CONSUMER TRENDS, INGREDIENT INNOVATION, AND THE EVOLVING SCIENCE BEHIND CHILDREN'S IMMUNE-HEALTH NUTRACEUTICALS

From "Immune Boosting" to Evidence-Based Paediatric Immune Resilience

A critical review of consumer behaviour, developmental immunology, ingredient science, formulation technology, clinical evidence and regulatory constraints

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INTABIOTECH

Structured Critical Review | Literature updated through 1 September 2026

Academic Article · 2026

Abstract

Children's immune health has evolved from a predominantly seasonal supplement category into a major field of paediatric nutritional innovation. Parents increasingly seek products positioned around immunity, gut health, cognitive development and broader resilience while simultaneously demanding convenient formats, low or no added sugar, natural or recognisable ingredients, clean-label positioning, transparency and credible scientific substantiation. Contemporary market data illustrate this transformation. In the United States, children's supplement sales across major measured channels reached approximately USD 1.29 billion between July 2025 and July 2026, with gummies accounting for approximately USD 581 million. Immune/cold-and-flu positioning represented approximately USD 170 million over the same period. International consumer research likewise places immune health among the leading priorities of parents of children aged 3-12 years. These commercial observations, however, constitute evidence of consumer demand rather than evidence of clinical efficacy.

The scientific landscape is substantially more complex. 'Immune support' is frequently communicated as if it were synonymous with infection prevention, yet immune competence is a multidimensional developmental state involving epithelial barrier function, innate and adaptive immune responses, immune tolerance, inflammatory regulation, immunological memory and bidirectional interactions with the microbiota. Deficiencies of micronutrients such as vitamins A and D, zinc, iron and selenium can compromise host defence, but correcting deficiency must be distinguished from supplementing already replete children in an attempt to obtain supra-physiological protection. Contemporary evidence therefore supports a shift from the poorly defined concept of 'immune boosting' toward the more biologically coherent construct of paediatric immune resilience.

At the same time, ingredient research is expanding beyond conventional vitamin-mineral combinations toward strain-specific probiotics, prebiotics and synbiotics, postbiotics, human-identical milk oligosaccharides (HiMOs), lactoferrin, milk fat globule membrane (MFGM), beta-glucans and other biologically active systems. These platforms offer compelling mechanistic rationales but markedly heterogeneous levels of clinical validation. Recent systematic reviews and randomized trials demonstrate why entire ingredient classes cannot legitimately inherit the evidence generated for individual strains, structures, preparations or formulations.

This structured critical review examines the convergence of paediatric immune development, consumer behaviour, nutritional science, microbiome research, ingredient innovation, formulation technology, safety assessment, clinical-trial methodology and regulatory science. It proposes two integrated conceptual frameworks - the Paediatric Immune Resilience Model and the Seven-Layer Evidence Architecture for Paediatric Immune Products - and argues that the next generation of clinically credible products will be distinguished not by the length of their ingredient lists but by biological coherence, age-appropriate dosing, analytical characterisation, formulation stability, clinically meaningful endpoints, transparent evidence hierarchies and regulatory-compatible communication.

Keywords: *paediatric nutrition; immune resilience; immune health; nutraceuticals; dietary supplements; probiotics; prebiotics; synbiotics; postbiotics; human milk oligosaccharides; lactoferrin; MFGM; beta-glucans; vitamin D; zinc; microbiome; respiratory infections; functional foods.*

Research highlights

- 'Immune boosting' is biologically imprecise; paediatric immune resilience is a more defensible research construct.
- Correcting nutrient deficiency is not equivalent to supplementing nutrient-replete children for infection prophylaxis.
- Evidence for probiotics, postbiotics, HMOs, beta-glucans, botanicals and biological fractions is product-, strain-, structure- and dose-specific.
- Biomarker modulation should support, not replace, clinically meaningful outcomes.
- The finished formulation - not the ingredient list - must ultimately become the validated intervention.

