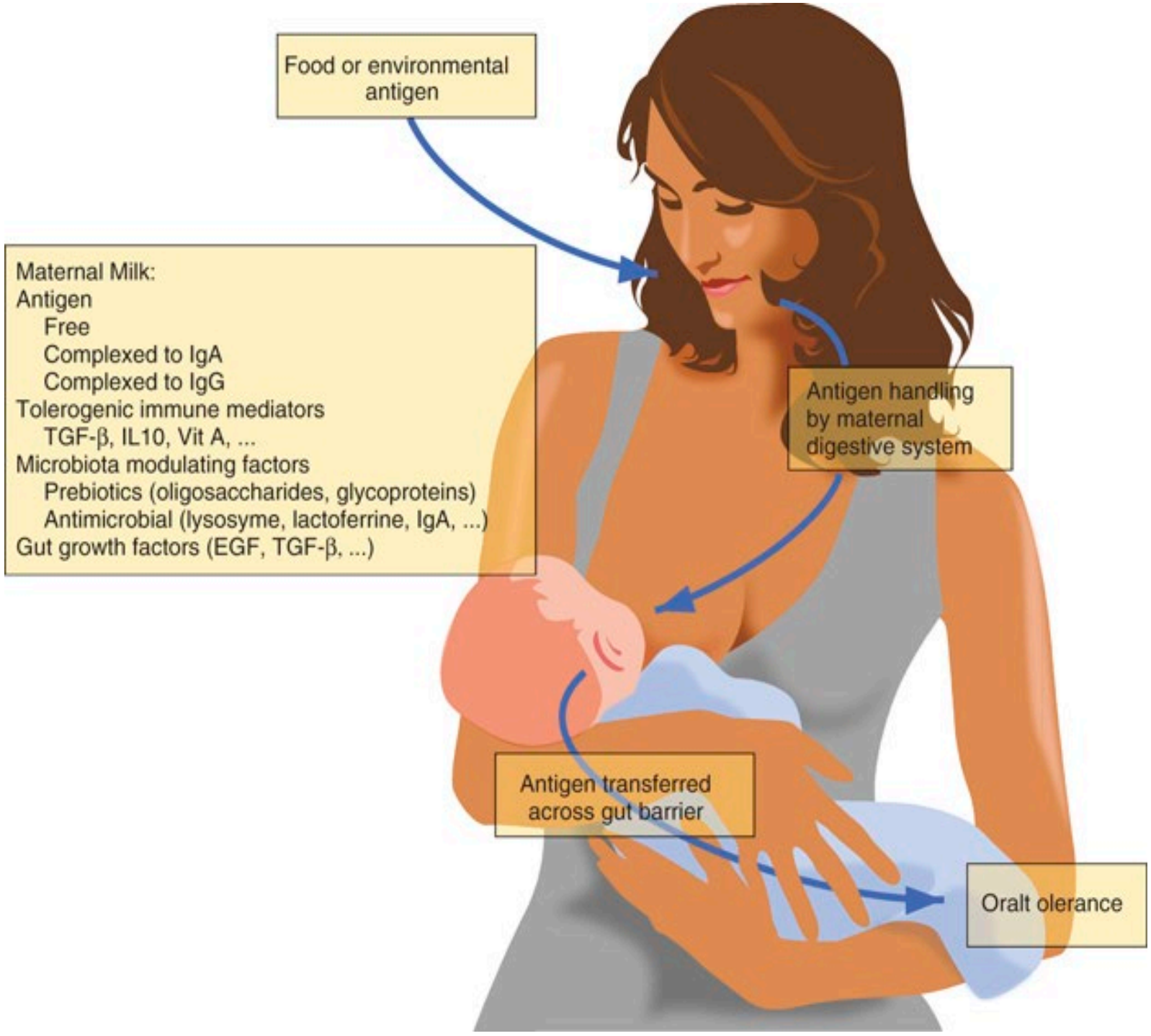
Una dieta sana e varia contenente latticini, pesce, noci, frutta e verdura, nonché l'integrazione di alimenti o micronutrienti secondo necessità, è essenziale per combattere la marcia atopica

Lack of iron, zinc, and vitamins as a contributor to the etiology of atopic diseases.

Diego G. Peroni, et al.

Front Nutr 2023



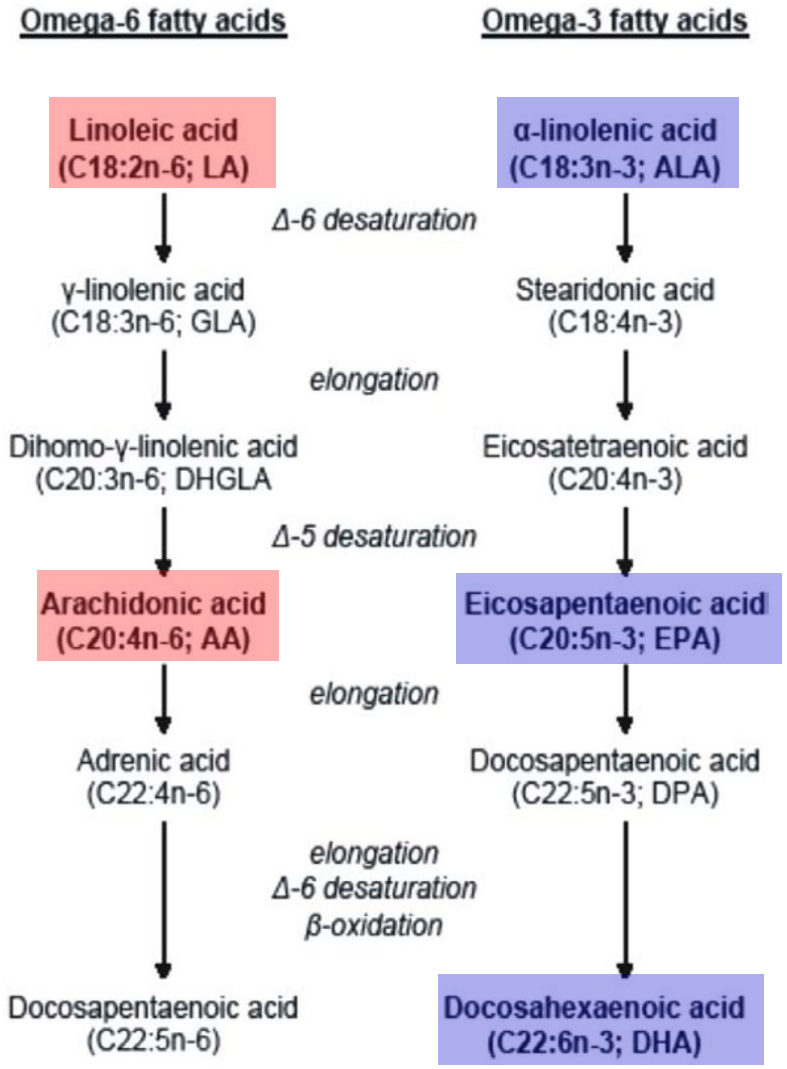

Food or environmental antigen
Maternal Milk:
Antigen
Free
Complexed to IgA
Complexed to IgG
Tolerogenic immune mediators
TGF-β, IL10, Vit A, ...
Microbiota modulating factors
Prebiotics (oligosaccharides, glycoproteins)
Antimicrobial (lysosyme, lactoferrine, IgA, ...)
Gut growth factors (EGF, TGF-β, ...)
Antigen handling by maternal digestive system
Antigen transferred across gut barrier
Oralt olerance

Breast milk fatty acid composition has a long-term effect on the risk of asthma, eczema, and sensitization

Van Elten T M, Allergy 2015;70:1468–1476

- In particolare, l'acido alfa-linoleico degli acidi grassi **polinsaturi n-6 (PUFA)** e i loro derivati a catena lunga, **l'acido arachidonico (AA),** sembrano essere associati a un incremento delle malattie allergiche.

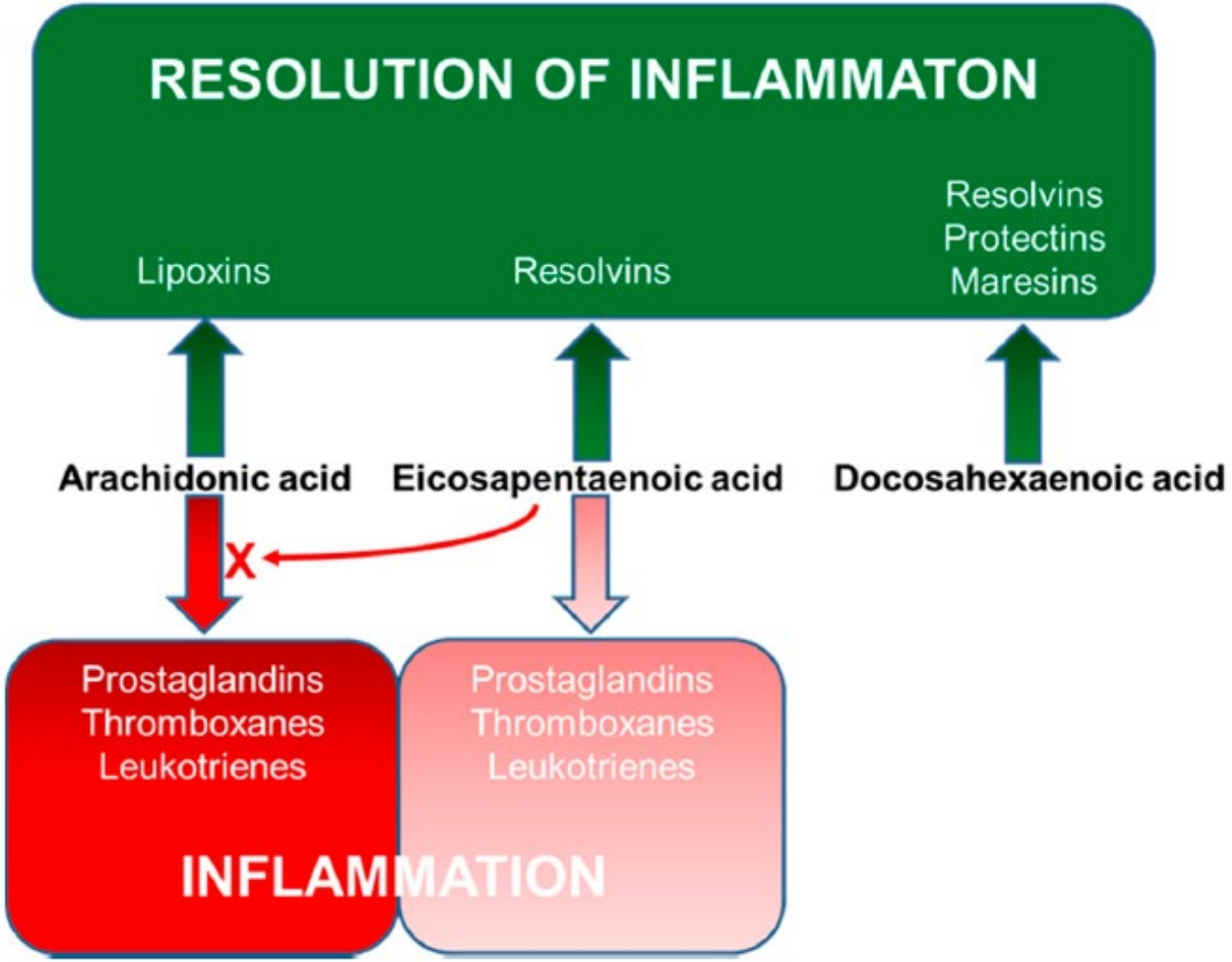
- **PUFA N-3: l'acido eicosapentaenoico (EPA) e l'acido docosaesaenoico (DHA)** sembrano avere un effetto protettivo, mentre un elevato apporto di PUFA n-6 sembra aumentare il rischio di malattie allergiche.



