

Ti ricordiamo che questo materiale
è di proprietà dell'Autore.
Come partecipante al
XXVIII CONGRESSO NAZIONALE SIMRI
questo materiale ti è fornito da SIMRI
per esclusivo uso personale
concesso dall'Autore



XXVIII CONGRESSO NAZIONALE SIMRI

Il respiro: scienza e terapia per la salute del bambino

Programma

Torino, 10-12 ottobre 2024

INFEZIONI RESPIRATORIE RICORRENTI

*Maria Angela Tosca
IRCCS G.Gaslini
Genova*

Seminar

The common cold



Fino al 25% dei bambini di età inferiore a 5 anni nei paesi industrializzati presenta infezioni respiratorie ricorrenti

THE LANCET • Vol 361 • January 4, 2003

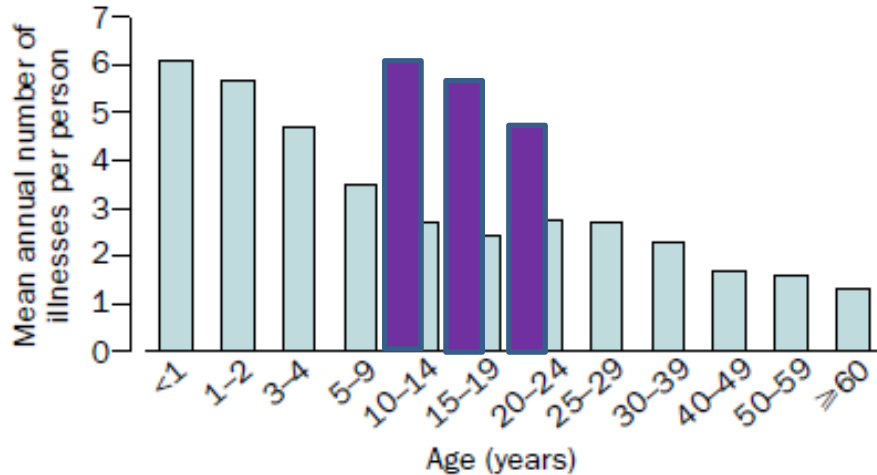


Figure 2: Mean annual incidence of respiratory illnesses per person by age group⁵

[JAMA Netw Open.](#) 2023 Oct; 6(10): e2339884.

Published online 2023 Oct 26. doi: [10.1001/jamanetworkopen.2023.39884](https://doi.org/10.1001/jamanetworkopen.2023.39884)

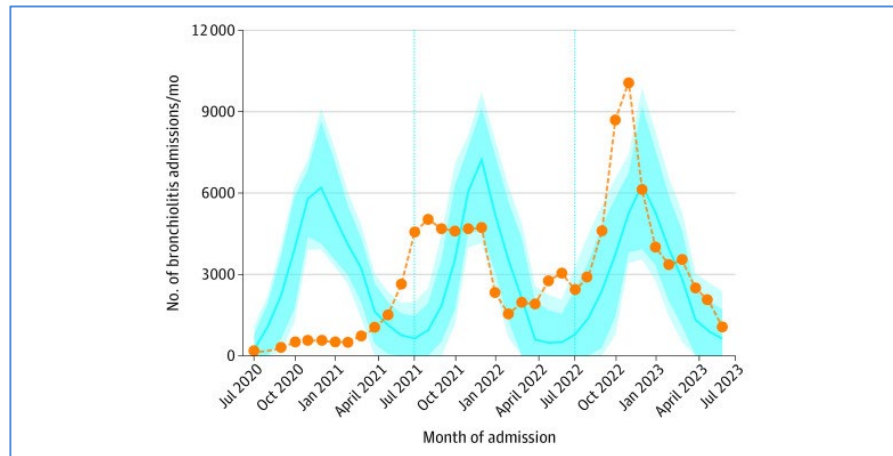
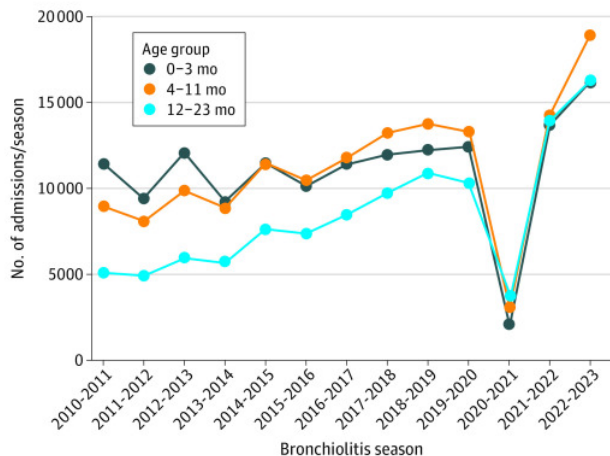
PMCID: PMC10603547

PMID: [37883085](https://pubmed.ncbi.nlm.nih.gov/37883085/)

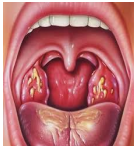
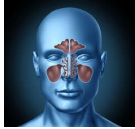
Admissions for Bronchiolitis at Children’s Hospitals Before and During the COVID-19 Pandemic

[Kailey A. Remien](#), DO,¹ [Justin Z. Amarin](#), MD,² [Christopher M. Horvat](#), MD, MHA,³ [Ryan A. Nofziger](#), MD, MBA,^{4, 5} [Christopher K. Page-Goertz](#), MD,^{4, 5} [James B. Besunder](#), DO,^{4, 5} [Brittany K. Potts](#), MD,^{5, 6} [Michael L. Forbes](#), MD,^{4, 5} [Natasha Halasa](#), MD, MPH,² and [Jonathan H. Pelletier](#), MD^{4, 5}

COVID-19 e bronchioliti
Riduzione della *trained*
Immunity



DEFINIZIONE - IRR



1-3 anni:

- 6 o più infezioni delle vie respiratorie (delle quali 1 può essere polmonite, anche grave) oppure
- 2 polmoniti non gravi confermate da criteri clinici e/o radiologici in un anno

3-6 anni:

- 5 o più infezioni delle vie respiratorie (delle quali 1 può essere polmonite, anche grave) o
- 2 polmoniti non gravi confermate da criteri clinici e/o radiologici in un anno

6-12 anni:

- 3 o più infezioni delle vie respiratorie (delle quali 1 può essere polmonite, anche grave) o
- 2 polmoniti non gravi confermate da criteri clinici e/o radiologici in un anno

LA PREVENZIONE DELLE
INFEZIONI RESPIRATORIE
RICORRENTI

Consensus intersocietaria 2020



CONSENSUS INTERSOCIETARIA 2020
LA PREVENZIONE DELLE INFEZIONI RESPIRATORIE RICORRENTI

Burden of Recurrent Respiratory Tract Infections in Children

A Prospective Cohort Study

Laura Toivonen, MD,*† Sinikka Karppinen, MD,*† Linnea Schuez-Havupalo, MD,*† Tamara Teros-Jaakkola, MD,*†
Juho Vuononvirta, PhD,‡ Jussi Mertsola, MD, PhD,*† Qiushui He, MD, PhD,‡ Matti Waris, PhD,§
and Ville Peltola, MD, PhD*†

**STEP: Steps to the
Healthy Development
And Well Being of
Children**

Studio di coorte prospettico

1089 pazienti dalla nascita fino ai 2
anni

-diario IRR

-tamponi nasofaringei a 2 mesi
e durante infezioni respiratorie acute

Fino al 10% dei bambini (< 2 a) presenta IRR

- Le OMA sono le infezioni più frequenti
- L' 80% dei bambini presenta la prima infezione respiratoria acuta entro i 3 mesi di vita
- Il 73% assume almeno 3 cicli antibiotici
- 21% viene ospedalizzato per infezione respiratoria acuta
- Il 13% va incontro a adenoidectomia
- Il 12% viene inquadrato come "asmatico"
- E' frequente la colonizzazione precoce nasofaringea da pneumococco
- Nel 58% si riscontra infezione da Rhinovirus

INQUADRAMENTO DEL PAZIENTE

Anamnesi familiare

- Infezioni gravi e/o decessi in età infantile
- consanguineità
- presenza di infezioni recidivanti nei familiari
- familiarità per allergopatie
- Fratelli

Anamnesi fisiologica

- Nascita a termine
- peso alla nascita
- allattamento al seno o con formula
- stato vaccinale

Anamnesi patologica

- sintomi respiratori insorti nei primi giorni di vita
- patologie di base (specie cardiopatie con clubbing, malformazioni dell'apparato respiratorio e patologie neurologiche)
- scarso accrescimento staturò-ponderale
- segni sintomi compatibili con allergopatie (specie DA grave o reazioni allergiche gravi)
- uso e abuso di FANS e corticosteroidi



Fattori favorenti le I.R.R.

- Et  < 6 anni (immaturit  S.I.)
- Basso peso alla nascita e/o prematurit 
- Vita in comunit 
- Inquinamento (outdoor ed indoor)
- Fumo anche di “terza mano”
- Clima e tipologia di riscaldamento
- Presenza di aero-allergeni
- Stress
- Dieta incongrua
- Disbiosi (intestino e vie aeree)
- Scarse condizioni igieno-sanitarie
- Basso livello socio-economico



10 CAMPANELLI DI ALLARME

delle Immunodeficienze Primitive



- sede
- frequenza
- durata
- difetto di crescita
- non benessere nel periodo inter-critico
- microorganismi inusuali

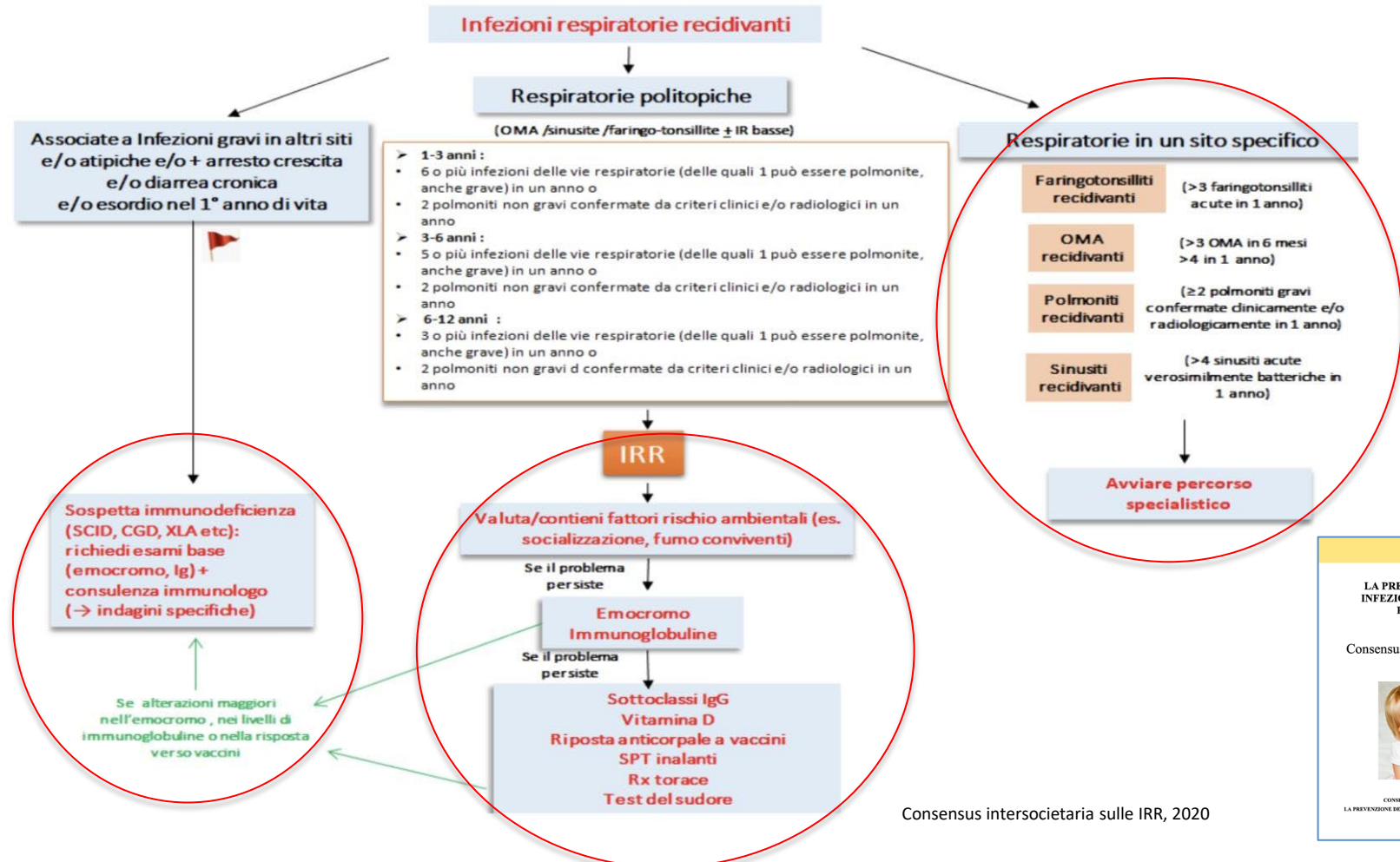
Almeno 2 dei seguenti: pensa a ID

10 CAMPANELLI DI ALLARME

delle Immunodeficienze Primitive



- complicanze recidivanti o gravi
- interessamento sistemico o extra-polmonare
- necessità di terapia e.v.
- accessi cutanei/sepsi
- familiarità per ID



IRR alte vie

I livello: emocromo e Ig

II livello: sottoclassi IgG, 25-OH vitamina D, prick test

III livello: visita ORL con FBS e tampone faringeo per SBEGA e altri germi

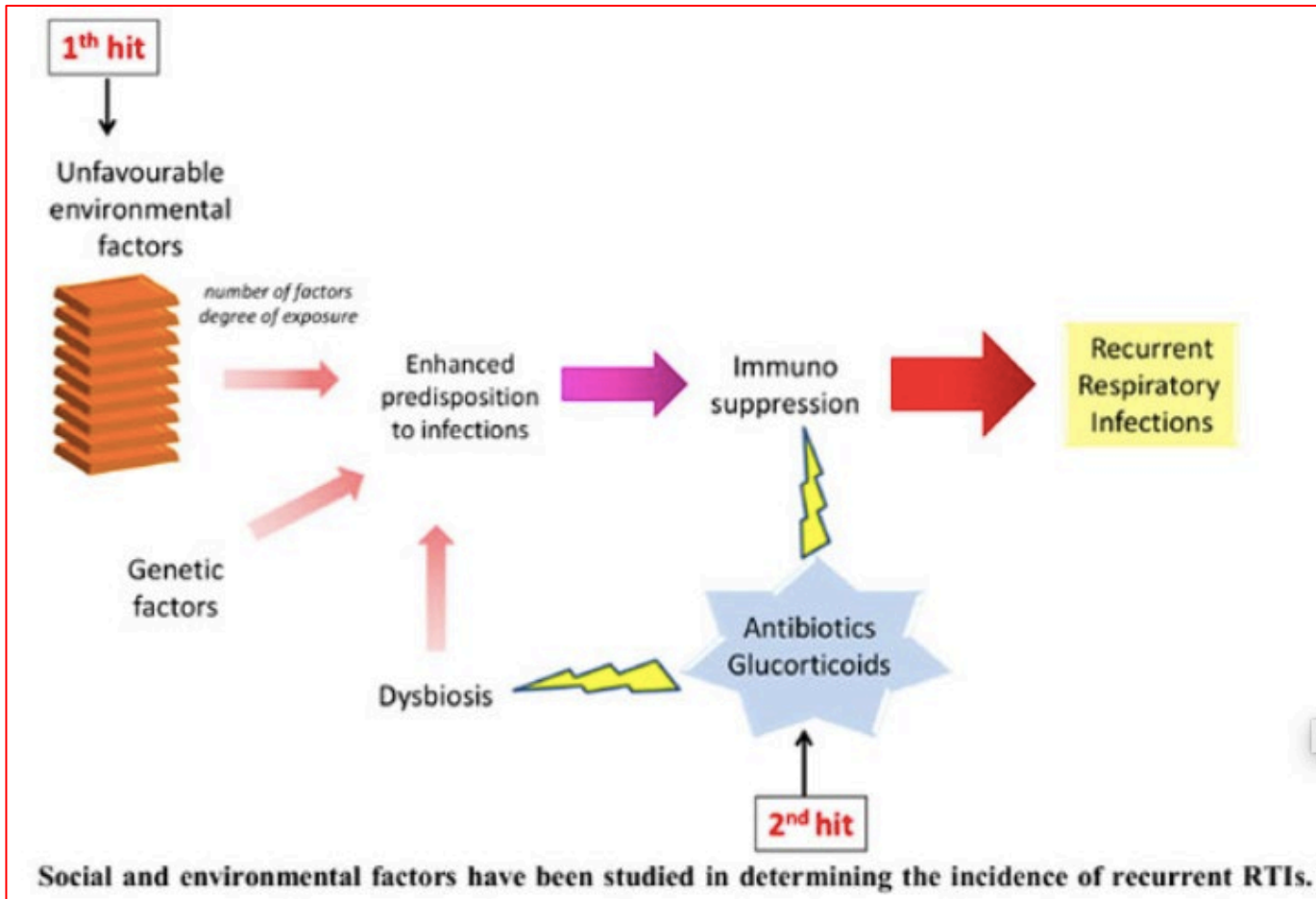
IRR basse vie

I livello: emocromo e Ig

II livello: sottoclassi IgG, 25-OH vitamina D, prick test, RX torace, **PFR**, test del sudore (se non effettuato screening FC)