1. Introduction: from category growth to scientific accountability

Paediatric immune-health products occupy an unusual position at the intersection of nutrition, preventive health, consumer psychology and biomedical science. Parents want to reduce the frequency and impact of childhood illness. Manufacturers seek nutritional interventions capable of satisfying that expectation. Researchers continue to uncover increasingly sophisticated interactions between nutrients, microbial ecosystems, epithelial tissues and immune development.

Yet these three domains - consumer expectation, commercial innovation and clinical evidence - do not necessarily evolve at the same speed. The consequence is a market in which biologically plausible mechanisms can rapidly become consumer-facing narratives before their clinical significance has been established. That is particularly problematic in children.

A product containing vitamin D, zinc, elderberry and a probiotic may appear scientifically sophisticated because every constituent can be associated with immune biology. That does not establish that the combination prevents infections, reduces disease burden or produces an additive or synergistic effect. The central problem is therefore epistemological as much as nutritional: what level of evidence is required before an immune-health concept becomes an evidence-based paediatric nutritional intervention?

This review argues that the sector is entering a transition from ingredient-led formulation toward evidence-led systems formulation. That transition should fundamentally alter ingredient selection, dose design, formulation technology, clinical validation, safety assessment and claims strategy.

The next generation of paediatric immune-health products should be designed around evidence, not assembled around ingredients.

2. Methodological approach and evidence hierarchy

This article constitutes a structured critical narrative review rather than a formal systematic review or meta-analysis. Literature was updated through 1 September 2026, prioritising systematic reviews and meta-analyses, randomized controlled trials, international consensus statements, major mechanistic reviews, authoritative public-health guidance, EFSA and European Commission materials, EUR-Lex legislation, FDA guidance and NIH Office of Dietary Supplements resources. Contemporary market-intelligence sources were used only where consumer behaviour, product format or commercial category evolution - rather than biomedical efficacy - was being evaluated.

Search concepts included combinations of child, paediatric, infant, immune, respiratory infection, nutritional supplement, vitamin D, vitamin A, zinc, probiotic, prebiotic, synbiotic, postbiotic, HMO, lactoferrin, MFGM, beta-glucan, echinacea, elderberry, microbiome and immune development. Particular weight was assigned to evidence published from 2024 to September 2026 while retaining earlier consensus publications and pivotal trials where necessary.

Evidence was interpreted hierarchically. Mechanistic plausibility was not considered equivalent to biomarker efficacy; biomarker efficacy was not considered equivalent to improvement in clinically meaningful outcomes; and evidence generated with one specific strain, extract, molecular structure or formulation was not automatically extrapolated to an entire ingredient category. Market performance was treated as evidence of demand, not evidence of efficacy.

Evidence level	What it establishes	What it does not establish
Mechanistic plausibility	A biologically credible pathway can be affected.	That children experience a clinically meaningful benefit.
Intermediate phenotype / biomarker	The intervention changes a biological marker, microbial feature or physiological process.	That infection incidence, severity or recovery improves.

Evidence level	What it establishes	What it does not establish
Clinical efficacy	A predefined clinically meaningful endpoint improves under controlled conditions.	That all formulations in the same ingredient class are equivalent.
Real-world effectiveness	The validated intervention performs under routine use.	That disease-treatment claims are legally permissible.
Regulatory compatibility	A given communication is permitted under the relevant framework.	That a broader implied disease claim is also permitted.

3. Consumer trends and the commercial transformation of paediatric immune health

3.1 Immunity as a baseline parental priority

The post-pandemic consumer environment has permanently changed the children's supplement category. International qualitative research involving parents across multiple geographical markets places immune, brain and gut health among the leading parental priorities. Immunity ranked among the three leading concerns in every geography examined and was the highest priority in several markets, while parents simultaneously expressed preferences for naturalness, convenience and scientific credibility (NutraIngredients, 2026a).