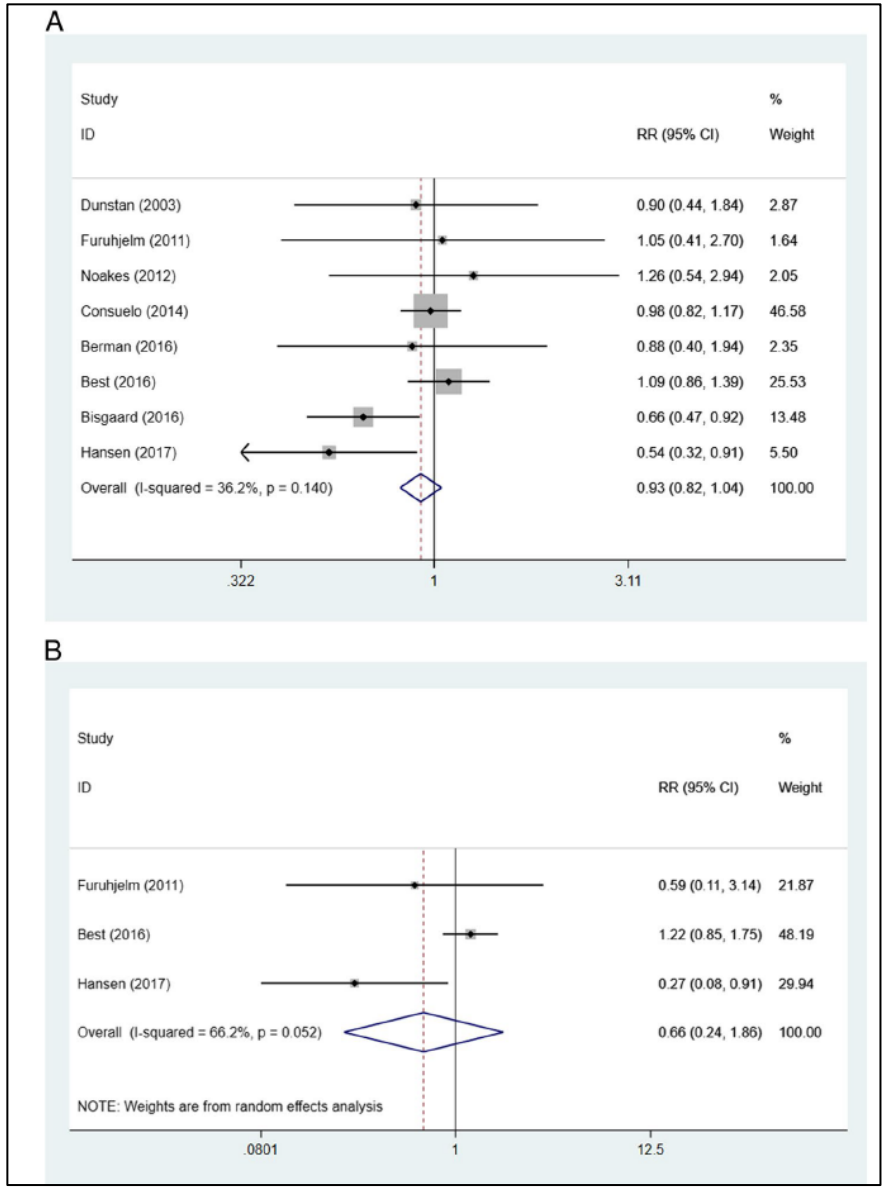
Long-Chain Polyunsaturated Fatty Acids (LCPUFAs) and the Developing Immune System: A Narrative Review. Miles, Nutrients 2021

Effetto protettivo

COME?



A dose-response meta-analysis of the association between the maternal omega-3 long-chain polyunsaturated fatty acids supplement and risk of asthma/wheeze in offspring. Y Jia, BMC Pediatrics 2022



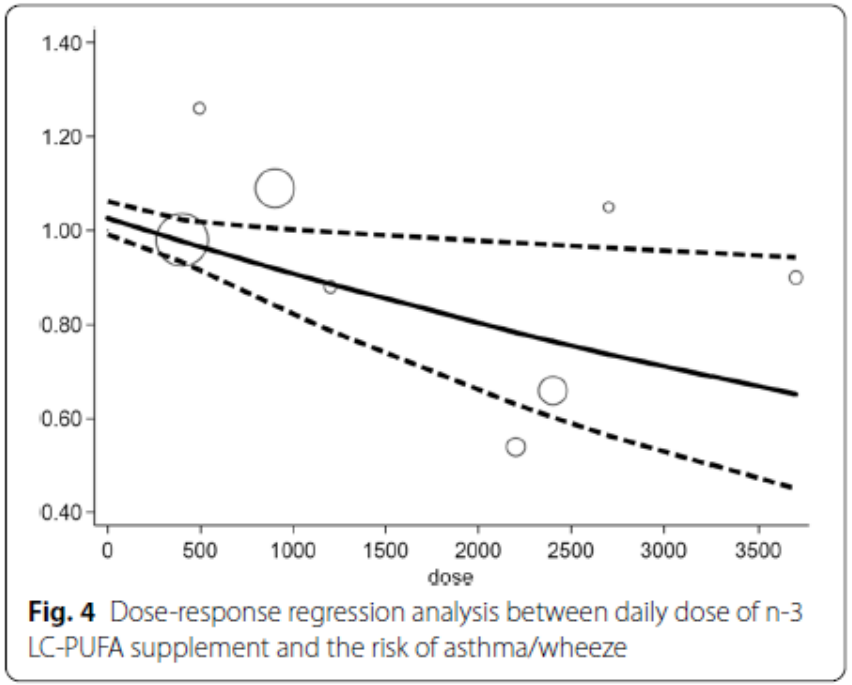


Fig. 4 Dose-response regression analysis between daily dose of n-3 LC-PUFA supplement and the risk of asthma/wheeze

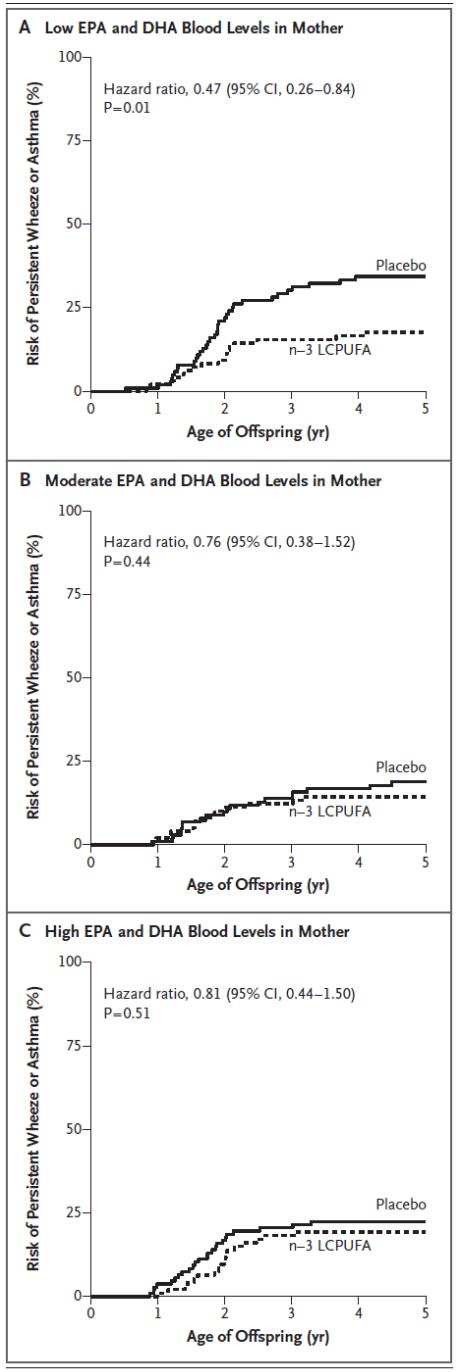
I risultati hanno mostrato che **l'integrazione prenatale con n-3 LC-PUFA può ridurre l'incidenza di asma/ respiro sibilante** o asma allergico nella prole in **determinate circostanze**.