III livello: Mantoux; studio genetica FC, indagini per DCP; studio della deglutizione; TC torace; FBS + BAL; **visita gastroenterologica, visita cardiologica**

-SEDI DIVERSE: pensa a ID, DCP, FC, RGE, asma
-STESSA SEDE: pensa ad anomalie strutturali, bronchiectasie, compressione extratoracica o ostruzione endoluminale (anche corpo estraneo)



FATTORI DI RISCHIO IRR - OBESITA' e SOVRAPPESO

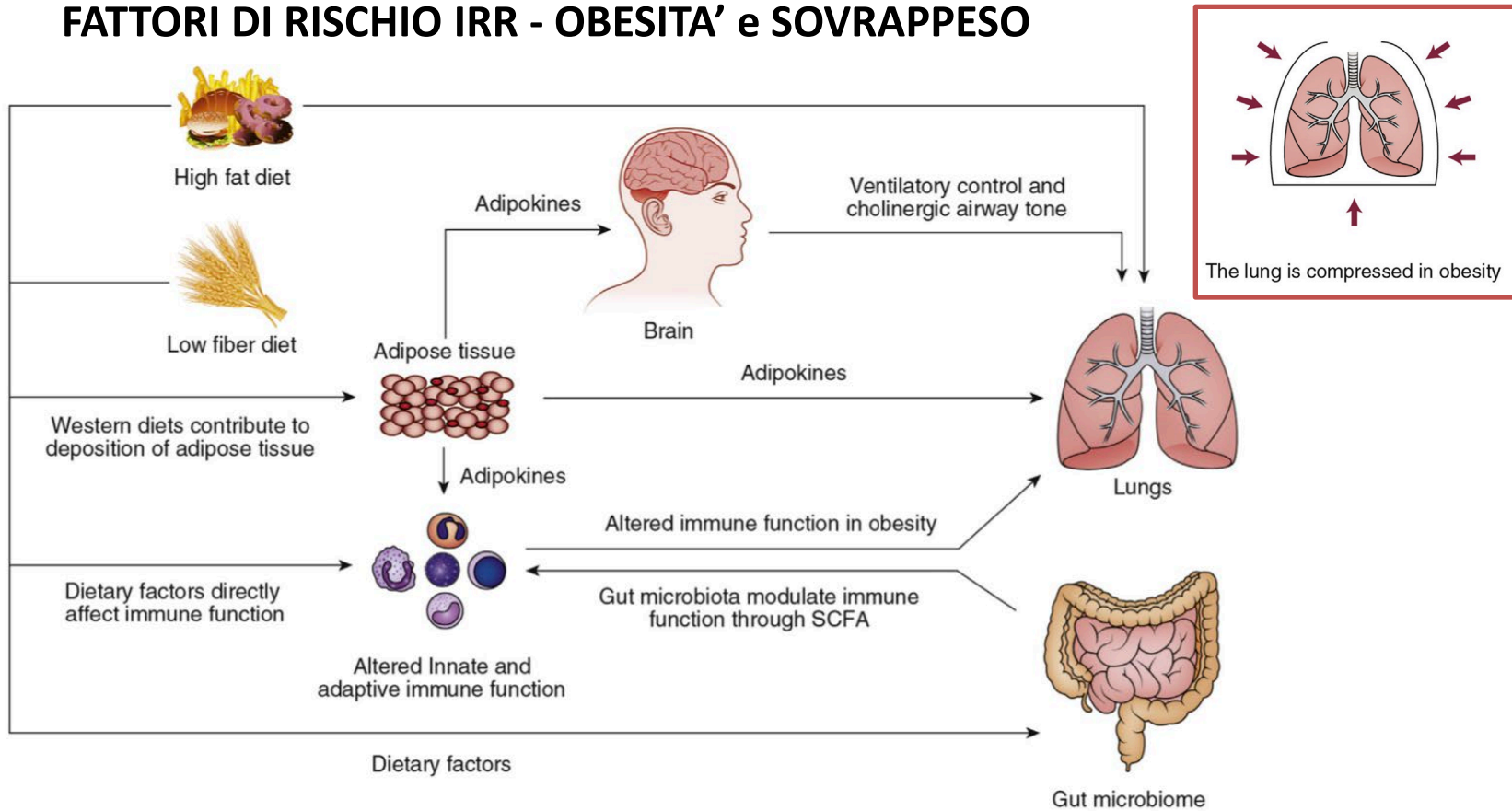


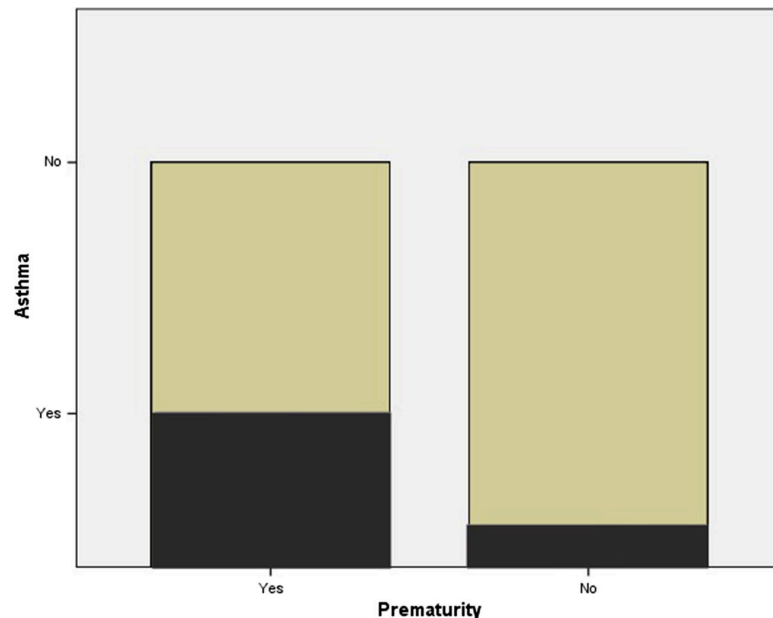
Figure 2 – Etiology of lung disease in obesity. High-fat and low-fiber diets are important contributors to increased adiposity. Increased adipose tissue mass can lead to lung function impairment through the release of adipokines that modulate immune response, ventilation, and airway smooth muscle tone. In addition, obesogenic diets have been associated with fundamental changes in the gut microbiome, which could also alter pulmonary host immune response. SCFA = short-chain fatty acid.



Respiratory morbidity, atopy and asthma at school age in preterm infants aged 32–35 weeks

Júlia Morata-Alba^{1,2}  · María Teresa Romero-Rubio¹ · Silvia Castillo-Corullón¹ · Amparo Escribano-Montaner¹

PTIs had a higher prevalence of bronchiolitis, recurrent wheezing and asthma; risk factors for asthma are the following: older siblings, allergic father, atopic dermatitis and antibiotic treatment in the first 3 years of life and prematurity itself.



Risk factors for atopic diseases and recurrent respiratory tract infections in children

Hannah M. Kansen MD, PhD^{1,2} | Melanie A. Lebbink MD³ | Joeri Mul MD³ |

Results: Children aged ≥ 5 years were more likely to have any atopic disease (adjusted odds ratio [OR]: 1.50-2.77) and less likely to have RRTIs (OR: 0.68-0.84) compared to children aged less than 5 years. Female sex (OR: 0.72; 95% confidence interval [CI]: 0.63-0.81), low birth weight (OR: 0.74; 95% CI: 0.57-0.97) and dog ownership (OR: 0.79; 95% CI: 0.66-0.95) reduced the odds of any atopic disease, but not of RRTIs. Daycare attendance (OR: 1.22; 95% CI: 1.02-1.47) was associated with RRTIs, but not with atopic diseases. A family history of asthma, allergic rhinitis, atopic dermatitis, and RRTIs was significantly associated with the same entity in children, with OR varying from 1.58 (95% CI: 1.35-1.85) in allergic rhinitis to 2.20 (95% CI: 1.85-2.61) in asthma.

Conclusion: Risk factors for atopic diseases are distinct from risk factors for RRTIs, suggesting that the changing prevalence of both entities is not related to shared risk factors.

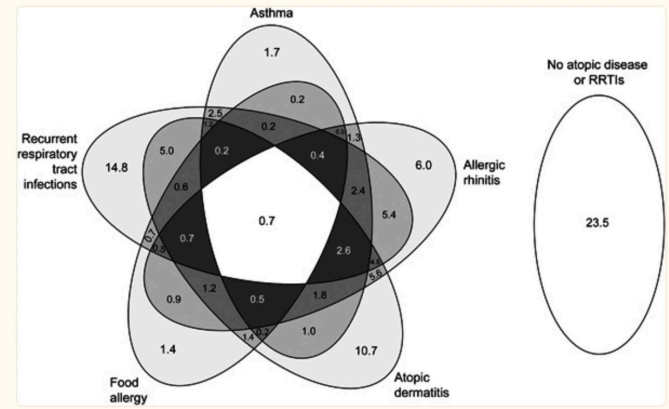


Figure 1

Venn diagram displaying the proportion of atopic diseases and respiratory tract infections in all included children. The numbers are percentages

Demographics	Any atopic disease		RRTIs	
	Adjusted OR (95% CI)	P value*	Adjusted OR (95% CI)	P value*
Food allergy	1.29 (1.09-1.52)	<.01	0.91 (0.79-1.06)	.23
Recurrent respiratory infections	0.91 (0.80-1.04)	.18	1.71 (1.50-1.96)	<.001
Comorbidities				
Asthma	NA		2.01 (1.68-2.39)	<.001
Allergic rhinitis	NA		1.39 (1.19-1.63)	<.001
Atopic dermatitis	NA		0.70 (0.61-0.81)	<.001
Food allergy	NA		0.62 (0.49-0.77)	<.001
Recurrent respiratory infections	0.94 (0.82-1.09)	.44	NA	

Note: *Significant P values are in bold. Analyses were mutually adjusted for all risk factors within the model and for centre (secondary care, tertiary care, or birth cohort).

Abbreviations: Adjusted OR, adjusted odds ratio; CI, confidence interval; NA, not applicable; RRTIs, recurrent respiratory tract infections.

Early nasal microbiota and acute respiratory infections during the first years of life

 Laura Toivonen^{1, 2}, Kohei Hasegawa¹, Matti Waris³, Nadim J Ajami⁴, Joseph F Petrosino⁴, Carlos A Camargo Jr¹, Ville Peltola²

Correspondence to Dr Laura Toivonen, Department of Emergency Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA 02114, USA; Itoivonen@mgh.harvard.edu

Toivonen L, et al. *Thorax* 2019;0:1–8. doi:10.1136/thoraxjnl-2018-212629

Conclusion *Moraxella*-dominant nasal microbiota profile in early infancy was associated with an increased rate of ARIs during the first 2 years of life.

Key messages

What is the key question?

- ▶ Are early infant airway microbiota profiles associated with susceptibility to acute respiratory infections (ARIs) in young children?

What is the bottom line?

- ▶ In this prospective, population-based birth-cohort study, we identified five distinct nasal microbiota profiles in healthy 2-month-old infants, and found that the incidence rate of ARIs was highest in children with an early *Moraxella*-dominant nasal microbiota profile and lowest in those with a *Corynebacteriaceae*-dominant profile.

Why read on?

- ▶ This large prospective cohort study shows that early infant airway microbiota profiles may play an important role in susceptibility to ARIs in children during the first years of life.

Bacterial microbiota of the upper respiratory tract and childhood asthma

Depner M. et al.

J ALLERGY CLIN IMMUNOL
MARCH 2017

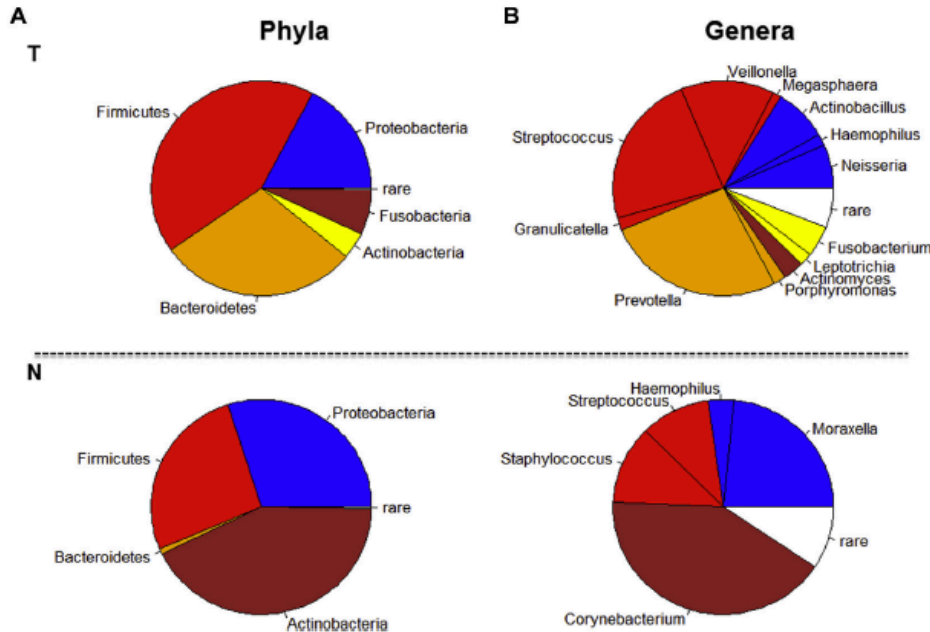


FIG 3. Taxonomic composition of the microbiota from throat and nose. Survey-weighted relative abundance of phyla (A) and genera (B) for throat (T) and nasal (N) samples. Genera belonging to the same phylum are represented by the color of the respective phylum. Phyla and genera representing less than 0.5% of all reads for phyla and less than 1% for genera in the combined throat and nasal sample, respectively, are grouped in "rare."

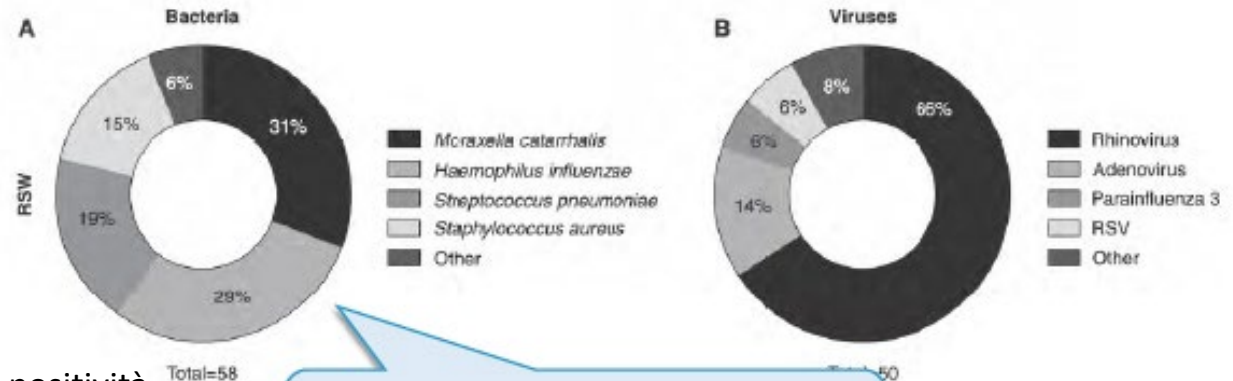
Key messages

- Asthma was associated with an altered diversity in the nasal, but not in the throat, microbiota and an increased *Moraxella* abundance in school-age children living in rural areas.
- The association of asthma with *Moraxella* colonization was restricted to nonfarm children.

**ASMA= DISBIOSI NASALE
(MORAXELLA) in età scolare**

Recurrent Severe Preschool Wheeze: From Prespecified Diagnostic Labels to Underlying Endotypes

136 bambini di età 1-5 anni (105 con **wheezing grave ricorrente** [RSW]; 31 con malattie respiratorie **senza wheezing** [NWRD])



- ✓ Il cluster non allergici presenta positività per **Haemophilus, Streptococcus e Staphylococcus**

H. influenzae, M. catarrhalis and Streptococcus pneumoniae in 50% of lower airway samples

- ✓ Il cluster allergici presenta positività per **Moraxella**

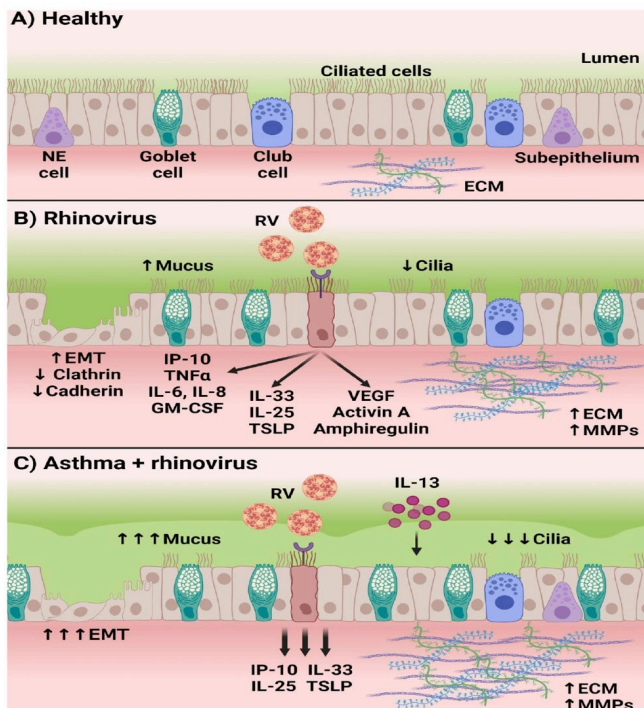
REVIEW

Open Access

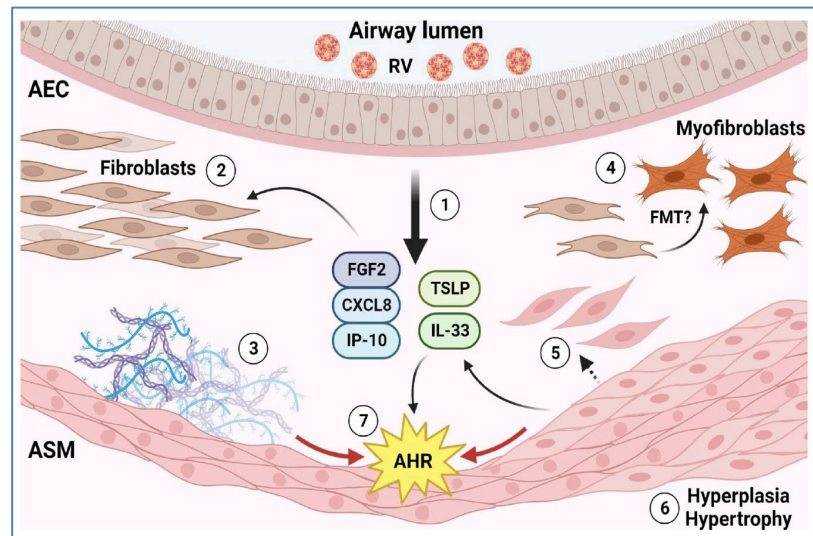


Rhinovirus induces airway remodeling: what are the physiological consequences?