The market has also shifted away from undifferentiated multivitamins. US SPINS data reported in 2026 placed children's supplement sales at approximately USD 1.29 billion across measured natural, multi-outlet, convenience and Amazon channels from July 2025 through July 2026. Gummies represented approximately USD 581 million, ahead of liquids, chewables, powders and conventional tablets. Immune/cold-and-flu positioning represented approximately USD 170 million during the same measured period (NutraIngredients, 2026b).

The commercial architecture is therefore changing from a broad 'multivitamin equals general health' proposition toward a more targeted sequence: defined age group, defined health need, targeted ingredients, convenient delivery, evidence narrative. This is commercially rational. Scientifically, however, it creates greater obligations rather than fewer.

Format	Approximate US sales (Jul 2025-Jul 2026)
Gummies	USD 581 million
Liquids	USD 252 million
Chewable tablets	USD 91 million
Powders	USD 54 million
Conventional tablets	USD 54 million

Source note: market figures are commercial category data, not clinical efficacy evidence. Figures reported from SPINS data in NutraIngredients (2026b).

3.2 Consumer popularity is not clinical validation

One of the most important principles for paediatric supplement development is that sales velocity does not constitute biological validation. Elderberry provides a useful example. It occupies a visible position in contemporary immune-health markets, yet a systematic review identified only five randomized trials investigating prevention or treatment of viral respiratory illness. The evidence suggested that elderberry may not reduce the probability of developing a common cold, while possible effects on severity and duration remained uncertain (Wieland et al., 2021).

The correct conclusion is not that elderberry is ineffective. The defensible conclusion is that the strength of the commercial narrative currently exceeds the strength of the clinical evidence. Commercial adoption can substantially precede evidentiary maturity, and responsible product development must explicitly recognise that gap.

4. Scientific framework: why immune resilience is a better construct than immune boosting

4.1 The biological inadequacy of "immune boosting"

The expression 'immune boosting' is intuitively attractive and biologically imprecise. The immune system is not a single quantitative variable. Protection depends upon coordinated activity among epithelial barriers, antimicrobial peptides, complement, phagocytes, innate lymphoid cells, natural killer cells, antigen-presenting cells, B and T lymphocytes, antibodies, immune memory, regulatory pathways, inflammatory-resolution mechanisms and the microbiota.

Increasing one component does not necessarily improve overall host defence. Excessive immune activation can itself become pathological. Allergic disease represents inappropriate immune responses toward otherwise harmless antigens; autoimmune disease involves loss of tolerance; and excessive inflammatory responses can increase tissue injury during infection. An effective immune system must therefore recognise, respond, regulate, resolve and remember.

4.2 Proposed concept: paediatric immune resilience

For nutritional research, immune resilience offers a more defensible framework. We propose the following operational definition:

> ***Paediatric immune resilience is the capacity of the developing immune system to maintain barrier integrity, mount proportionate innate and adaptive responses to biological challenges, preserve immune tolerance, regulate inflammation and restore homeostasis after challenge while normal immune maturation proceeds.***

This construct encompasses at least six domains to know: barrier resilience, innate defensive competence, adaptive immune competence, immune tolerance, inflammatory regulation, and recovery with return to homeostasis. Unlike the idea of "boosting", resilience recognises that both insufficient and excessive responses can be undesirable.