Secondo l'analisi della dose-risposta, dosi più elevate suggeriscono effetti protettivi più forti

Fish Oil–Derived Fatty Acids in Pregnancy and Wheeze and Asthma in Offspring Hans Bisgaard, NEJM 2016

736 donne gravide dalla 24a settimana di gestazione hanno ricevuto **2,4 g di n-3 LCPUFA** (olio di pesce) o placebo (olio di oliva) al giorno.

I loro figli hanno formato il gruppo Copenhagen Prospective Studies on Asthma in Childhood 2010 (**COPSAC 2010**) e sono stati seguiti in modo prospettico con un'ampia fenotipizzazione clinica



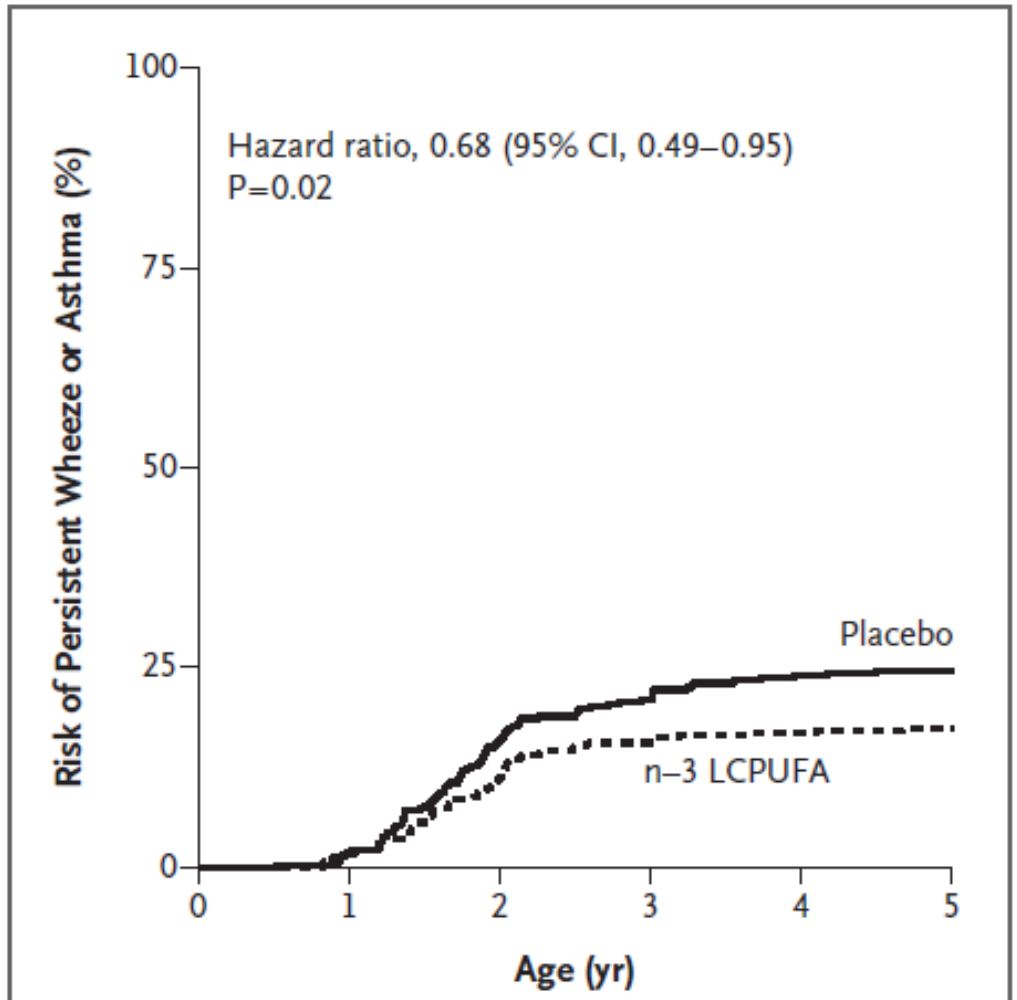


Figure 1. Risk of Persistent Wheeze or Asthma in Children According to n–3 LCPUFA Supplementation or Placebo during Pregnancy.

LCPUFA denotes long-chain polyunsaturated fatty acids.

Fish Oil–Derived Fatty Acids in Pregnancy and Wheeze and Asthma in Offspring Hans Bisgaard, NEJM 2016

La supplementazione con n-3 LCPUFA nel terzo trimestre di gravidanza ha **ridotto il rischio di respiro sibilante** persistente o asma e infezioni del tratto respiratorio inferiore nella prole di **circa 7 punti percentuali, ovvero un terzo**.

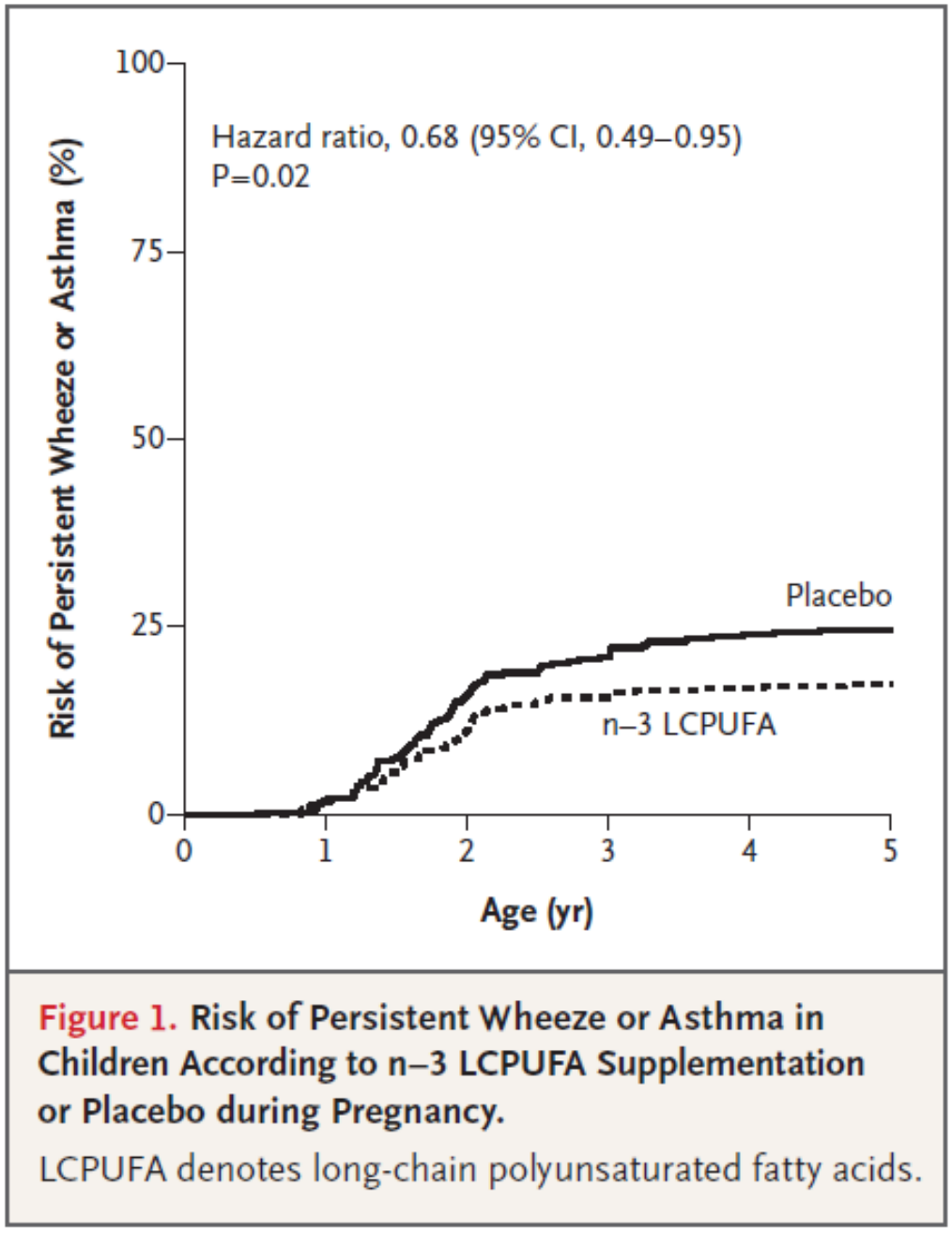


Figure 1. Risk of Persistent Wheeze or Asthma in Children According to n–3 LCPUFA Supplementation or Placebo during Pregnancy.