Cassandra Spector¹, Camden M. De Sanctis¹, Reynold A. Panettieri Jr.¹ and Cynthia J. Koziol-White^{1*}



L'infezione da RV determina una risposta immunologica favorente il rimaneggiamento strutturale delle vie aeree



Spector *C Respir Res* 2023
Hayashi *Y. Viruses* 2022

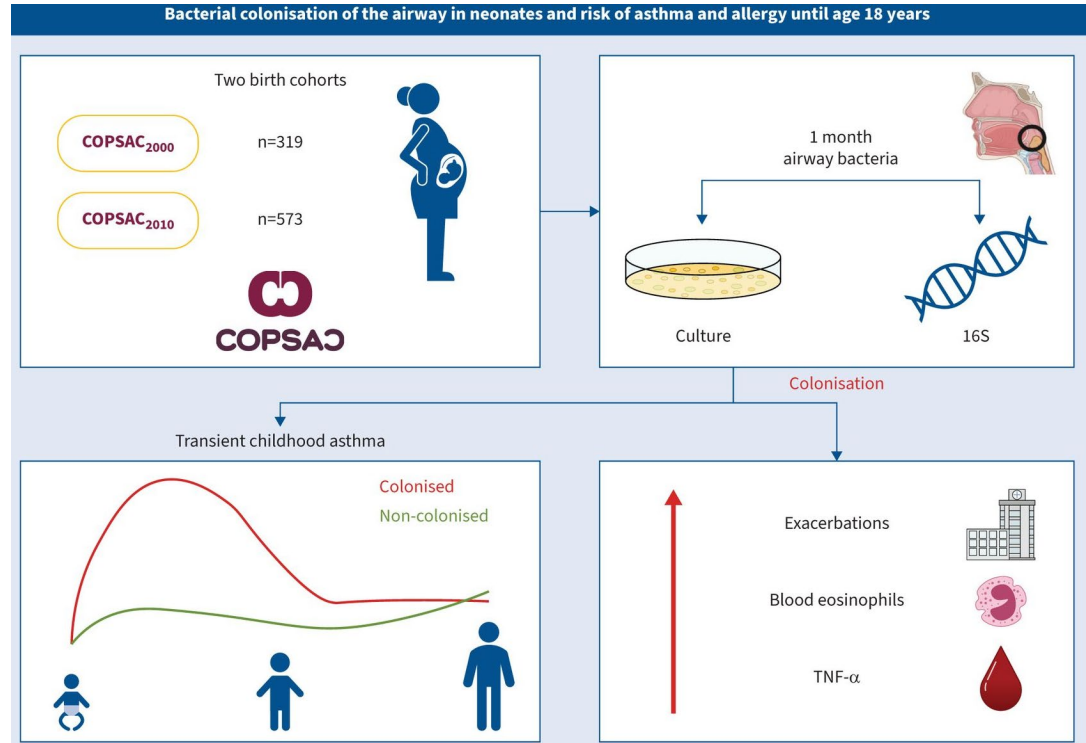


Bacterial colonisation of the airway in neonates and risk of asthma and allergy until age 18 years

Rikke Bjersand Sunde, Jonathan Thorsen, Min Kim, Ann-Marie Malby Schoos, Jakob Stokholm, Klaus Bønnelykke, Hans Bisgaard, Bo Chawes
European Respiratory Journal 2024 63: 2300471; DOI: 10.1183/13993003.00471-2023

2024

Associazione tra colonizzazione delle vie aeree (*St. pneumoniae*, *M. catarrhalis* e/o *H. influenzae*) in neonati di 1 mese (COPSAC 2000) e lo sviluppo di wheeze/asma persistente fino all'età di 18 anni (studio replicato nel COPSAC 2010)

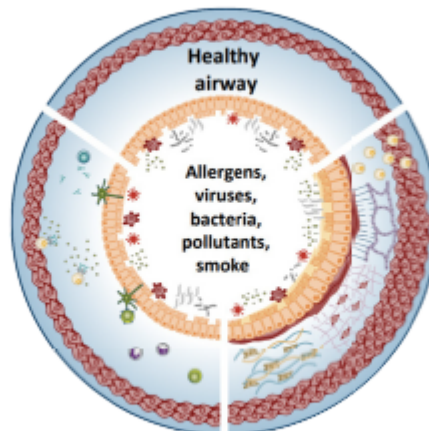


Airway hyperresponsiveness in asthma: The role of the epithelium

Check for updates

Peter Bradding, DM,^a Celeste Porsbjerg, MD, PhD,^b Andréanne Côté, MD, MSc,^{c,d} Sven-Erik Dahlén, MD, PhD,^{a,d}
Teal S. Hallstrand, MD, MPH,^{a,h} and Christopher E. Brightling, PhD^a *Leicester, United Kingdom; Copenhagen, Denmark;
Laval, Quebec, Canada; Stockholm, Sweden; and Seattle, Wash*

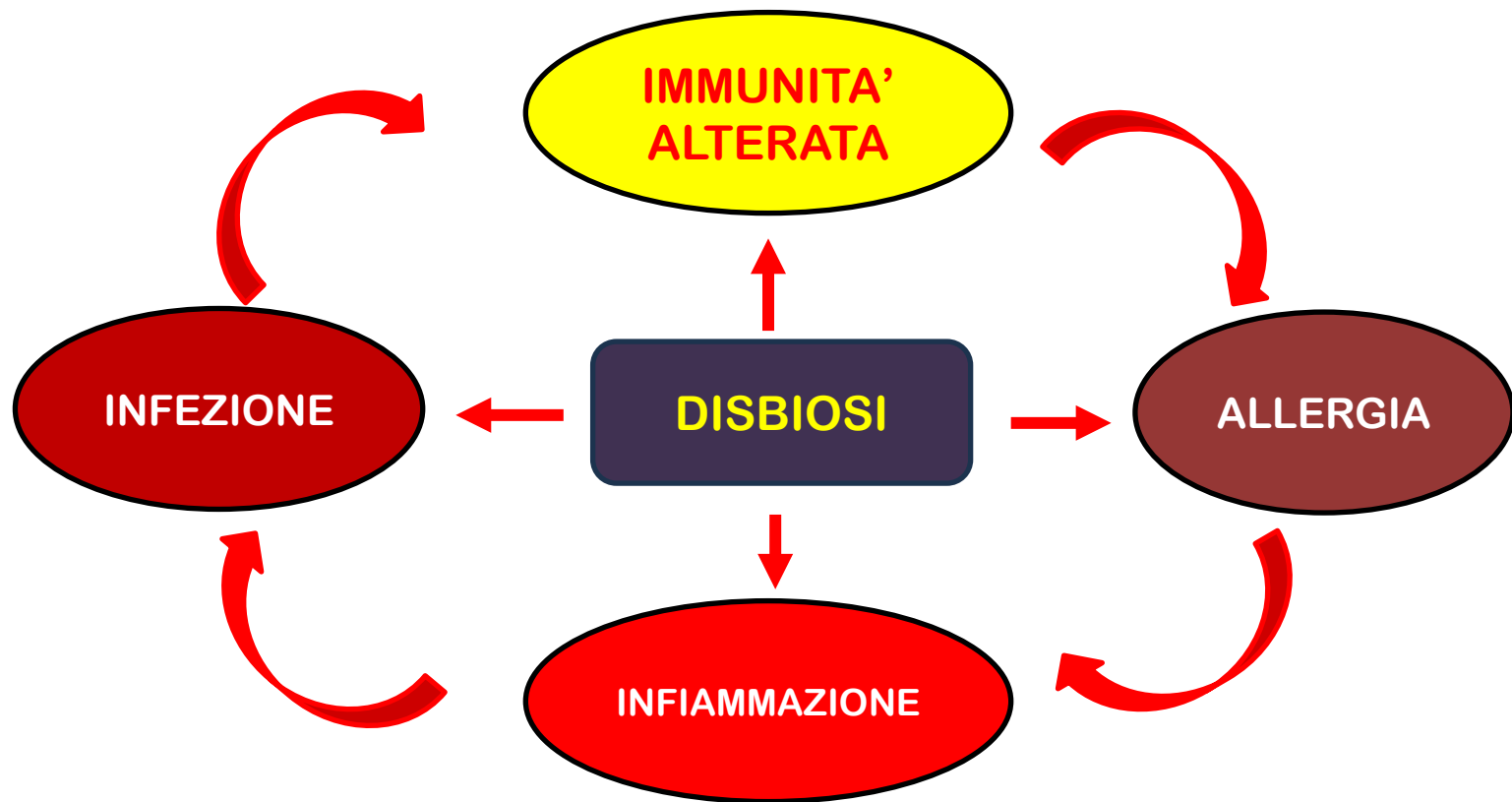
Airway inflammation
Triggers include allergens, infections, occupational triggers and environmental triggers
Epithelial cytokines are released from epithelial cells that may drive inflammation, bronchoconstriction and AHR
Intraepithelial mast cells are associated with indirect AHR
Eosinophils are associated with indirect AHR and T2 inflammation
Severity of AHR positively correlates with the number of eosinophils and mast cells in the airways



Airway remodeling and structural changes
Epithelial damage
Epithelial cell hyperplasia/airway wall thickening
Possible loss of airway tethering to parenchyma
Reticular basement membrane thickening
Airway smooth muscle hypertrophy and hyperplasia
Altered extracellular matrix
Subepithelial fibrosis

Bradding et al. JACI 2024

CIRCOLO VIZIOSO CHE PROMUOVE LE INFEZIONI RECIDIVANTI



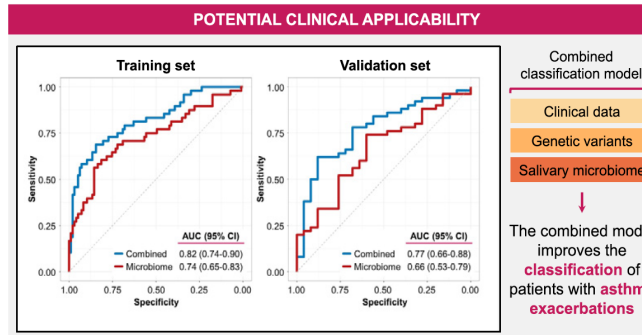
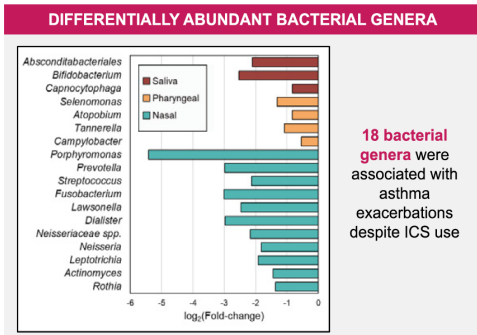
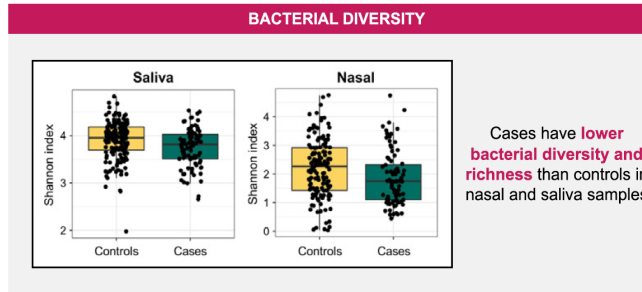
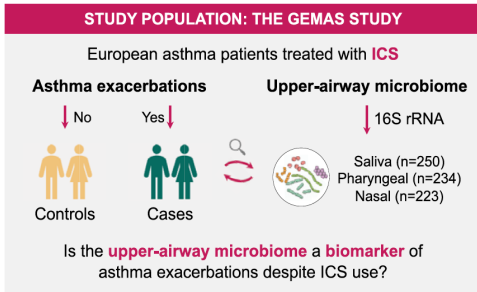
The upper-airway microbiome as a biomarker of asthma exacerbations despite inhaled corticosteroid treatment

Javier Perez-Garcia, PharmD,^a Mario González-Carracedo, PhD,^{b,c} Antonio Espuela-Ortiz, MSc,^a José M. Hernández-Pérez, MD, PhD,^{d,e} Ruperto González-Pérez, MD, PhD,^f Olaia Sardón-Prado, MD, PhD,^{g,h} Elena Martín-Gonzalez, MSc,^a Elena Mederos-Luis, MD, PhD,ⁱ Paloma Poza-Guedes, MD, PhD,^f Paula Corcuera-Elosegui, MD, PhD,^g Ariel Callero, MD, PhD,^j Inmaculada Sánchez-Machín, MD, PhD,ⁱ Javier Korta-Murua, MD, PhD,^{g,h} José A. Pérez-Pérez, MD, PhD,^{k,l} **Isa Pino-Yanes, PhD,^{a,k,n}** and **Fabian Lorenzo-Diaz, PhD^{a,c}**
Tenerife, La Palma, San Sebastián, Madrid, and Las Palmas de Gran Canaria, Spain; and Toronto, Ontario, Canada

Disbiosi delle VA quantitativa e qualitativa nei soggetti con esacerbazione asmatica nonostante terapia con CSI



The Upper-Airway Microbiome as a Biomarker of Asthma Exacerbations Despite Inhaled Corticosteroid Treatment



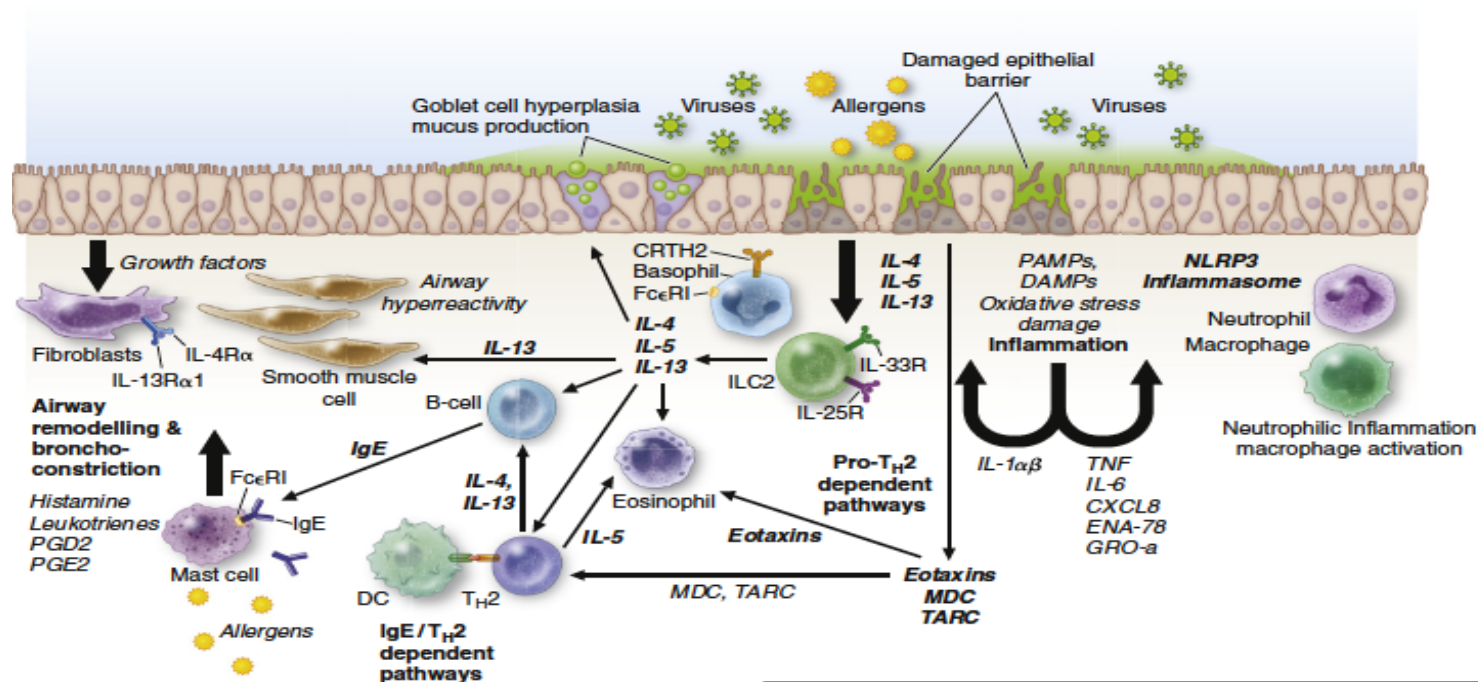
Abbreviations: 16S rRNA: 16S ribosomal ribonucleic acid gene; GEMAS: Genomics and Metagenomics of Asthma Severity; ICS: Inhaled corticosteroids