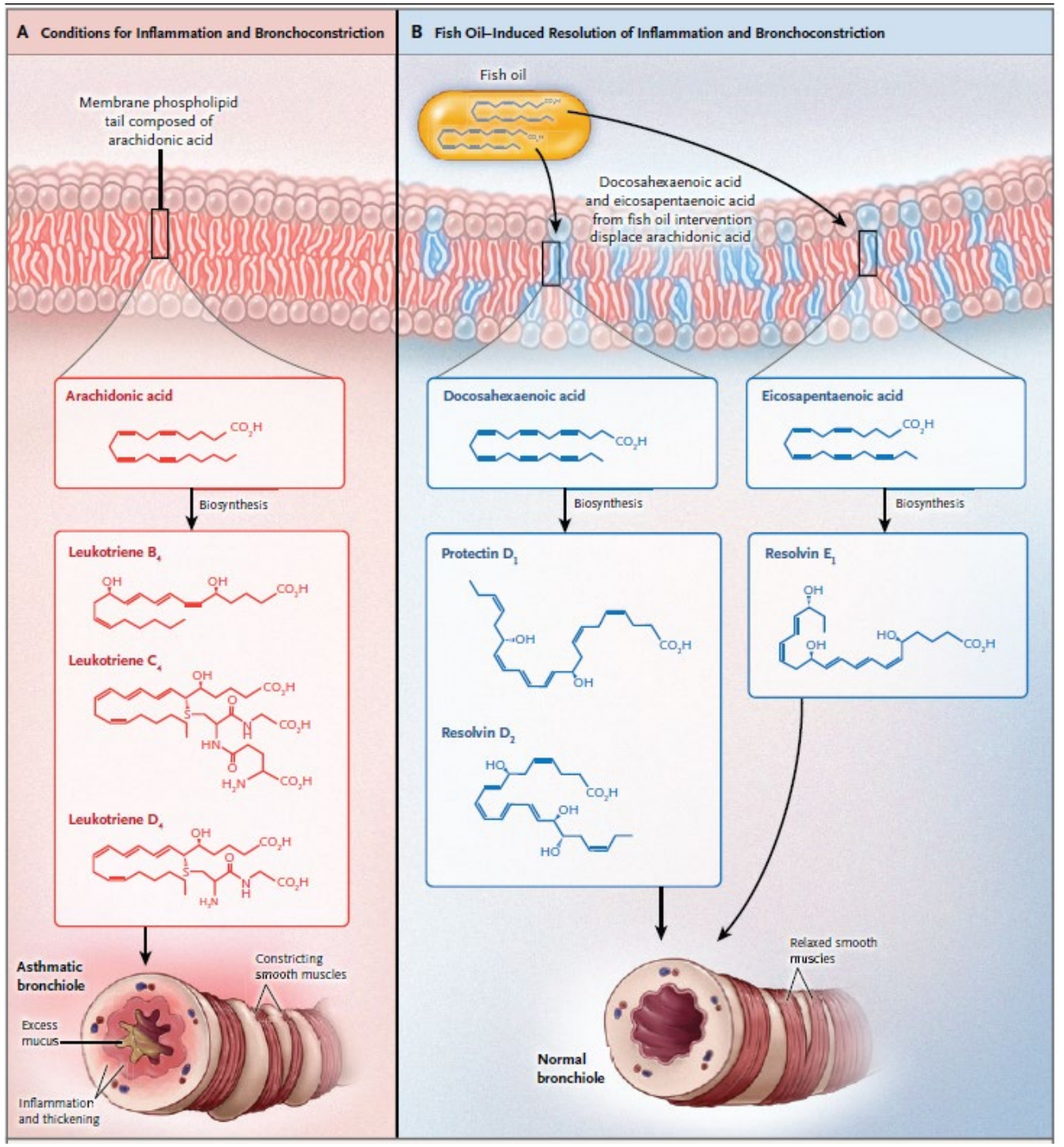
LCPUFA denotes long-chain polyunsaturated fatty acids.

Breathing Easier with Fish Oil — A New Approach to Preventing Asthma? Christopher E. Ramsden NEJM

I leucotrieni sintetizzati dall'acido arachidonico mediano la broncocostrizione e l'infiammazione delle vie aeree.

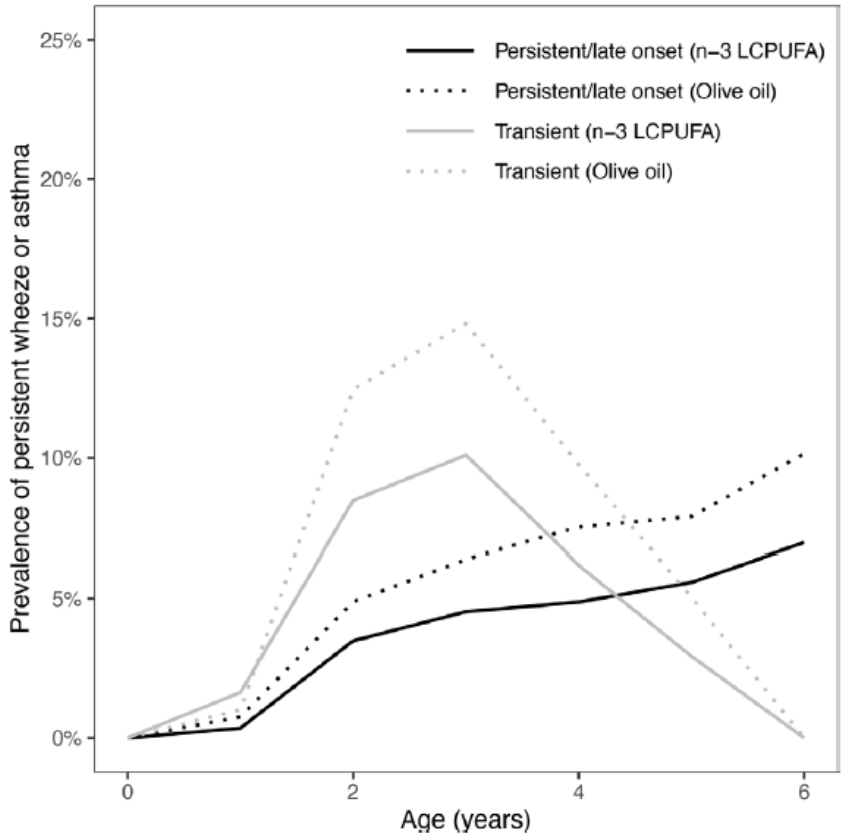
L'acido docosaesaenoico e l'acido eicosapentaenoico nell'olio di pesce sostituiscono l'acido arachidonico nei fosfolipidi di membrana, che fungono da precursori per la biosintesi dei mediatori lipidici.

Questo effetto sposta l'equilibrio dai mediatori dell'infiammazione e della broncocostrizione verso la risoluzione dell'infiammazione e la difesa dell'ospite.



Atopic and non-atopic effects of fish oil supplementation during pregnancy.

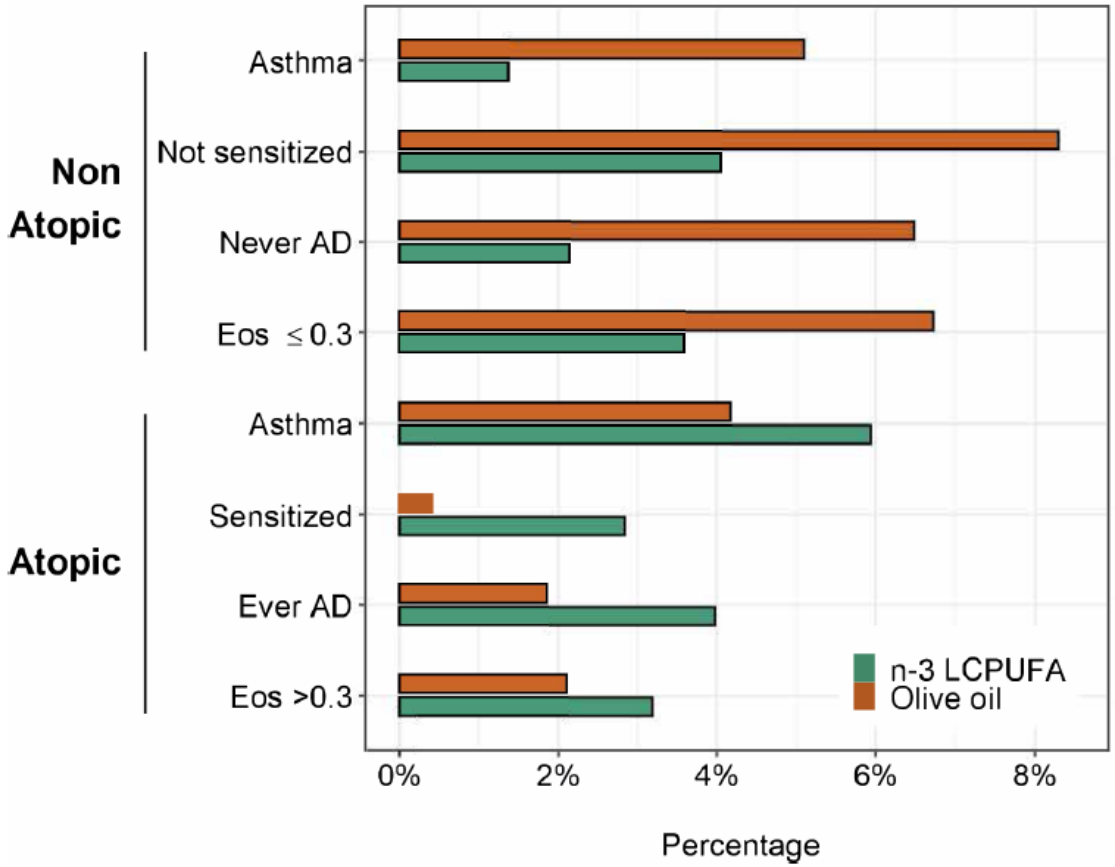
H Bisgaard, Thorax 2022



L'integrazione di n-3 LCPUFA in gravidanza ha mostrato effetti protettivi sull'asma e sulle infezioni non atopiche. Gli effetti protettivi sull'asma atopico **dipendevano**

1. **dal genotipo FADS materno**
2. **2. dai livelli di LCPUFA n-3**.

Frequenza di asma non atopico e sottogruppi di asma atopico all'età di 6 anni nella n-3 LCPUFA e strati di olio d'oliva



The association between n-3 polyunsaturated fatty acid intakes and asthma in US children and adolescents: A cross-sectional study from NHANES.