Viral infections in allergy and immunology: How allergic inflammation influences viral infections and illness



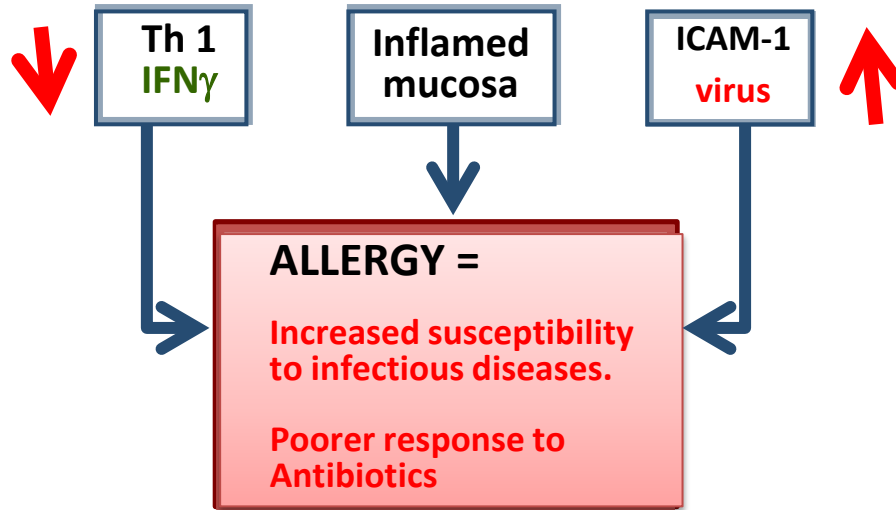
J ALLERGY CLIN IMMUNOL
OCTOBER 2017

Michael R. Edwards, PhD,^{a,b} Katherine Strong, BSc,^{a,b} Aoife Cameron, PhD,^{a,b} Ross P. Walton, PhD,^{a,b}
David J. Jackson, MD, PhD,^{a,b,c} and Sebastian L. Johnston, MD, PhD^{a,b} London, United Kingdom



I virus stimolano l'immunità innata verso una risposta Type2 in un milieu già Type2

Natural course of allergic patient



Children with recurrent otitis show defective IFN γ -producing cells in adenoids

Antonia Avanzini¹, Anna Maria Castellazzi¹, Massimo Marconi¹, Chiara Valsecchi¹, Alessia Marseglia¹, Giorgio Ciprandi², Annalisa De Silvestri³ and Gian Luigi Marseglia¹

I bambini con IRR producono meno IFN- γ

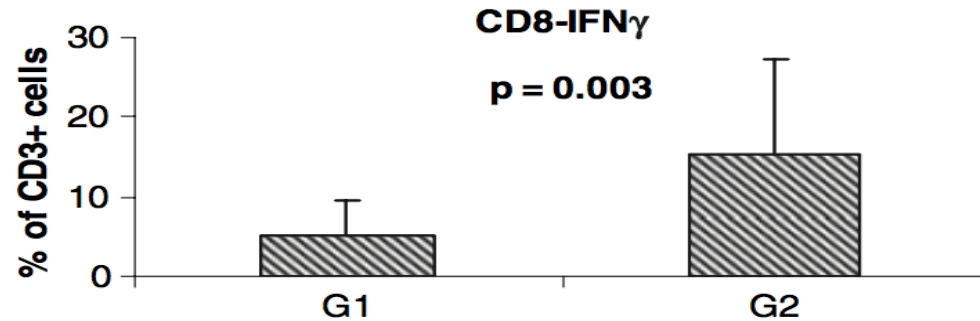


Fig. 1. Percentage of CD8 + cells producing interferon- γ in adenoid of G1 (≥ 3 otitis media per year) and G2 (< 3 otitis media per year) children.

Short Report

Allergic children have more numerous and severe respiratory infections than non-allergic children

Ciprandi G, Tosca MA, Fasce L. Role of allergy in children with recurrent respiratory infections.
Pediatr Allergy Immunol 2006.
© 2006 The Authors

Giorgio Ciprandi¹, Maria Angela Tosca² and Lilia Fasce²
¹Azienda Ospedaliera Universitaria San Martino, Genova, Italy, ²Istituto Giannina Gaslini, Genova, Italy

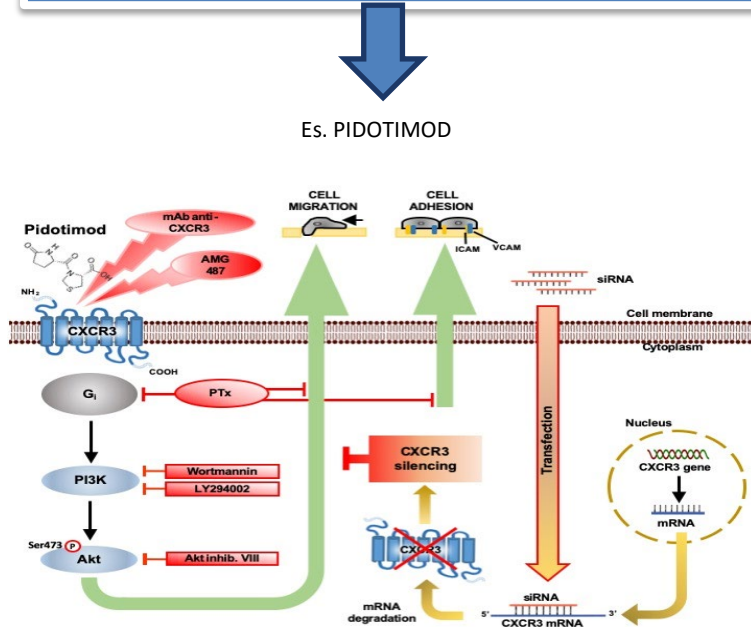
Table 1. Weighted mean \pm s.d. of number and duration of respiratory infections (RI) in children with recurrent RI

	Non-allergic children (n = 71)	Allergic children (n = 46)
Total number and forms of RI		
Total RI number (p = 0.0001)	0.94 \pm 1.37	1.26 \pm 0.73
Mild RI number (p < 0.00001)	0.53 \pm 0.64	1.02 \pm 0.7
Total RI duration (days) (p = 0.009)	4.85 \pm 5.24	8.92 \pm 9.64
Mild RI duration (days) (p = 0.0007)	2.99 \pm 3.91	7.82 \pm 9.87

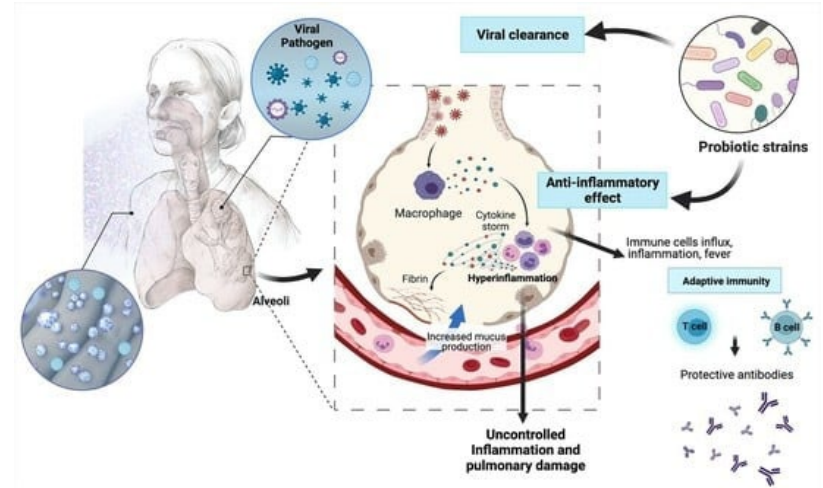
**I Bambini Allergici
sviluppano un maggior numero
di infezioni e di maggior durata**

PROPOSTE TERAPEUTICHE

BIOLOGIC RESPONDER MODIFIERS



PROBIOTICI



Caccuri, F.; Bugatti, A.; Corbellini, S.; Roversi, S.; Zani, A.; Mazzuca, P.; Marsico, S.; Caruso, A.; Giagulli, C. The Synthetic Dipeptide Pidotimod Shows a Chemokine-Like Activity through CXC Chemokine Receptor 3 (CXCR3). *Int. J. Mol. Sci.* **2019**, *20*, 5287. <https://doi.org/10.3390/ijms20215287>

Wahab, S.; Almaghaslah, D.; Mahmood, S.E.; Ahmad, M.F.; Alsayegh, A.A.; Abu Haddash, Y.M.; Rahman, M.A.; Ahamd, I.; Ahmad, W.; Khalid, M.; et al. Pharmacological Efficacy of Probiotics in Respiratory Viral Infections: A Comprehensive Review. *J. Pers. Med.* **2022**, *12*, 1292. <https://doi.org/10.3390/jpm12081292>

Pidotimod in Pediatrics: new evidence and future perspectives.

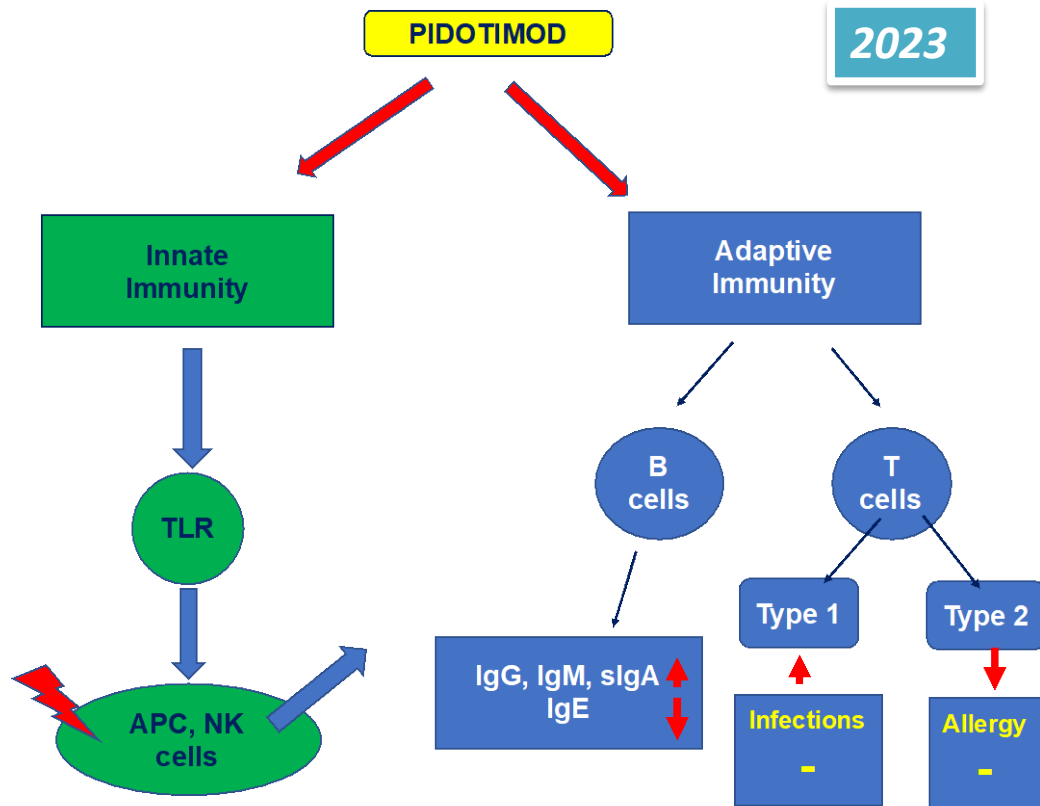
Gian Luigi Marseglia ^{1,2}, Giorgio Ciprandi ^{3*}

2023

Pidotimod is a synthetic dipeptide that exerts immunomodulatory activity, modifying innate and adaptive immunity.

Pidotimod firstly acts on Toll-Like Receptors, then on antigen-presenting cells and other immunocompetent cells.

Pidotimod also affects immunoglobulin production and their switching.



Pidotimod may prevent recurrent respiratory infections in children

A Licari ¹, M De Amici, S Nigrisoli, A Marseglia, S Caimmi, L Artusio, G L Marseglia

Affiliations + expand

PMID: 25253184

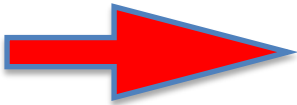
Abstract

Aim: Recurrent respiratory infections (RRI) constitute a social problem for both the pharmacoeconomic impact and the burden for the family. Pidotimod is a synthetic immunostimulant. The aim of this study was to evaluate the effects of pidotimod on RRI prevention in children.

Methods: Globally, 100 children (49 males, mean age 4.7 ± 1.2 years) with RRI were enrolled in the study. At baseline, children were randomly assigned to the treatment with pidotimod 400 mg/die or not for two months. Children were visited at baseline, after 30 (T1) and 60 (T2) days, and at follow-up (120 days; T3). Number of children with upper and lower airways symptoms, medications use, school attendance, and paediatric visits for RRI were evaluated.

Results: Pidotimod treatment was able of significantly reducing the number of children with upper and lower airways symptoms, and medications use, increasing school attendance, and reducing pediatric visits for RRI.

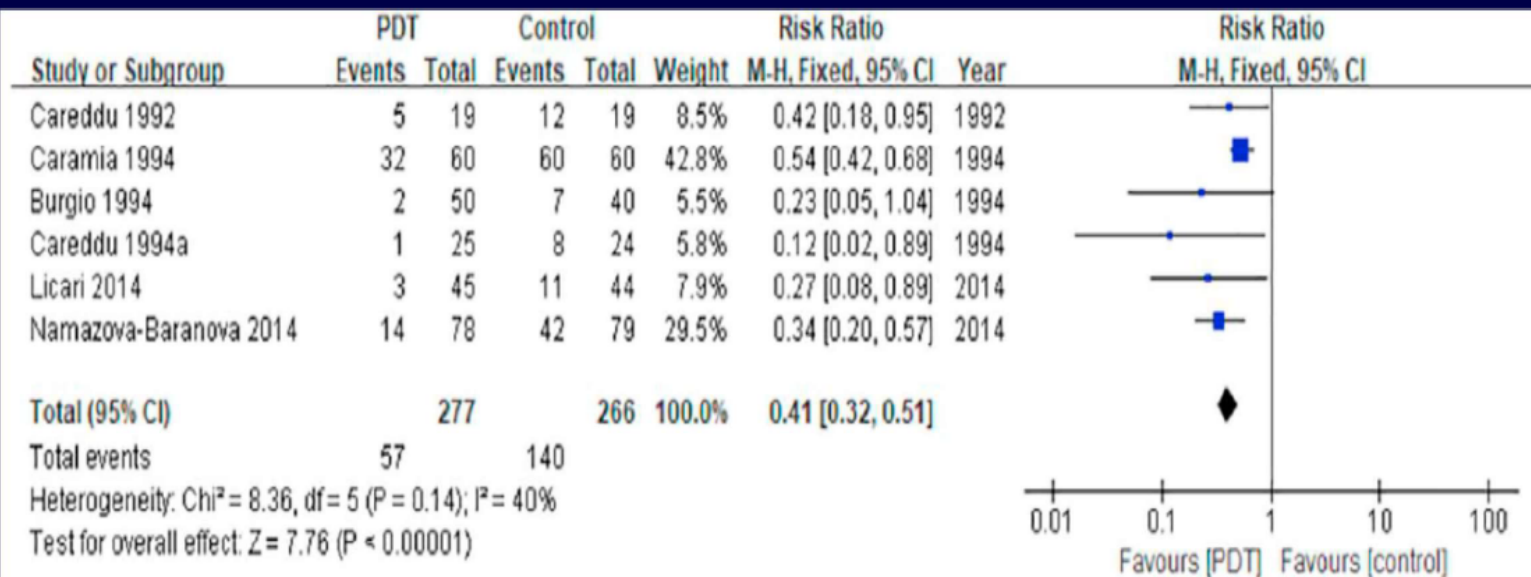
Conclusion: This study provided the evidence that pidotimod may be able of preventing RRI in children.



Pidotimod, an immunostimulant in pediatric recurrent respiratory tract infections: A meta-analysis of randomized controlled trials

Hui Niu, Rui Wang, Yu-ting Jia, Yun Cai*

International Immunopharmacology 67 (2019) 35–45



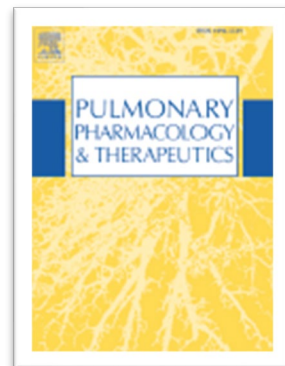
Pidotimod treatment significantly decreased the number of patients in using antibiotics (RR 0.41; 95% CI 0.32–0.51, $I^2=40\%$, $p < 0.00001$) compared with the conventional treatment

Effects of pidotimod and bifidobacteria mixture on clinical symptoms and urinary metabolomic profile of children with recurrent respiratory infections: A randomized placebo-controlled trial

Francesca Santamaria, Silvia Montella, Matteo Stocchero, Paola Pirillo, Sara Bozzetto, Giuseppe Giordano, Marco Poeta, Eugenio Baraldi

PII: S1094-5539(19)30051-3

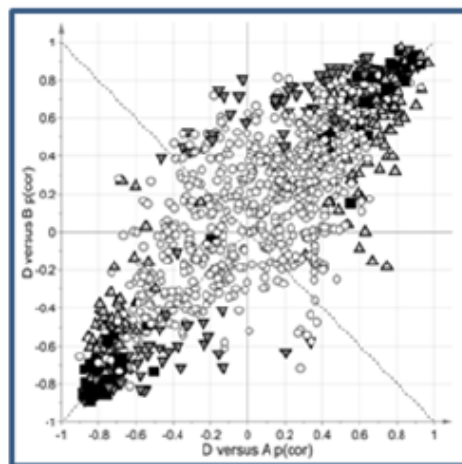
DOI: <https://doi.org/10.1016/j.pupt.2019.101818>



Clinical Examination

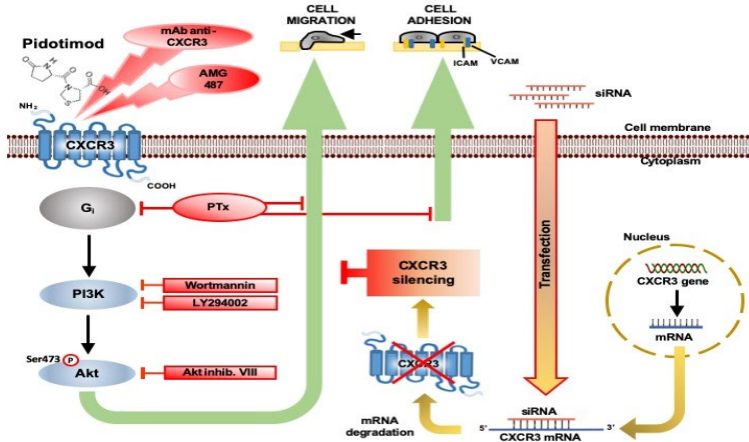
	Group A (n = 13) P value <u>vs D</u>	Group B (n = 13) P value <u>vs D</u>	Group C (n = 13) P value <u>vs D</u>
Symptom-free days	0.02	0.003	>0.05
Days with common cold	0.004	0.005	>0.05

Metabolomic Analysis

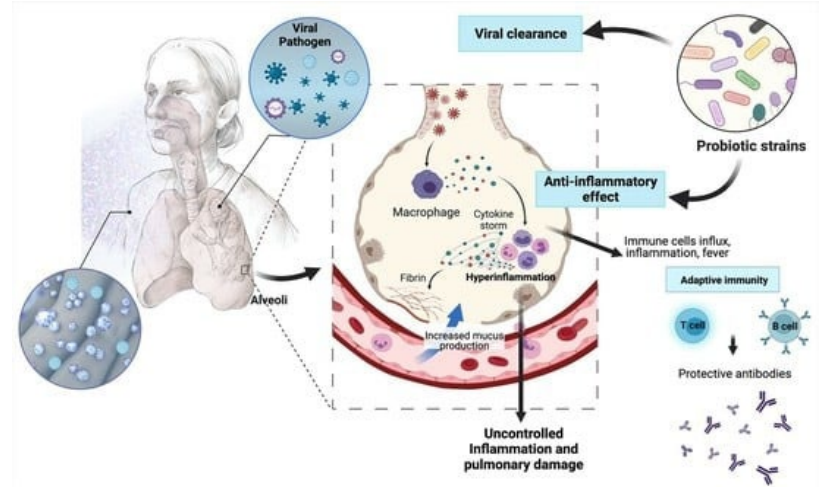


PROPOSTE TERAPEUTICHE

BIOLOGIC RESPONDER MODIFIERS



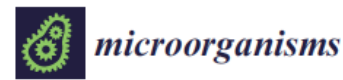
PROBIOTICI



Caccuri, F.; Bugatti, A.; Corbellini, S.; Roversi, S.; Zani, A.; Mazzuca, P.; Marsico, S.; Caruso, A.; Giagulli, C. The Synthetic Dipeptide Pidotimod Shows a Chemokine-Like Activity through CXC Chemokine Receptor 3 (CXCR3). *Int. J. Mol. Sci.* **2019**, *20*, 5287. <https://doi.org/10.3390/ijms20215287>

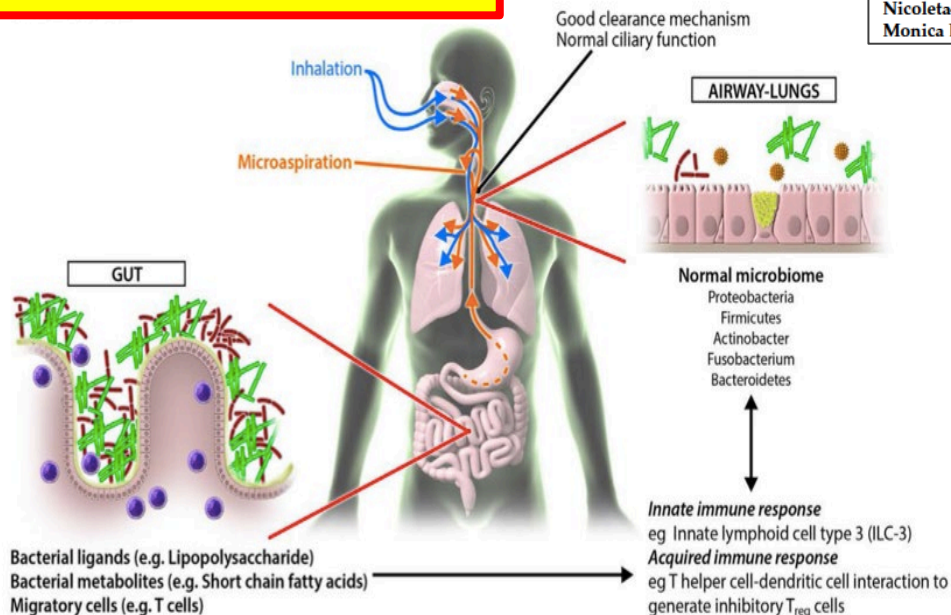
Wahab, S.; Almaghaslah, D.; Mahmood, S.E.; Ahmad, M.F.; Alsayegh, A.A.; Abu Haddash, Y.M.; Rahman, M.A.; Ahamd, I.; Ahmad, W.; Khalid, M.; et al. Pharmacological Efficacy of Probiotics in Respiratory Viral Infections: A Comprehensive Review. *J. Pers. Med.* **2022**, *12*, 1292. <https://doi.org/10.3390/jpm12081292>

Airway microbial dysbiosis in asthmatic patients: A target for prevention and treatment?



Kian Fan Chung, MD, DSc, FRCP London, United Kingdom

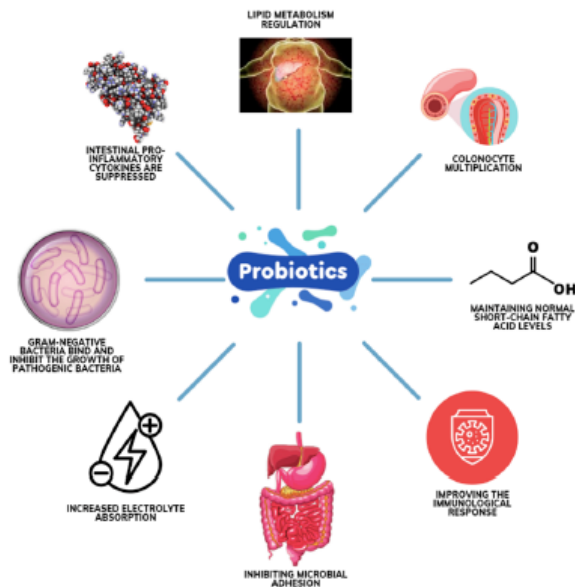
Asse Intestino-Vie Aeree



Review

The Potential Impact of Probiotics on Human Health: An Update on Their Health-Promoting Properties

Nicoleta-Maricica Maftai^{1,2,3}, Cosmin Raducu Raileanu⁴, Alexia Anastasia Balta⁵, Lenuta Ambrose⁴, Monica Boev^{1,3,*}, Denisa Bafir Marin^{1,3,*} and Elena Lacramioara Lisa^{1,3}

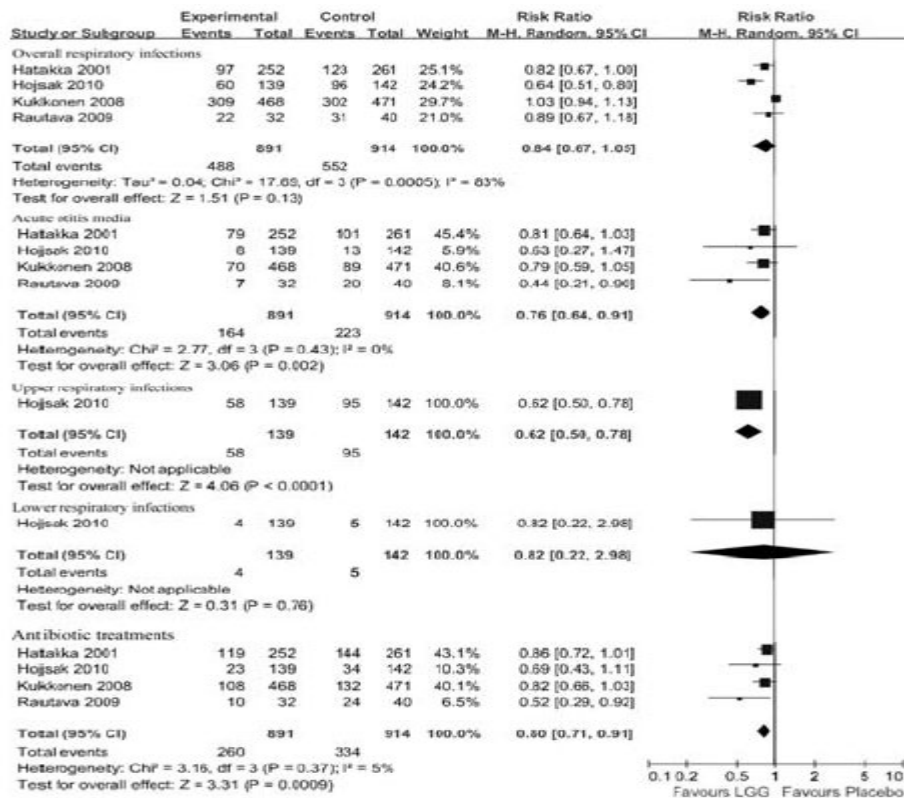


2024

Lactobacillus rhamnosus GG Supplementation for Preventing Respiratory Infections in Children: A Meta-analysis of Randomized, Placebo-controlled Trials

SHAN LIU, PENG-WEI HU, XIAOXIN DU, TAO ZHOU AND XIAOFANG PEI

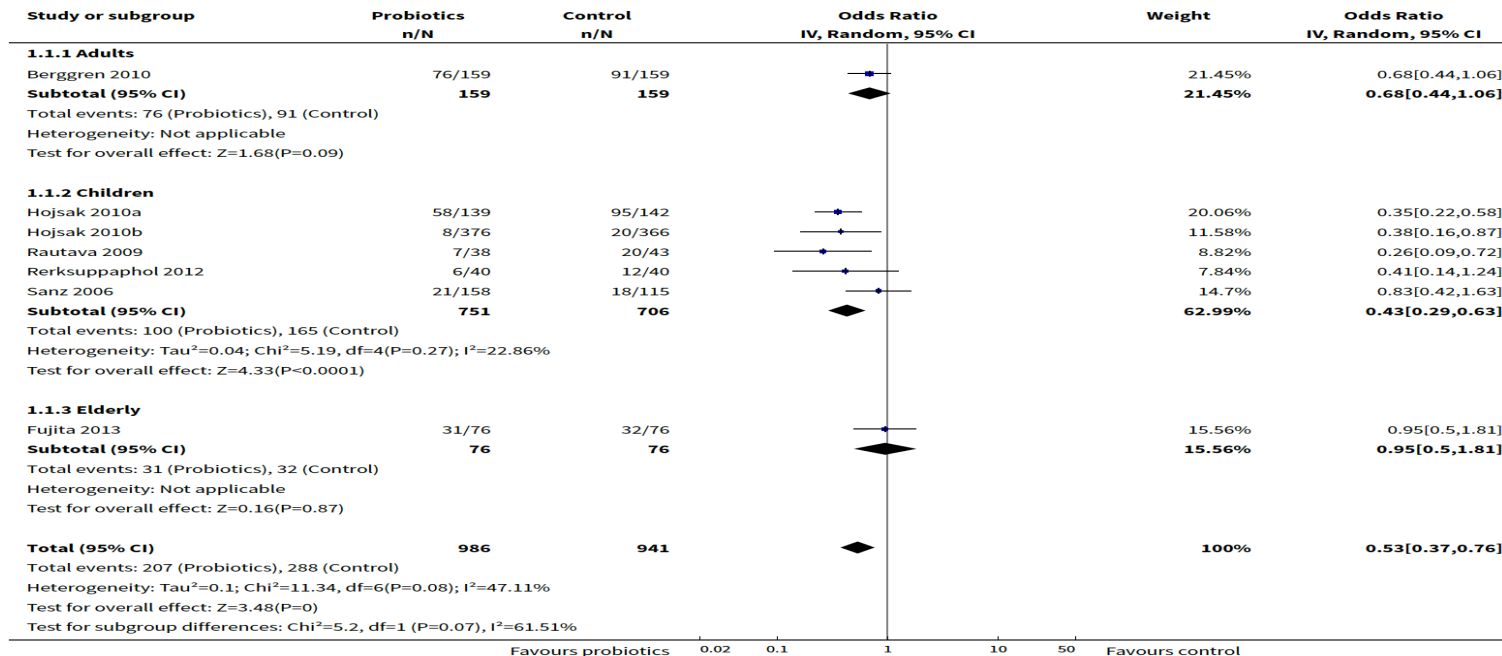
VOLUME 50—APRIL 16, 2013



Meta-Analisi
Lactobacillus GG
previene!

FIG.2 Effect of Lactobacillus GG on respiratory infections.

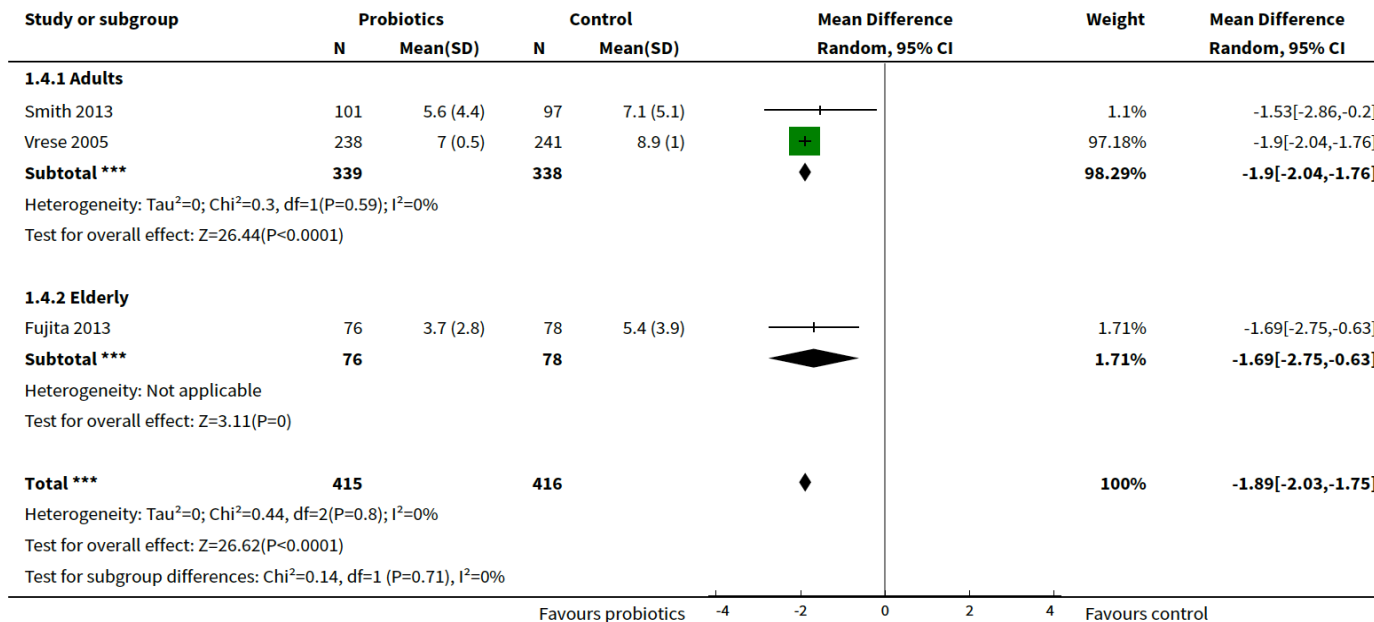
Analysis 1.1. Comparison 1 ITT analysis: probiotics versus placebo - primary outcome measures, Outcome 1 The number of participants who experienced URTI episodes: at least 1 event.