Zhang, PAI 2023

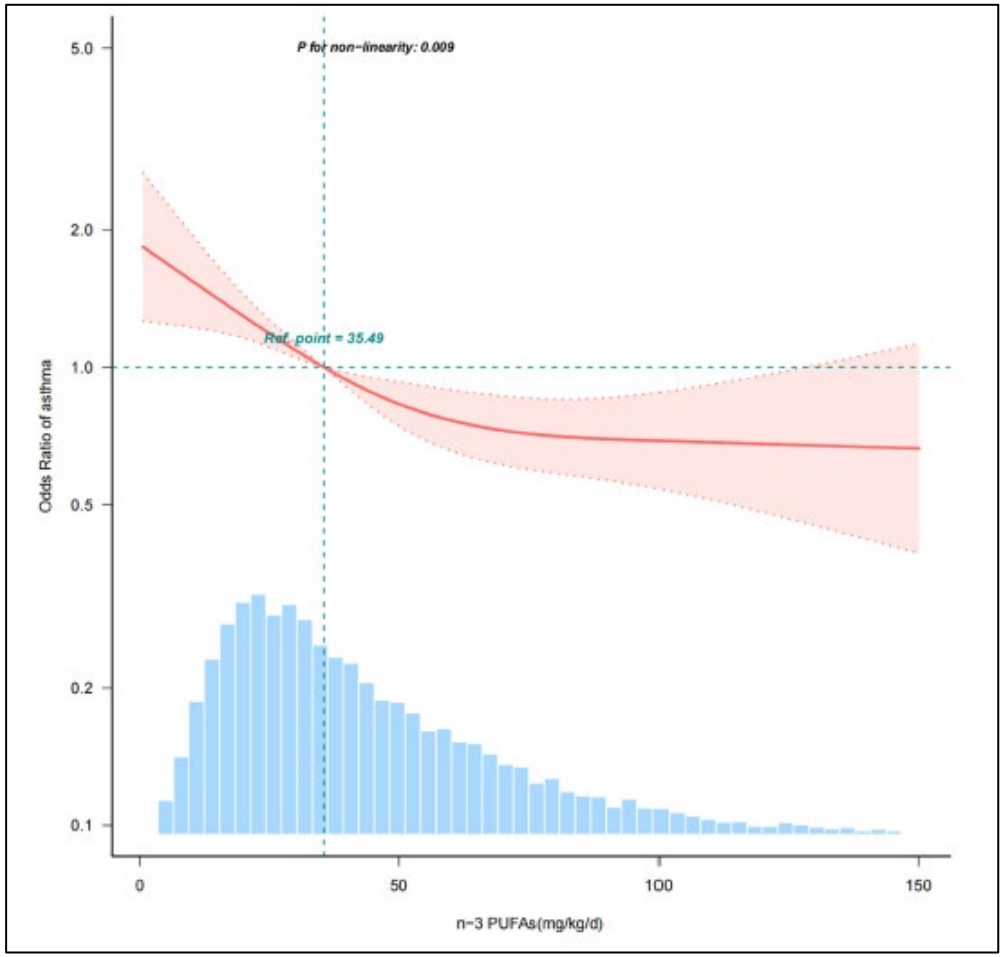
8543 bambini e adolescenti del National Health and Nutrition Examination Survey (NHANES)

Dopo aver aggiustato per potenziali fattori confondenti,

rispetto agli individui nel gruppo con il consumo più basso di PUFA n-3
(T1, <26,07 mg/kg/giorno),

l'odds ratio (OR) aggiustato per l'asma era **0,71** (IC 95%: 0,6–0,84, p < 0,001) nel secondo gruppo (T2, 26,07–48,93 mg/kg/giorno)

e **0,58** (IC 95%: 0,47–0,73, p < 0,001) nel terzo gruppo (T3, >48,93 mg/kg/giorno).



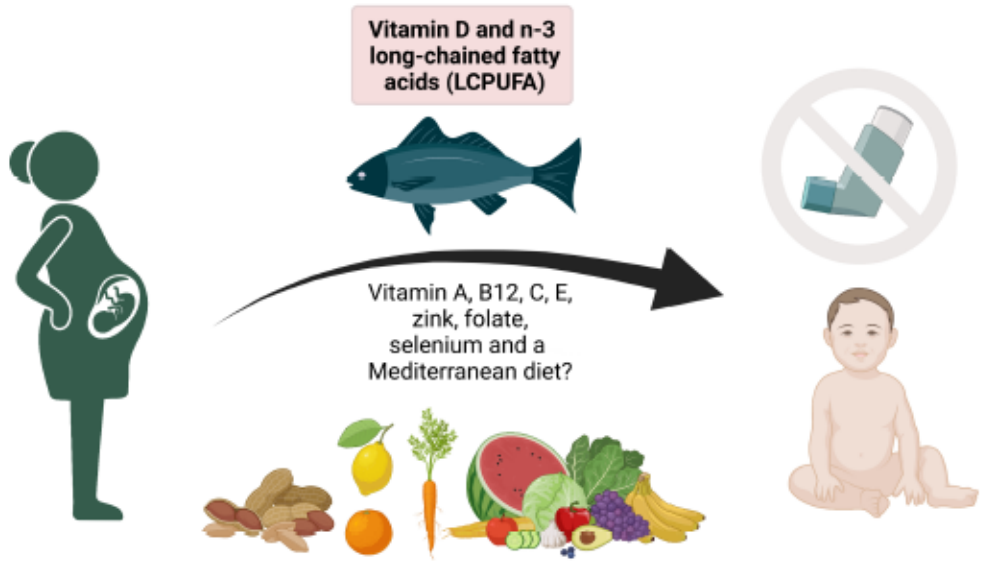
REVIEW ARTICLE

WILEY

Dietary prevention strategies for childhood asthma

Nicklas Brustad | Klaus Bønnelykke | Bo Chawes

Dietary primary prevention of early childhood asthma

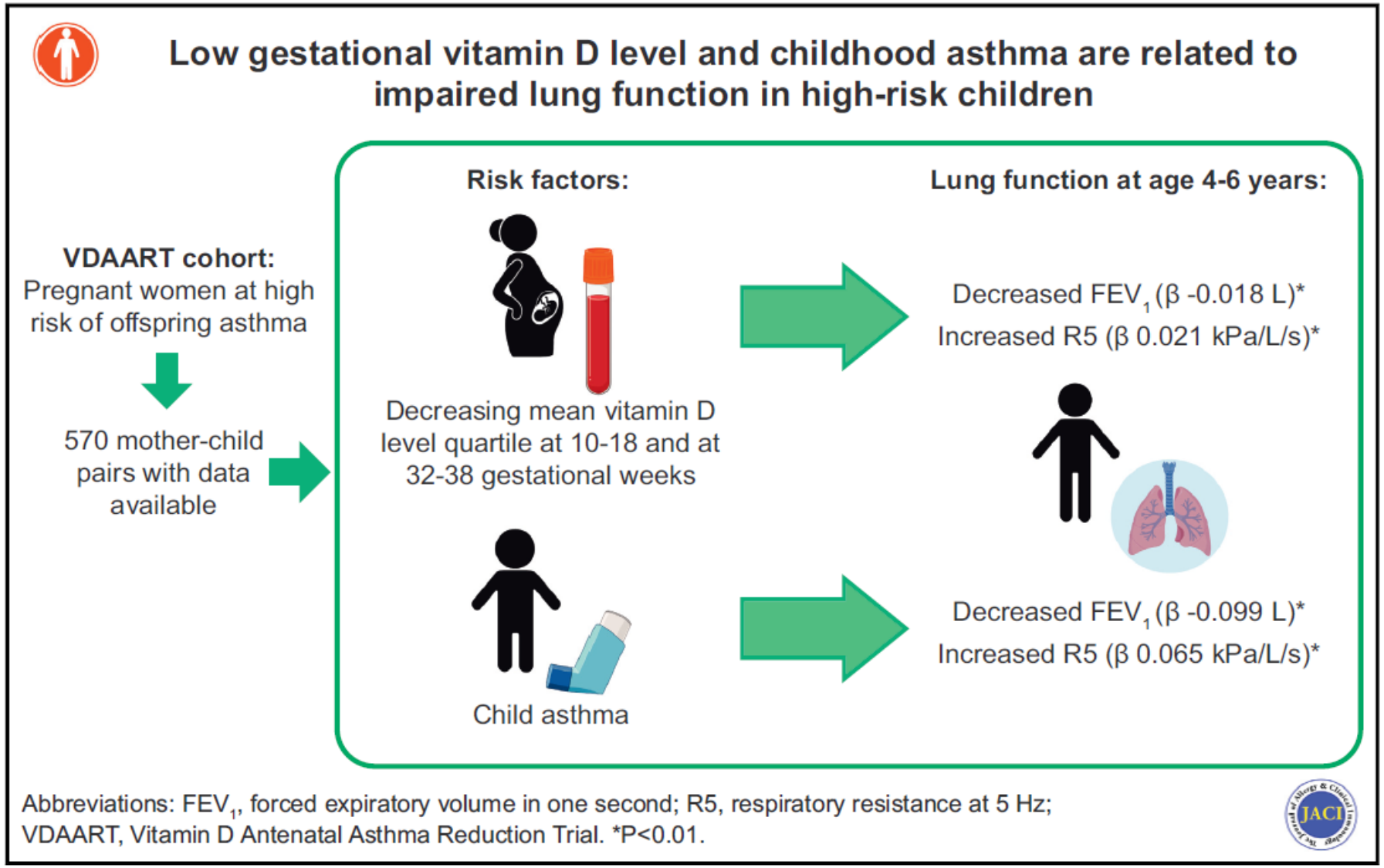


LCPUFA	Fatty fish (salmon, herring, mackerel etc.)	Antioxidant effects, reduced airway inflammation and fetal lung development	*Primary*: One large pregnancy RCT ($COPSAC_{2010}$) showing reduction in asthma and respiratory infections until age 6 years. A meta-analysis only showing reduction among European populations. In early childhood, one large RCT did not find an effect from supplementation on wheeze at age 1 year. *Secondary*: Promising effect from observational studies on lung function and medication use. One small RCT showed reduction in symptoms among school aged children with asthma. *Future research needs*: Large primary RCTs for secondary prevention.

Low gestational vitamin D level and childhood asthma are related to impaired lung function in high-risk children

Hanna M. Knihtilä, MD, PhD,[a] Benjamin J. Stubbs, BA,[a] Vincent J. Carey, PhD,[a] Nancy Laranjo, BA,[a] Su H. Chu, PhD,[a] Rachel S. Kelly, PhD,[a] Robert S. Zeiger, MD, PhD,[b] Leonard B. Bacharier, MD,[c] George T. O'Connor, MD, MS,[d] Jessica Lasky-Su, ScD,[a] Scott T. Weiss, MD, MS,[a]* and Augusto A. Litonjua, MD, MPH[e]* *Boston, Mass; San Diego and Pasadena, Calif; St Louis, Mo; and Rochester, NY*

Low gestational 25(OH)D level and childhood asthma are important risk factors for decreased lung function in early childhood.