Meta-analysis

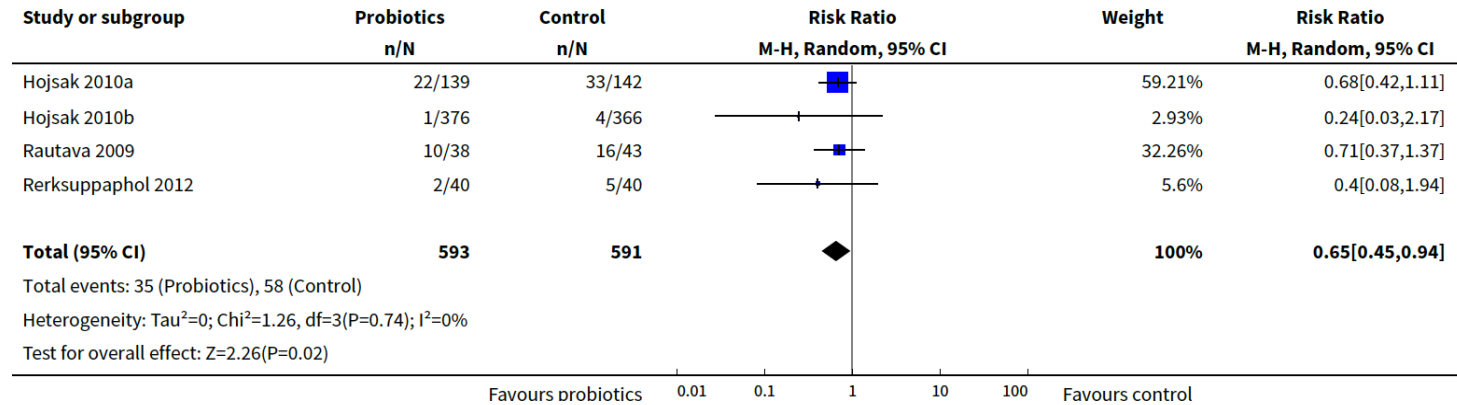
Meno episodi di IR

Analysis 1.4. Comparison 1 ITT analysis: probiotics versus placebo - primary outcome measures, Outcome 4 The mean duration of an episode of URTI.



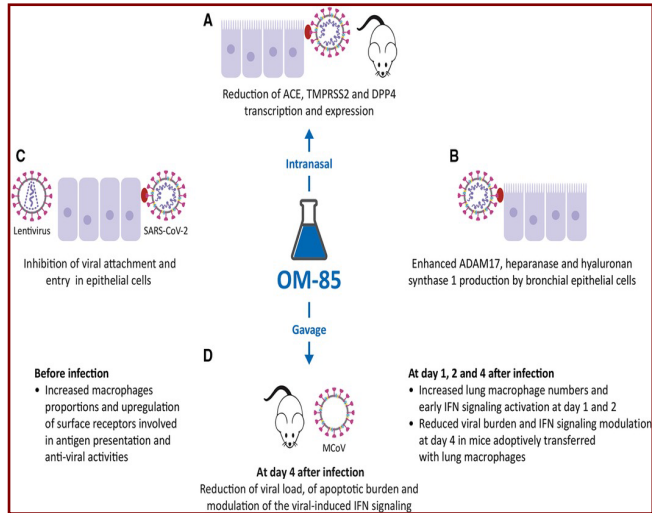
Minor durata degli episodi di IR

Analysis 3.1. Comparison 3 ITT analysis: probiotics versus placebo - prescribed antibiotics for acute URTIs, Outcome 1 The number of participants who used antibiotics.



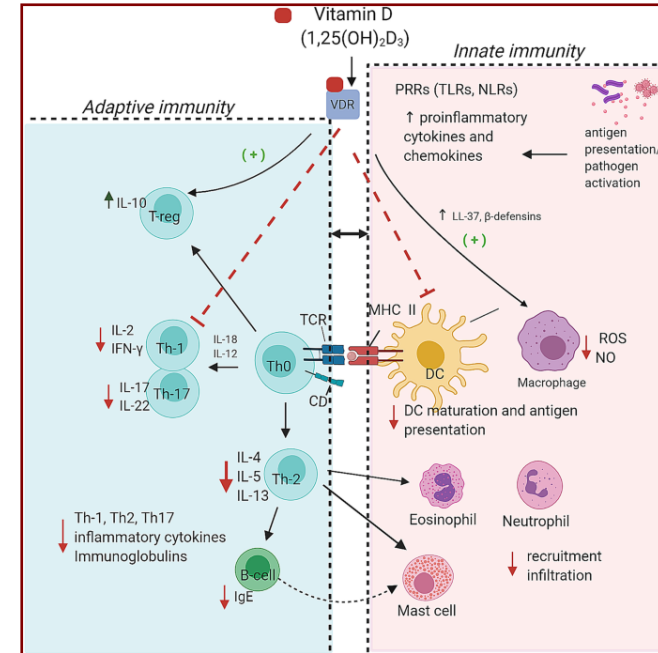
Meno antibiotici

LISATI BATTERICI



Ballarini S, Arduso L, Ortega Martell JA, Sacco O, Feleszko W and Rossi GA (2022) Can bacterial lysates be useful in prevention of viral respiratory infections in childhood? The results of experimental OM-85 studies. *Front. Pediatr.* 10:1051079. doi: 10.3389/fped.2022.1051079

VITAMINA D



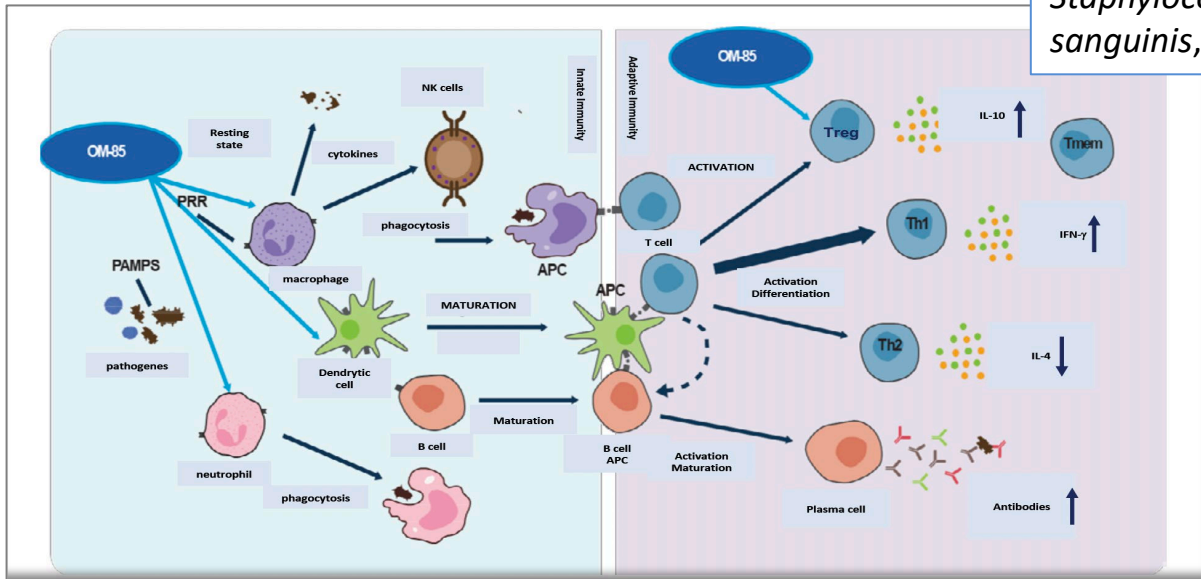
Gaudet, M., Plesa, M., Mogas, A. *et al.* Recent advances in vitamin D implications in chronic respiratory diseases. *Respir Res* 23, 252 (2022). <https://doi.org/10.1186/s12931-022-02147-x>

REVIEW



**OM-85 in the prevention of respiratory infections:
State-of-the-art and future perspectives in clinical practice**

G.L. Marseglia¹, M. Benazzo², P. Biasci³, F. Blasi⁴, C. Cricelli⁵, M. Doria³, S. Leonardi⁶,
D.G. Peroni⁷, F. Scaglione⁸ and G. Ciprandi⁹

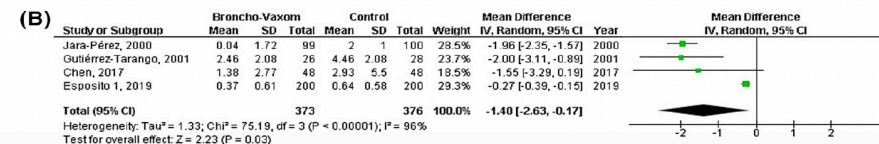
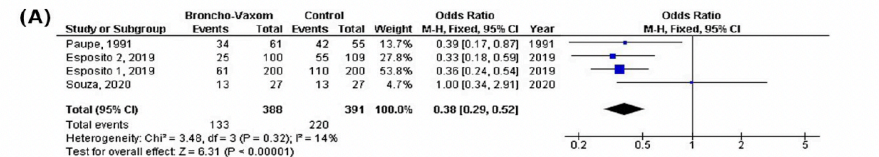
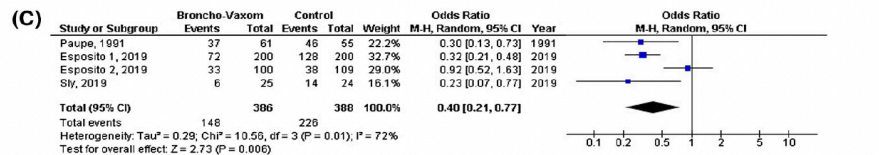
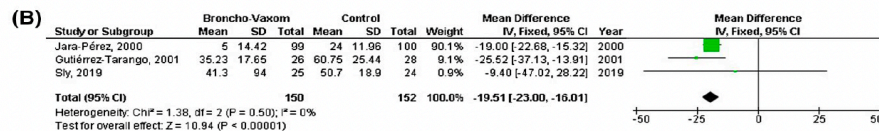
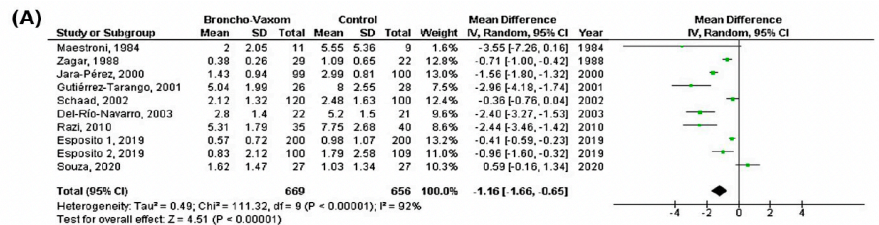
Lisati batterici liofilizzati di *Haemophilus influenzae*, *Streptococcus pneumoniae*, *Klebsiella pneumoniae* ssp. *pneumoniae* e ssp. *ozaenae*, *Staphylococcus aureus*, *Streptococcus pyogenes* e *sanguinis*, *Moraxella (Branhamella) catarrhalis*.



Efficacy and safety of OM-85 in paediatric recurrent respiratory tract infections which could have a possible protective effect on COVID-19 pandemic: A meta-analysis

Changqing Cao¹ | Jinghua Wang² | Yuning Li¹ | Yumei Li¹ | Liyan Ma³ | Mohamed E. A. Abdelrahim⁴  | Yi Zhu⁵ 

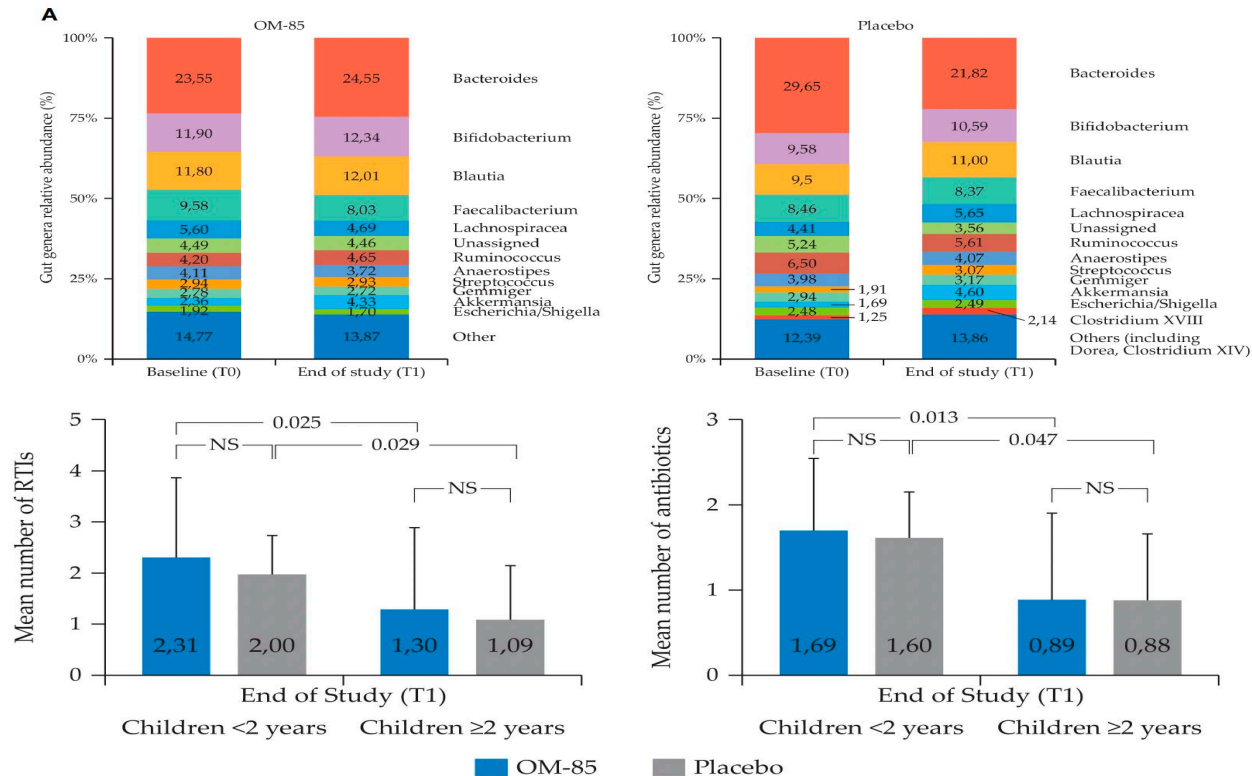
OM-85 riduce le infezioni respiratorie ricorrenti e l'uso di antibiotici in età pediatrica.



Microbiota profiles in pre-school children with respiratory infections: Modifications induced by the oral bacterial lysate OM-85

OM-85 modifica il microbiota respiratorio prevenendo le infezioni respiratorie e riducendo gli antibiotici

Susanna Esposito^{1*}, Stefania Ballarini², Alberto Argentiero¹, Luca Ruggiero³, Giovanni A. Rossi⁴ and Nicola Principi⁵



Expert consensus on the role of OM-85 in the management of recurrent respiratory infections: A Delphi study

[Susanna Esposito](#),^a [Michele Cassano](#),^b [Renato Cutrera](#),^c [Francesco Menzella](#),^d [Alfonso Varricchio](#),^e
and [Marzio Uberti](#)^f

RRIs are associated with a relevant mortality and morbidity risk in both adults and children, with a significant impact on QoL and health-care costs. According to the results of the present Delphi study, prevention is unanimously recognized as the most important intervention to reduce disease burden, and the use of immunomodulation to improve the effectiveness of vaccination is gaining increasing favor among clinicians. In this respect, OM-85 is recognized as the most studied immunomodulating agent currently available, whose efficacy and safety profile makes it a valuable tool to optimize the management of RRIs in both adults and children. In particular, the combined use of OM-85 and influenza vaccine was recognized as an effective and safe approach to improve the current prevention strategies in order to reduce the burden of RRIs in children.

Can bacterial lysates be useful in prevention of viral respiratory infections in childhood? The results of experimental OM-85 studies

Review che riassume i meccanismi d'azione di OM-85

Stefania Ballarini¹, Ledit Arduso², José Antonio Ortega Martell³,
Oliviero Sacco⁴, Wojciech Feleszko⁵ and Giovanni A. Rossi^{6*}

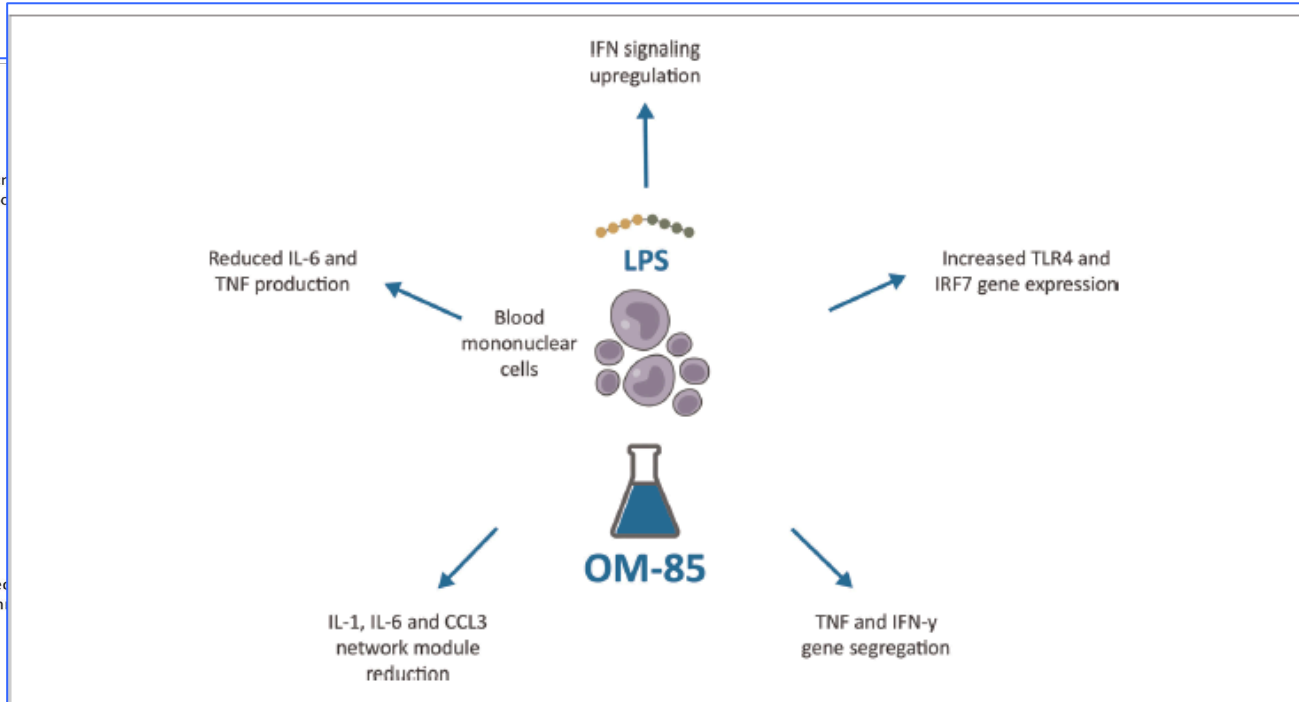
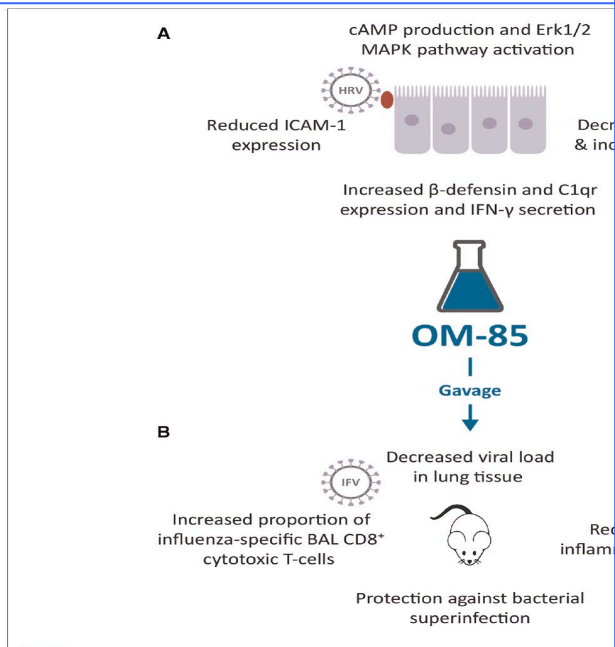


FIGURE 4 Potential immune training-based effects induced by OM-85 leading to protection against severe lower respiratory tract infections in children. LPS, Lipopolysaccharide; TLR 4, Toll Like Receptor; IRF1, Interferon Regulatory Factor 1.