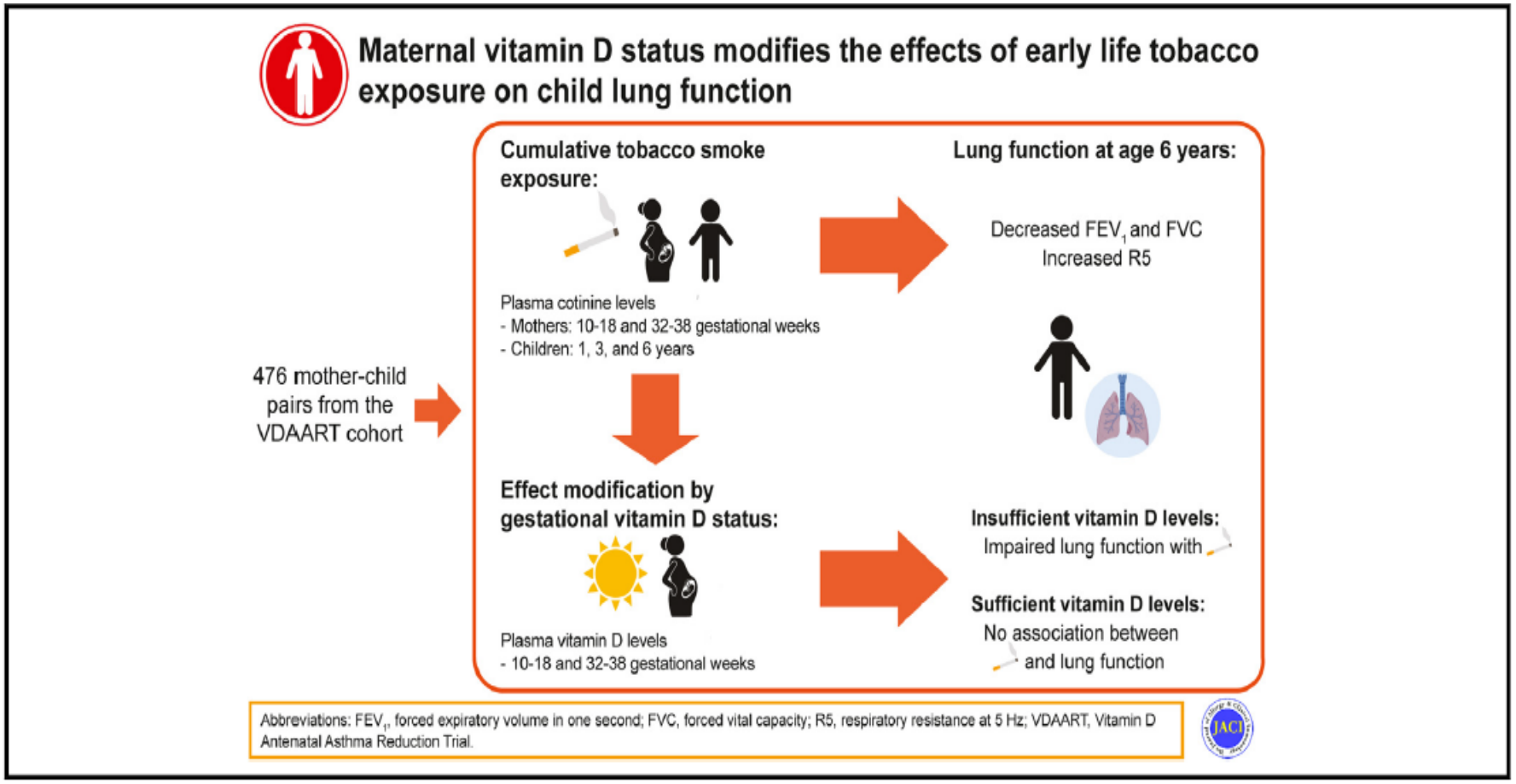


Maternal vitamin D status modifies the effects of early life tobacco exposure on child lung function

Hanna M. Knihtilä, MD, PhD,[a,b] Mengna Huang, PhD,[a] Nicole Prince, PhD,[a] Benjamin J. Stubbs, BA,[a]

Cumulative TSE from pregnancy to childhood is associated with dose- and duration-dependent decreases in child lung function at 6 years even in the absence of reported maternal smoking.

Gestational vitamin D may modulate this effect and have therapeutic potential for minimizing the adverse effect of TSE on lung throughout early life



NEWS AND VIEWS

Groundbreaking Discoveries in Immunology

Allergy EAACI WILEY

Vitamin D supplementation in pregnancy does not prevent school-age asthma

Pasquale Comberiati[1,2] | Diego G. Peroni[1]

[1]Department of Clinical and Experimental Medicine, Section of Pediatrics, University of Pisa, Pisa, Italy

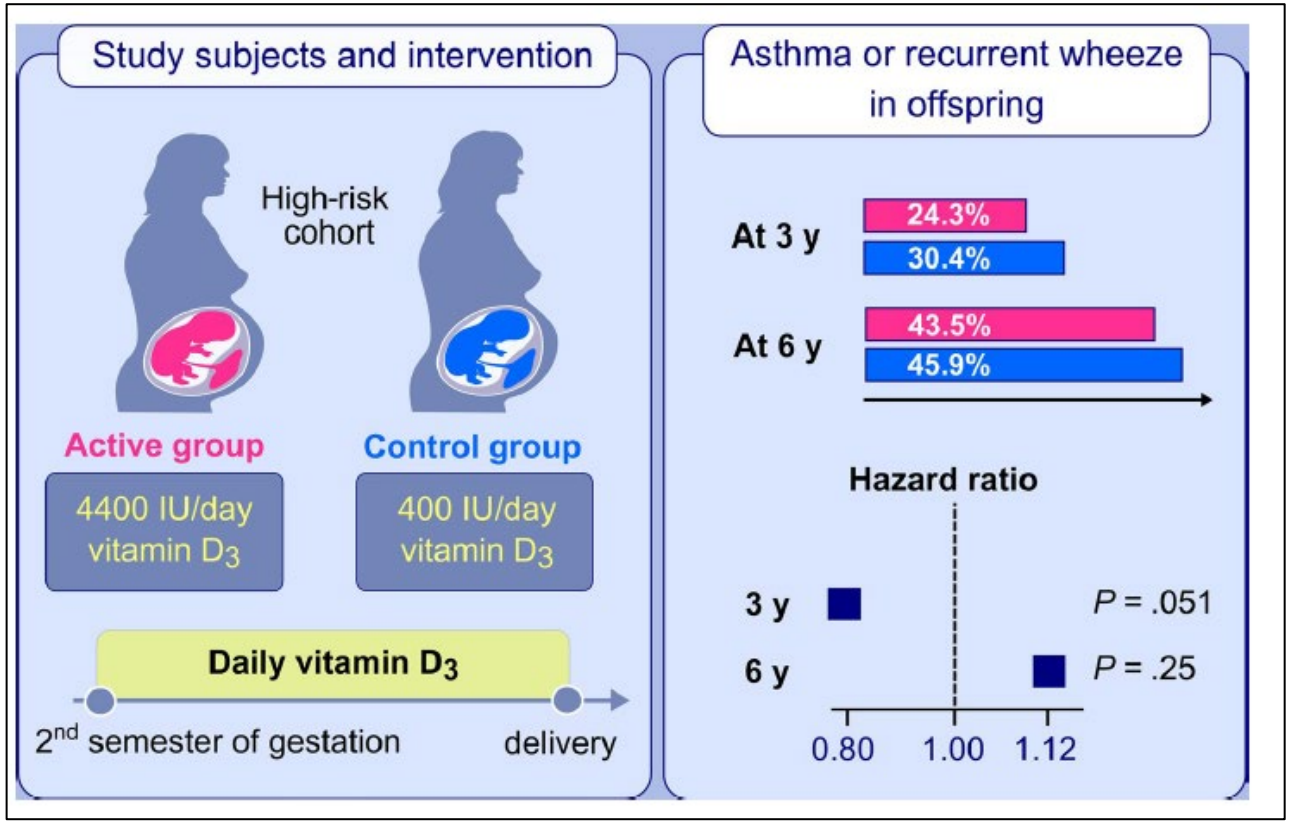
Several **knowledge gaps need** to be addressed :

(a) the **timing to start** prenatal vitamin D intake,

(b) the **maternal ethnicity and baseline** serum vitamin D level,

(c) the effect of **combined pre- and post-natal** vitamin D supplementation

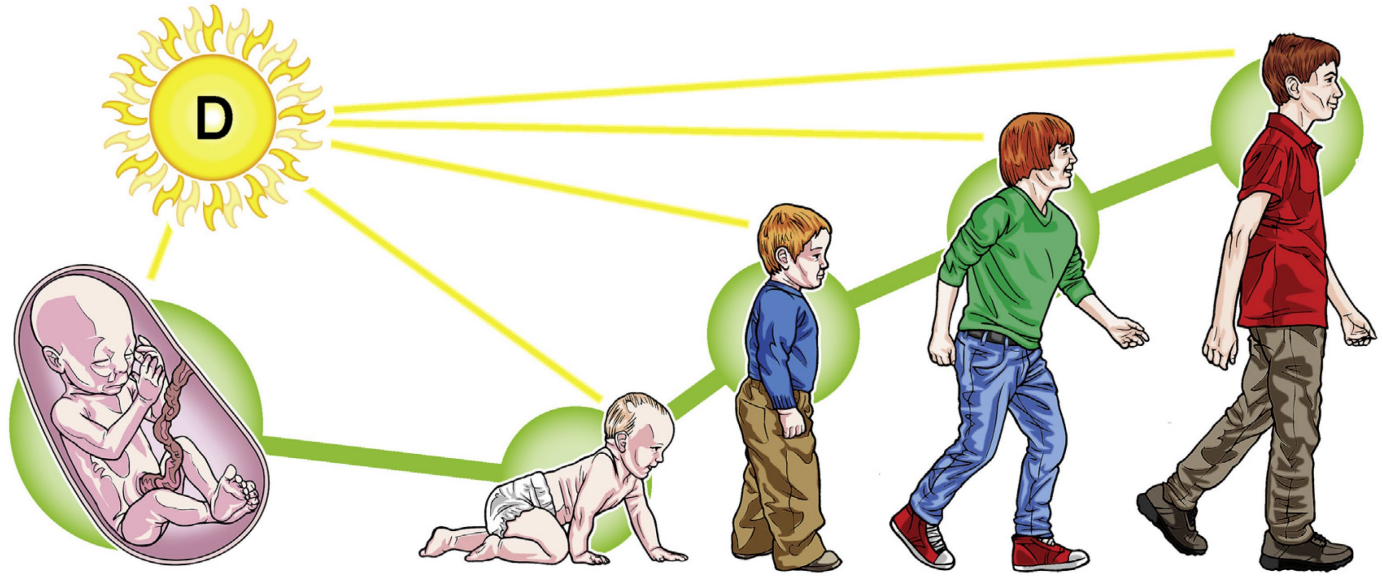
(d) the **microbiological characterization** of wheezing episodes



Vitamin D status through the first 10 years of life: A vital piece of the puzzle in asthma inception.