Inhibition of RV and influenza virus



Comunicazione EMA su medicinali a base di Lisati Batterici

L'Agenzia Europa per i Medicinali (EMA) raccomanda che i medicinali a base di lisati batterici autorizzati per le malattie respiratorie siano utilizzati soltanto per la prevenzione delle infezioni respiratorie ricorrenti, con l'esclusione della polmonite. Tale decisione è stata presa a seguito di una revisione da cui è emerso che non ci sono dati robusti che dimostrino l'efficacia di tali medicinali nel trattare le affezioni respiratorie in corso o nella prevenzione della polmonite, pertanto essi non devono essere utilizzati a tali scopi.

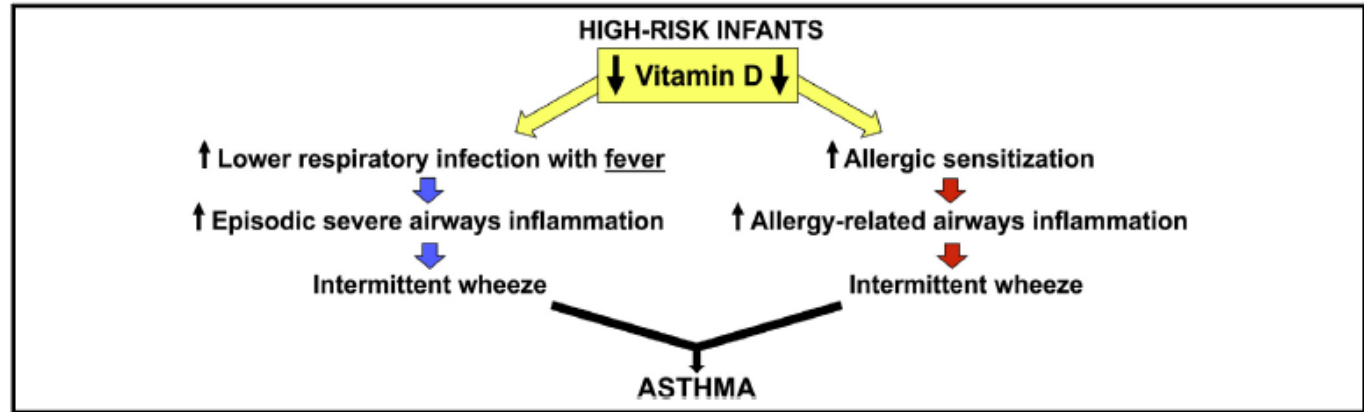
In questa revisione, il Comitato per i Medicinali per uso Umano dell'EMA (CHMP) ha preso in considerazione i risultati di studi clinici, i dati sugli effetti avversi segnalati per questi medicinali e il parere di un gruppo di esperti sulle malattie infettive.

Sebbene i dati siano limitati, dalla loro rivalutazione sono emerse alcune evidenze di efficacia di tali prodotti nella prevenzione delle infezioni ricorrenti delle vie respiratorie ed il profilo di sicurezza è in linea con l'atteso per questa tipologia di prodotti. Il CHMP, pertanto, raccomanda che l'uso di questi medicinali nella profilassi venga mantenuto, tuttavia le ditte dovranno fornire ulteriori dati sulla sicurezza ed efficacia attraverso nuovi studi clinici entro il 2026.

Vitamin D over the first decade and susceptibility to childhood allergy and asthma



Elysia M. Hollams, PhD,^a Shu Mei Teo, PhD,^{b,c,d} Merci Kusel, MBBS, PhD,^a Barbara J. Holt, BSc,^a Kathryn E. Holt, PhD,^{b,c}

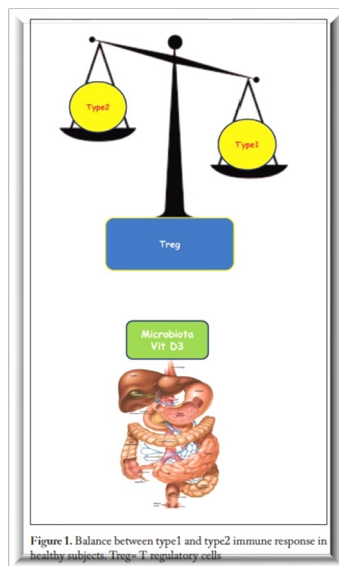


The most commonly used categorical levels to define serum 25(OH)D sufficiency, insufficiency and deficiency were ≥ 30 ng/ml (≥ 75 nmol/l), 20–29.9 ng/ml (50–74.9 nmol/l) and < 20 ng/ml (50 nmol/l), respectively

Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data

Adrian R Martineau ^{1 2}, David A Jolliffe ³, Richard L Hooper ³, Lauren Greenberg ³, John F Aloia ⁴, Peter Bergman ⁵, Gal Dubnov-Raz ⁶, Susanna Esposito ⁷, Davaasambuu Ganmaa ⁸, Adit A Ginde ⁹, Emma C Goodall ¹⁰, Cameron C Grant ¹¹, Christopher J Griffiths ^{3 2 12}, Wim Janssens ¹³, Ilkka Laaksi ¹⁴, Semira Manaseki-Holland ¹⁵, David Mauger ¹⁶, David R Murdoch ¹⁷, Rachel Neale ¹⁸, Judy R Rees ¹⁹, Steve Simpson Jr ²⁰, Iwona Stelmach ²¹, Geeta Trilok Kumar ²², Mitsuyoshi Urashima ²³, Carlos A Camargo Jr ²⁴

<20	5	629/1321 (47.6)	619/1435 (43.1)	0.94	0.006
				0.90 (0.79 to	
20-50	9	945/2796 (33.8)	1023/3077 (33.2)	1.01	0.08



What this study adds

Meta-analysis of IPD from 10 933 participants in 25 randomised controlled trials showed an overall protective effect of vitamin D supplementation against acute respiratory tract infection (number needed to treat (NNT)=33)

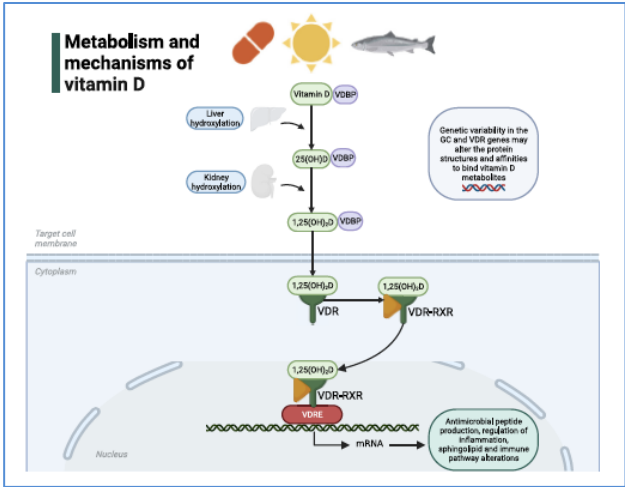
Benefit was greater in those receiving daily or weekly vitamin D without additional bolus doses (NNT=20), and the protective effects against acute respiratory tract infection in this group were strongest in those with profound vitamin D deficiency at baseline (NNT=4)

These findings support the introduction of public health measures such as food fortification to improve vitamin D status, particularly in settings where profound vitamin D deficiency is common

Vitamin D Primary Prevention of Respiratory Infections and Asthma in Early Childhood: Evidence and Mechanisms

Nicklas Brustad, MD, PhD, and Bo Chawes, MD, PhD, DMSc *Copenhagen, 1*

JACI pract 2024



Effect of vitamin D on respiratory infections and asthma in early childhood



No prenatal effect on asthma at school age from two RCTs^{13,25}. Umbrella review of prenatal vitamin D studies suggested effect on wheezing but not asthma in childhood³⁸

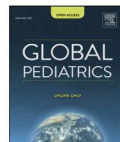
Pregnancy RCTs suggested reduced persistent wheeze but no effect on LRTI until age 18 months and 3 years^{13,25}. Reduced croup and ARI in two RCTs^{35,36}. No effect on ARI in another RCT¹⁸.

Two child RCTs suggested no effect on URTI and LRTI^{35,36}. One RCT found effect on influenza A episodes²⁷. Meta-analysis showed effect on ARI at age 1-16 years²⁸. No effect on wheezing and asthma in a meta-analysis⁴⁰



- Biologic response modifiers
- Probiotici
- Lisati batterici
- Vitamina D

Sulla base delle evidenze ad oggi disponibili, l'uso delle terapie sopracitate non è indicato routinariamente per la prevenzione delle infezioni respiratorie ricorrenti, tuttavia possono essere raccomandate in popolazioni selezionate di bambini, considerando il rapporto rischio/beneficio



Innesco di un Circolo Vizioso Possiamo interromperlo?



Nutraceuticals for allergic diseases: A brief overview

Giorgio Ciprandi ^{a,*}, Maria Angela Tosca ^b

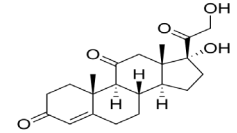
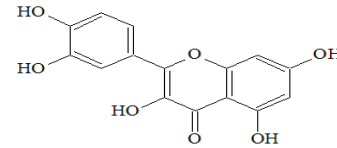


Synthetic list of the most common food supplements used in clinical practice.

Vitamins	Vitamin C, Vitamin D, Vitamin E, β -caroten
Polyphenols	Resveratrol, Catechins (green tea), Curcumin, Rosmarinic acid, Gingerol
ω -3 fatty acids	Fish oil, flaxseed oil
Probiotics	Lactobacilli, Bifidobacteria strains
Prebiotics	Inulin, FOS (fructo-oligosaccharides)
Postbiotics	Short chain fatty acids
Oligo-elements	Selenium, Zinc, Iron
Flavonoids	Quercetin, rutin, spirein
Immuno-modulants	Lactoferrin, Melatonin, Glucans

QUERCETINA

Quercetina



Cortisone

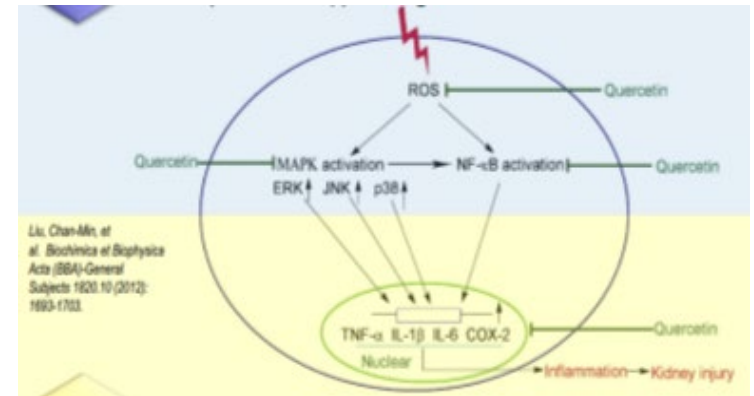
La **quercetina** è un **flavonoide** presente nella frutta e nei vegetali, ed è uno dei principali **antiossidanti** che si possono introdurre con la dieta

È isolabile da numerose specie vegetali: ippocastano, calendula, biancospino, camomilla, iperico e **Ginkgo biloba**

Alimenti particolarmente ricchi di quercetina sono: il **cappero** (è la pianta che ne contiene la maggior quantità rispetto al peso), l'uva rossa e il vino rosso, la cipolla rossa, il tè verde, il mirtillo, la mela, la propoli, il sedano, il radicchio.¹

QUERCETINA

La Quercetina esercita un importante effetto inibitorio sui **fattori di trascrizione (NF- κ B)** e sugli enzimi preposti al metabolismo dell'acido arachido: **cicloossigenasi (COX)** e **lipoossigenasi (LOX)**. Quindi può svolgere anche una **attività anti-infiammatoria**, riducendo la produzione di mediatori pro-infiammatori (**LT, PG**).



QUERCETINA effetti modulatori dell'immunità

- **Stabilizzazione delle membrane cellulari** agendo da antagonista della calmodulina e prevenendo il rilascio di mediatori
- **Riduzione della liberazione di istamina** da parte dei mastociti e dei basofili¹
- **Riduzione del rilascio di citochine** (es. TNF- α) e interleuchine da parte dei mastociti e dei basofili²
- **Riduzione della produzione di IgE**¹

QUERCETINA ed **attività antivirale**

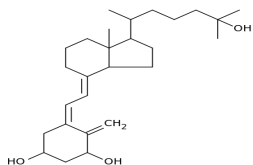
Studi *in vitro* hanno dimostrato che è in grado:

- Di inibire la produzione e la replicazione del virus dell'epatite C
- Di inibire la replicazione virale dei Rhinovirus e ridurre le citochine pro-infiammatorie
- Di prevenire l'ingresso nelle cellule dei virus dell'influenza A (anche H1N1s + H3N2)
- Di inibire le proteasi essenziali per la replicazione del virus Coronavirus Sars-Cov-2

Complementary treatment of allergic rhinoconjunctivitis: the role of the nutraceutical Lertal®

Gianluigi Marseglia¹, Amelia Licari¹, Giorgio Ciprandi²

¹ Department of Pediatrics, Fondazione IRCCS Policlinico San Matteo, University of Pavia, Pavia, Italy; ² Allergy Clinic, Villa Montallegro, Genoa, Italy



- **Quercetin 150 mg**: a natural flavonoid that inhibits the release of **histamine**, leukotrienes, PGD₂, IL (IL-6, IL-8, TNF-alpha).
- **Perilla frutescens 80 mg**: a dry extract of the seeds containing rosmarinic acid, luteolin, apigenin and crysoeriol that inhibits the release of **histamine** and expression of interleukins (IL-6, TNF-alpha).
- **Vitamin D3 5 mcg (200 IU)**, which contributes to the **normal function of the immune system**.