Litonjua A, J Allergy Clin Immunol 2017;139:459

Adequate vitamin D status prenatally and throughout childhood in the prevention of asthma and allergies. FVC, Forced vital capacity.



In utero

- Placental development
- Fetal programming
  - Gene expression
  - Epigenetic programming
- Lung development
  - Maturation
  - Sufactant production
- Immune development

Childhood

- Protection against allergies
- Establishment of a favorable microbiome (airway, intestinal)
  - Improved handling of respiratory infections
  - Decreased post-infection inflammation
- Normal lung growth
  - Normal FEV1 and FVC
  - Prevention of smooth muscle hypertropy and decreased inflammation
  - No airway hyperresponsiveness
- Immune regulation
  - Balanced Th1/Th2 response
  - Modulation of Th17 response
  - Potentiates tolerogenic potential of dendritic cells
- Genomic effects
  - Gene expression and regulation

nutrients

MDPI

Article

Vitamin D Supplementation and Allergic Diseases during Childhood: A Systematic Review and Meta-Analysis

Qinyuan Li [1], Qi Zhou [2], Guangli Zhang [1], Xiaoyin Tian [1], Yuanyuan Li [1], Zhili Wang [1], Yan Zhao [1], Yaolong Chen [2,3,4,5,6] and Zhengxiu Luo [1,*]

Vit D supplementation did not reduce asthma exacerbation risk in children overall but may reduce asthma exacerbation risk in children with serum 25(OH)D concentration < 10 ng/mL.

Vit D supplementation reduces the severity of atopic dermatitis and symptoms of allergic rhinitis in children.

Cochrane Library

Cochrane Database of Systematic Reviews

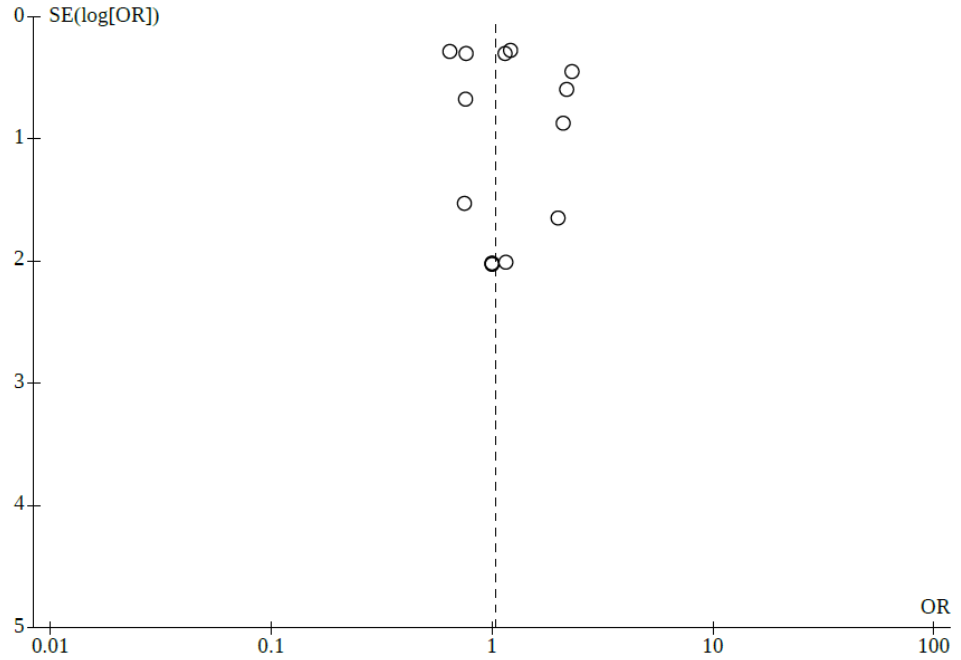
Vitamin D for the management of asthma (Review)

Williamson A, Martineau AR, Sheikh A, Jolliffe D, Griffiths CJ

In contrast to findings of our previous Cochrane Review on this topic, this updated review **does not find evidence to support a role for vitamin D supplementation or its hydroxylated metabolites to reduce risk of asthma exacerbations** or improve asthma control.

Participants **with severe asthma and those with baseline 25(OH)D concentrations < 25 nmol/L were poorly represented**, so further research is warranted here.

Figure 3. Forest plot of comparison: vitamin D versus placebo (all studies), outcome 1.1: proportion of participants experiencing one or more asthma exacerbations treated with systemic corticosteroids



Further research is required to clarify potential effects of calcidiol on risk of asthma exacerbation, and to determine whether **vitamin D supplementation may yet have an effect in people with severe asthma or those with the lowest levels of baseline vitamin D (25(OH)D < 25 nmol/L),** in whom a significant protective effect cannot currently be excluded.

The FEBS Journal
FEBS PRESS science publishing by scientists
COMMENTARY

Vitamin D to prevent COVID-19: recommendations for the design of clinical trials

Carlos A. Camargo Jr.[1] and Adrian R. Martineau[2]

1 Department of Emergency Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA
2 Institute for Population Health Sciences, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, UK

As investigators design and implement RCTs of vitamin D supplementation to prevent COVID-19, we encourage consideration of the issues raised here. Likewise, we encourage a greater tolerance for 'mixed' results given the likely heterogeneity of future trial designs—and the inherent challenges of RCT research on vitamin D.

1 Population (trial participants)
- Age-group (e.g., newborns *vs* elderly adults)
- Baseline vitamin D status (e.g., 25OHD level < 25 *vs* 75+ nM)
- Race/ethnicity (e.g., European white *vs* African black)
- Body mass index (e.g., adults < 25 *vs* 30+)
- Comorbidities (e.g., chronic diseases and immunodeficiencies)

2 Vitamin D intervention (dosing regimen)
- Frequency (daily *vs* less often)
- Initial bolus dose (yes/no)
- Regular dose (e.g., standard *vs* high; with amounts dependent on participant)
- Trial duration (e.g., 3 *vs* > 12 months)

Association between adherence to the Mediterranean diet and oxidative stress.

Dai J, Am J Clin Nutr. 2008;88:1364-70.

The association between the Mediterranean diet and lower plasma oxidative stress is robust and is not confounded by genetic or shared environmental factors.

Influence of Mediterranean diet on asthma in children: a systematic review and meta-analysis.

Garcia-Marcos L, PAI 2013;24:330-8.

8 STUDI CROSS_SECTIONAL

- current wheeze
- current severe wheeze
- asthma ever

Adherence to the Mediterranean diet tended to be associated with lower occurrence of the three respiratory outcomes.

Dietary patterns, lung function and asthma in childhood: a longitudinal study.

Talaei, Respir Res 2023

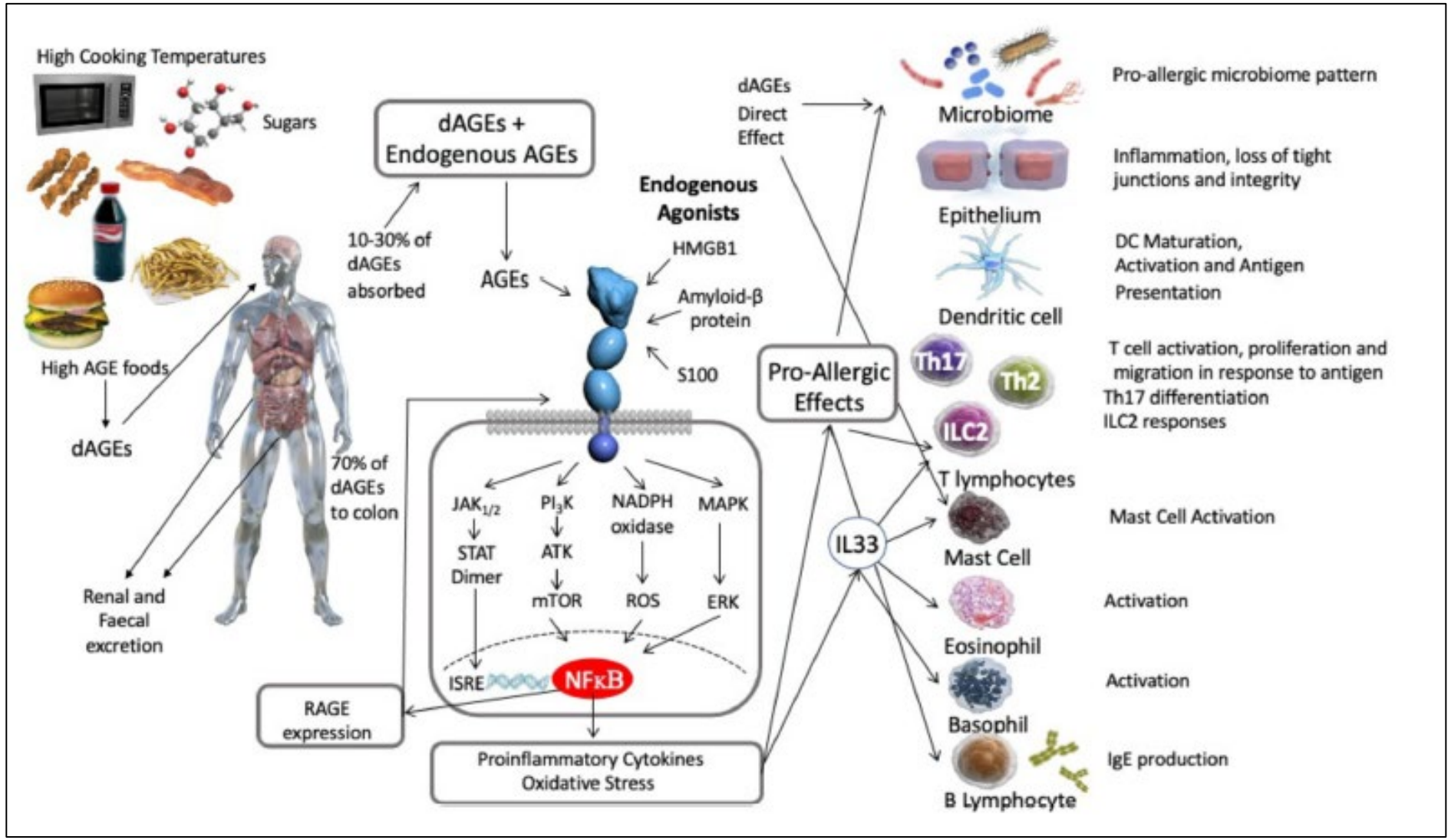
We used three previously defined dietary patterns, 'health-conscious', 'traditional', and 'processed', which were derived using PCA on 57 standardised food items [Northstone K, Emmett P. Multivariate analysis of diet in children at four and seven years of age and associations with socio-demographic characteristics. Eur J Clin Nutr. 2005;59:751] collected by food frequency questionnaire (FFQ) at ~ 7 years (81 months) of age [Emmett P. Dietary assessment in the Avon Longitudinal Study of parents and children. Eur J Clin Nutr. 2009;63(Suppl 1):S38].

In multivariable-adjusted models, the **'health-conscious' pattern** was positively associated with FEV1
(regression coefficient comparing top versus bottom quartile of pattern score 0.16, 95% CI 0.01 to 0.31, P for trend 0.04)
and FVC (0.18, 95% CI 0.04 to 0.33, P for trend 0.02),

while the **'processed' pattern** was negatively associated with FVC (– 0.17, 95% CI – 0.33 to – 0.01, P for trend 0.03).

Ultra-processed foods, allergy outcomes and underlying mechanisms in children: An EAACI task force report. Berni canani et al, PAI 2024

Advanced Glycation end products and the immune system. It gives a graphic overview of the role of how advanced Glycation end products modulates the immune system.



Ultra-processed foods, allergy outcomes and underlying mechanisms in children: An EAACI task force report. Berni canani et al, PAI 2024

BOX 2 Ultra-processed foods and the immune system

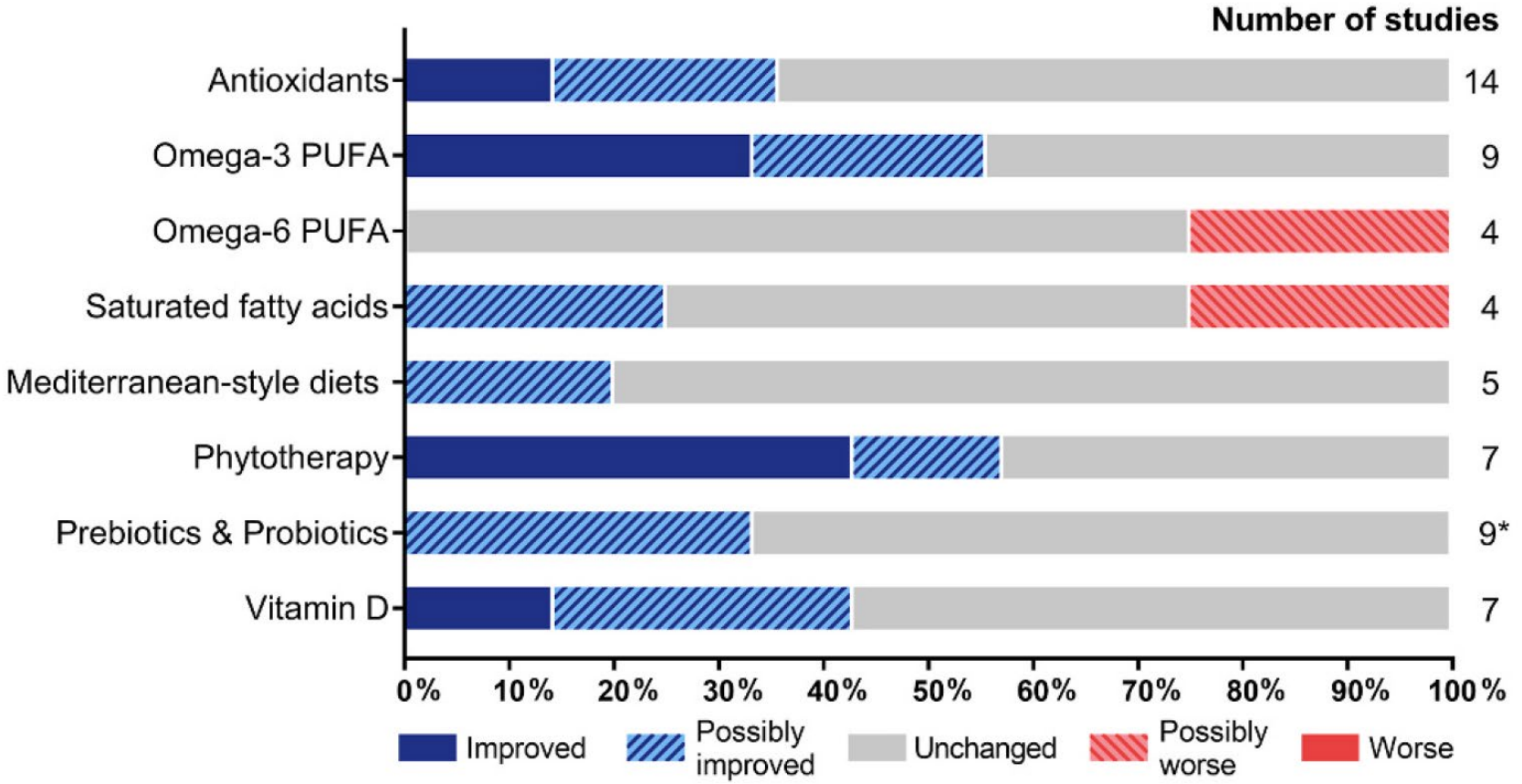
1. Higher UPF consumption has been associated with increased levels of inflammatory markers like CRP, interleukin-6, and 8.
2. Intake of emulsifiers such as polysorbate (P) 20, P80, and CMC have been associated with disruption of the gut epithelial barrier which might promote alterations of the immune tolerance mechanisms with local and systemic inflammatory responses.
3. Sweeteners such as Steviol may affect T-cell responses.
4. AGEs may induce alterations in gut barrier, inflammation, and Th2 response.

BOX 3 Ultra-processed foods and allergy outcomes

1. Maternal consumption of fructose and free sugars during pregnancy has been associated with an increased risk of childhood asthma, similarly the consumption of carbonated soft drinks during pregnancy resulted in higher prevalence of childhood asthma and allergic rhinitis in the offspring.
2. Early childhood consumption of commercial baby food has been linked to the development of OFC-confirmed food allergies in children.
3. Higher intake of free fructose beverages and fruit juice drinks has been associated with increased self-reported allergic symptoms and asthma prevalence in children and adolescents.
4. High carbohydrate-rich food consumption was associated with increased asthma severity in children.
5. Restricting monosodium glutamate in the diet could improve atopic dermatitis symptoms in children.
6. Consuming UPFs has been associated with asthma, allergic rhinitis, and atopic dermatitis in children
7. AGE exposure, may facilitate the occurrence of atopic dermatitis, allergic rhinitis, asthma, food allergy, and sensitization

Effect of dietary interventions on markers of type 2 inflammation in asthma: A systematic review
Edith Visser, Respir Med 2024.

Effetto degli interventi dietetici sui marcatori di infiammazione T2 in pazienti con asma



Perspective: Nutrition Health Disparities Framework: A Model to Advance Health Equity.

Agurs-Collins, Advances in Nutrition 2024

		Levels of Influence			
		Individual	Interpersonal	Community	Societal
Domains of Influence *(Over the Life Course)*	Biological	Taste Predispositions, Nutritional Status, Nutrition Metabolism, Nutrigenomics, Metabolomics, Microbiome, Food Allergies and Intolerances	Maternal -Child Interaction, Feeding Practices (e.g., breastfeeding), Family Microbiome	Community Illness Food Contaminant	Sanitation Pathogen Exposure (e.g., E Coli)
	Behavioral	Dietary Intake, Dietary Habits, Eating Patterns, Coping Strategies	Family Dietary Practices (e.g., family meals) School/Work Dietary Behavior	Farmers Markets Community engagement (lobbying for full- service grocery stores)	Nutrition Policies and Laws (e.g., food assistance programs and access) State- and City-level Food and Nutrition Policies (soda taxes)
	Physical/Built Environment	Personal Food Environment and Access (exposure to fast food at home)	Household Food Environment School/Work Food Environment	Community Environment Community Resources Neighborhood Food Environment (e.g., food deserts, food marketing)	Societal Structures (e.g., zoning laws) Dept. of Education and School System
	Sociocultural Environment	Food Preferences, Sociodemographic (discretionary income) Food Literacy and Preparation Skills Limited English Cultural Identity/Acculturation Response to Discrimination	Social Networks Family/Peer Norms Interpersonal Discrimination (e.g., dietary practice, body image)	Community Norms Local Structural Discrimination (e.g., dietary practice, body image)	Social Norms Food System (e.g., supply chain) Societal Structural Discrimination
	Health Care System	Insurance Coverage, Access, Utilization Health Literacy Treatment Preferences Medical Nutrition Therapy	Patient-Clinician Relationship Medical Decision-Making (referral to Registered Dietitian)	Availability of Services Safety Net Nutrition Services (WIC, SNAP, food pantries, produce prescriptions)	Quality of Care Health Care Policies for Nutrition Services (screening & treatment) Medically Tailored Meals
Health Outcomes		Individual Health	Family/Organizational Health	Community Health	Population Heath