Respiratory infections in allergic children: the preventive role of a multicomponent nutraceutical

Anna Maria Zicari¹, Giovanan De Castro¹, Giulia Brindisi¹, Maria Papale², Guido Marinelli³, Amelia Licari⁴, Gianluigi Marseglia⁴, Giorgio Ciprandi⁵

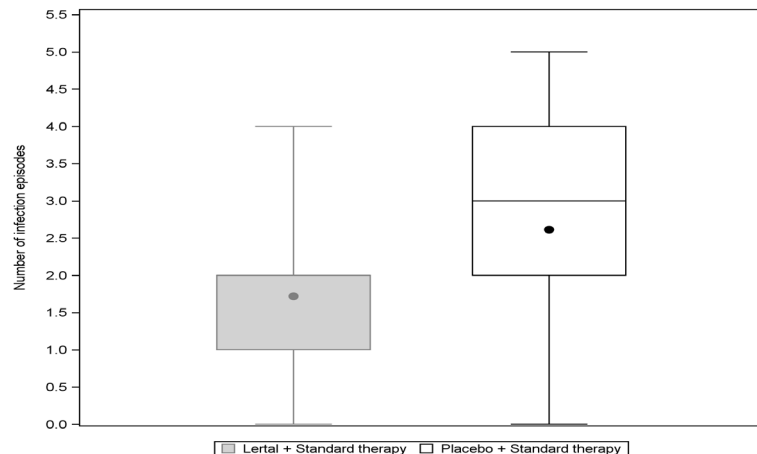


Figure 1. Box-plot of the number of respiratory infections in active group (grey) and control group (white). Data are expressed as medians, IQR, and minimum and maximum values

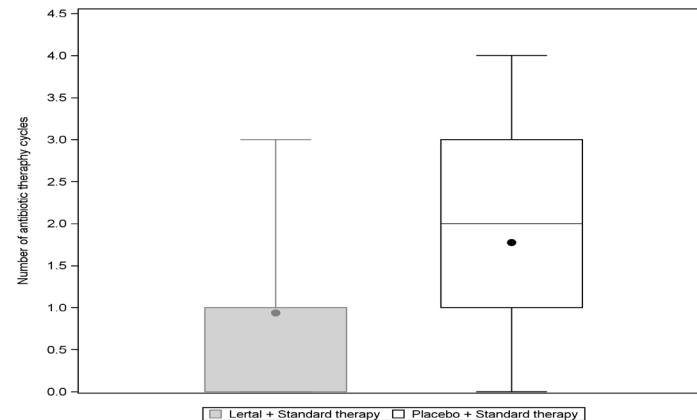
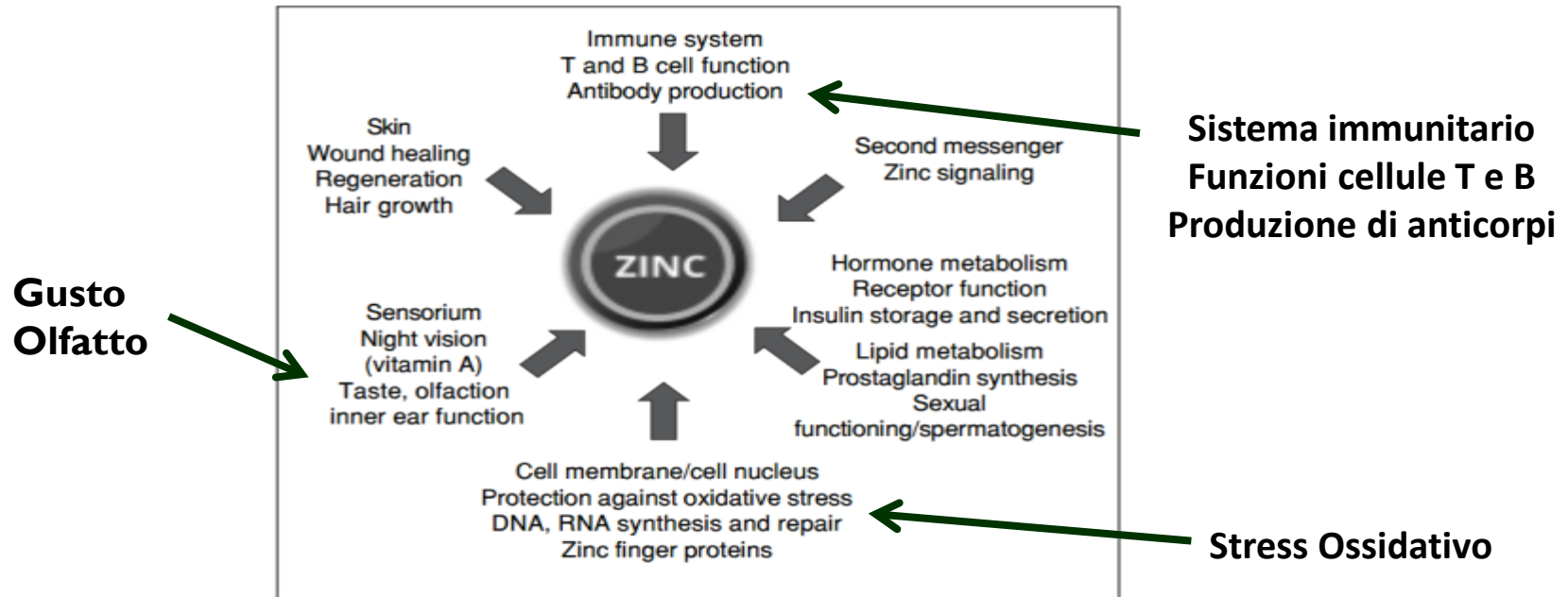


Figure 2. Box-plot of the number of courses of antibiotic therapy in active group (grey) and control group (white). Data are expressed as medians, IQR, and minimum and maximum values

Zinco: funzioni nell'organismo



**Lo zinco è il secondo più abbondante dei metalli presente nell'organismo umano:
ne contiene dai 2 ai 4 grammi**

Zinco e infezioni respiratorie

L'integrazione con zinco ha dimostrato di avere effetti benefici sulla funzionalità del sistema immunitario

- ✓ aumento azioni citotossiche¹
- ✓ maturazione di anticorpi¹
- ✓ bilanciamento di Th1/Th2¹
- ✓ riduzione dell'eccessiva espressione della cascata infiammatoria attraverso azione antiossidante¹
- ✓ mantenimento integrità epitelio¹
- ✓ riduzione della replicazione virale²

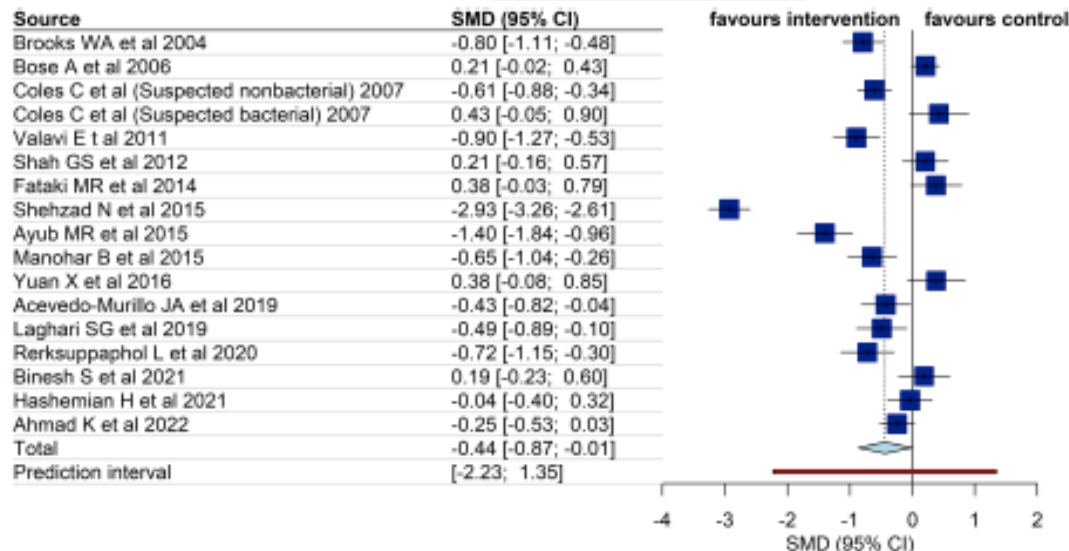
1. Wessels I. et Al. The Potential Impact of Zinc Supplementation on COVID-19 Pathogenesis. *Frontiers in Immunology* July 2020
2. Jothimani D. et Al. COVID-19: Poor outcomes in patients with zinc deficiency . *International Journal of Infectious Diseases* 2020

A systematic review and meta-analysis on nutritional and dietary interventions for the treatment of acute respiratory infection in pediatric patients: An EAACI taskforce

2024

Studies included in meta-analysis:
Zinc (length of hospital stay), $n = 16$
Zinc (time to recovery), $n = 10$
Vitamin D (length of hospital stay), $n = 3$
Vitamin D (time to recovery), $n = 3$

FIGURE 3 Meta-analysis and forest plot about pooled standardized mean difference of length of hospitalization in children with pneumonia treated with zinc or placebo. The area of the squares indicates the weight of each study in the analysis.



Exclusive breast-feeding, the early-life microbiome and immune response, and common childhood respiratory illnesses



J ALLERGY CLIN IMMUNOL
VOLUME 150, NUMBER 3

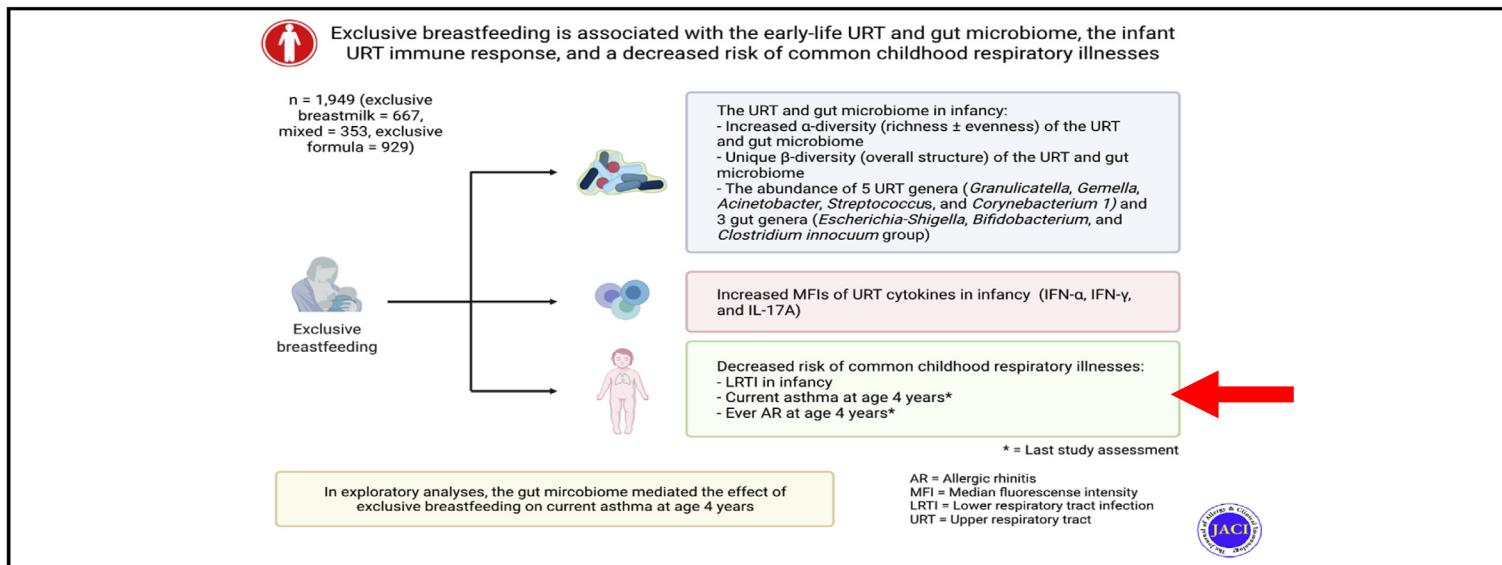


Christian Rosas-Salazar, MD, MPH,^a Meghan H. Shilts, MHS, MS,^b Zheng-Zheng Tang, PhD,^c Qilin Hong, MS,^c Kedir N. Turi, PhD,^b Brittany M. Snyder, PhD,^b Derek A. Wiggins, MS,^b Christian E. Lynch, MPH,^b Tebeb Gebretsadik, MPH,^d R. Stokes Peebles, Jr, MD,^b Larry J. Anderson, MD,^e Suman R. Das, PhD,^{b,f} and Tina V. Hartert, MD, MPH^b *Nashville, Tenn; Madison, Wis; and Atlanta, Ga*

Protezione del latte materno

Key messages

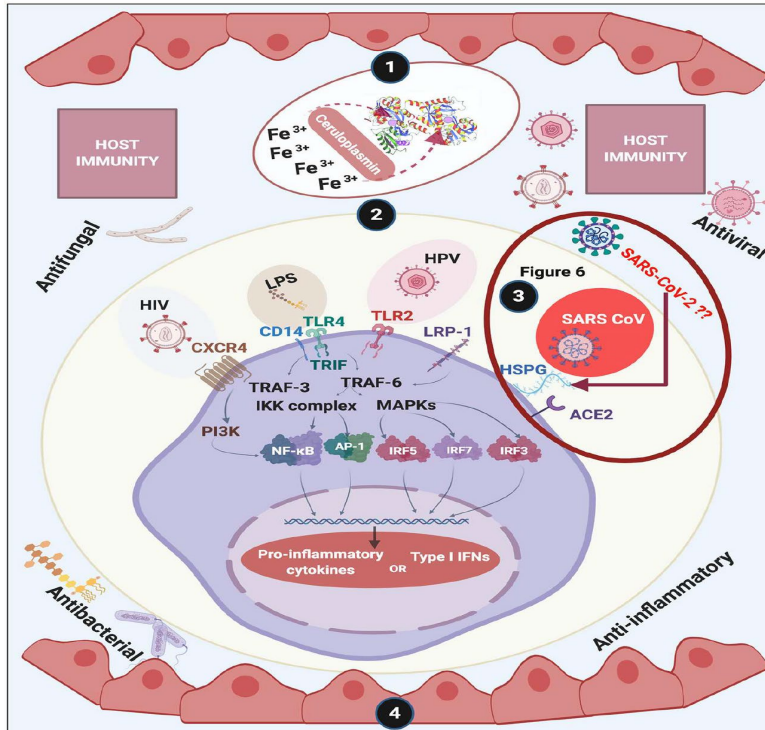
- Our results support a protective causal role of exclusive breast-feeding in the risk of developing an LRTI in infancy and asthma and AR in childhood.
- In addition, they shed light on potential mechanisms of these associations, including the effect of exclusive breast-feeding on the gut microbiome.
- For its respiratory and multiple nonrespiratory benefits for both the infant and the mother, exclusive breast-feeding should continue to be strongly recommended to all families.



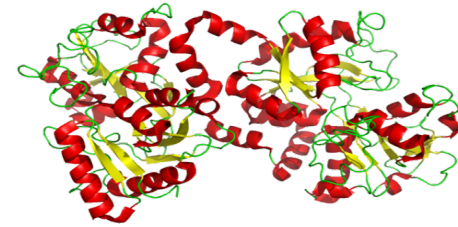


The Biology of Lactoferrin, an Iron-Binding Protein That Can Help Defend Against Viruses and Bacteria

Douglas B. Kell^{1,2,3*†}, Eugene L. Heyden¹ and Ethersia Pretorius^{3*†}



La Lattoferrina ha un'attività antimicrobica ed antinfiammatoria



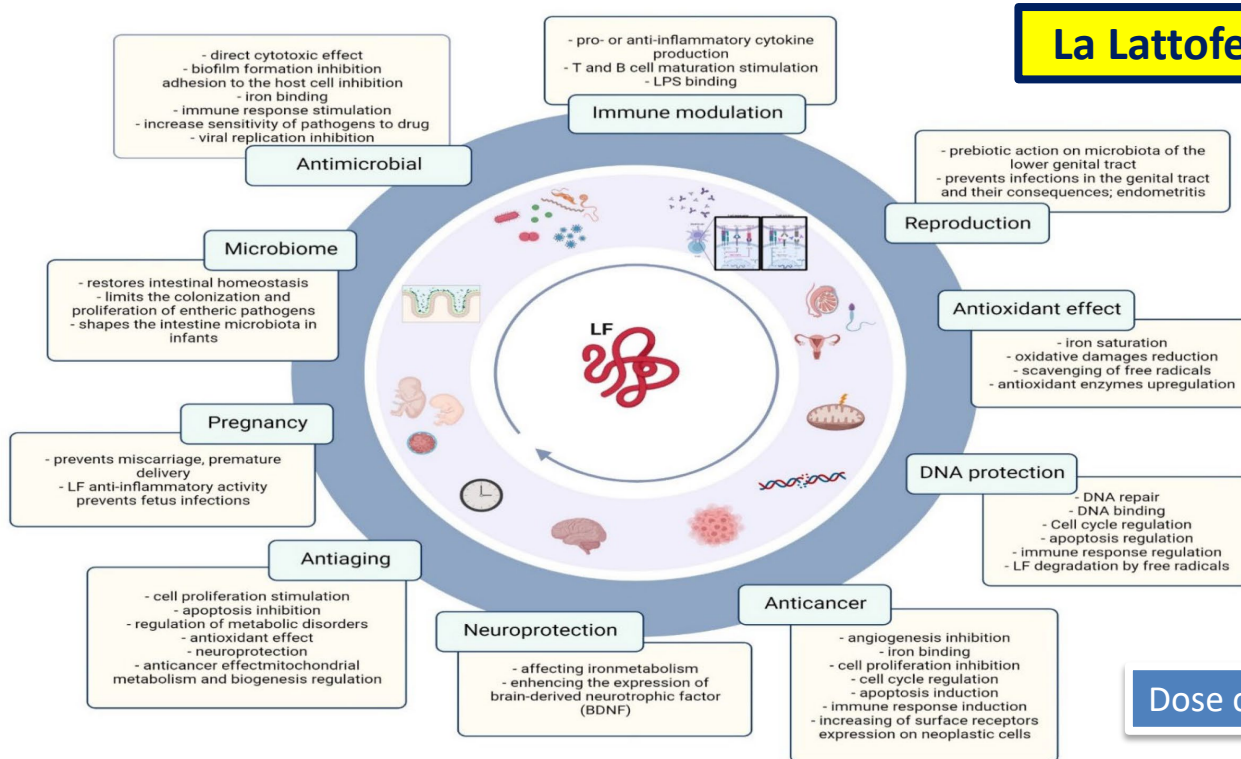
Il latte umano ha una concentrazione di 2g/L, 10-100 volte maggiore di altri mammiferi.



Review

The Lactoferrin Phenomenon—A Miracle Molecule

Paweł Kowalczyk ¹, Katarzyna Kaczyńska ², Patrycja Kleczkowska ^{3,4,*}, Iwona Bukowska-Oško ⁵, Karol Kramkowski ⁶ and Dorota Sulejczak ^{7,*}



La Lattoferrina è pleiotropica

Dose consigliata: 100 mg/giorno



Centro di Allergologia IGG

*mariangelatosca
robertaolcese
chiaratrincianti
valentinanosratian
claudiasalmaso
matteonaso
@gaslini.org*

***Grazie
a tutti!***