Figure 1. Paediatric Immune Resilience Model

A systems framework linking developmental inputs, host biology and clinically meaningful outcomes

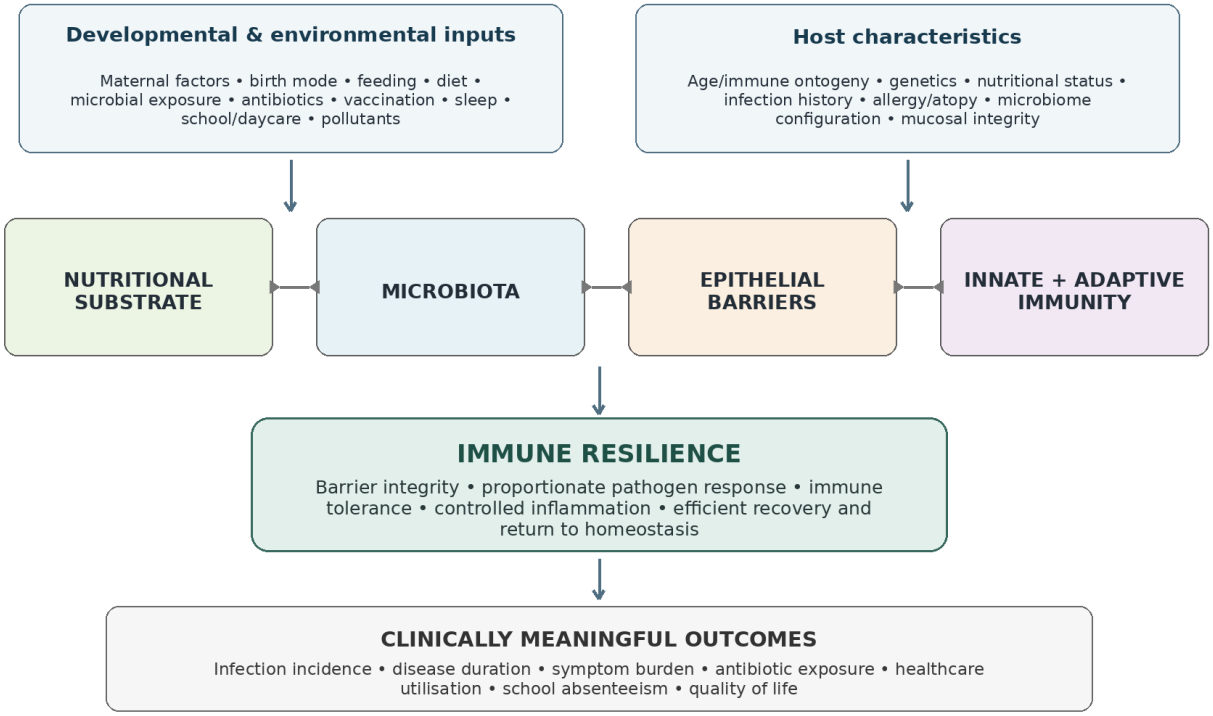

Figure 1. Paediatric Immune Resilience Model. Nutraceutical interventions may target one or more biological nodes, but clinically meaningful outcomes remain the ultimate test of utility. Original conceptual framework developed for this review.

4.3 Children are not small adults: immune ontogeny matters

The immune systems of newborns, infants, preschool children, school-age children and adolescents are biologically distinct. Recent work in developmental immunology emphasises that perinatal and early-life immune development follows ontogeny-specific programmes shaped by prenatal, maternal and postnatal signals (Palma et al., 2026).

Early-life immune development prioritises not only protection against pathogens but also tolerance. A newborn is suddenly exposed to large quantities of food antigens, commensal microorganisms, environmental microbes and novel proteins. Responding aggressively to every unfamiliar antigen would be physiologically disastrous. Immune maturation therefore requires education, not simply activation.

4.4 The microbiota as an immune-development partner

Microbiota research has radically altered understanding of early immune development. The intestinal microbiota communicates with epithelial tissues and immune cells through microbial structures and metabolites. Short-chain fatty acids and many other microbial-derived molecules can influence epithelial integrity, regulatory T-cell function, mucosal immunity, cytokine signalling, oral tolerance and inflammatory regulation.

A 2025 Nature Immunology review describes early life as a critical period of microbiota-mediated immune imprinting and highlights nutrition as a central modifier of that process (Iliev et al., 2025). Earlier work likewise established that early-life microbiota composition and immune maturation are reciprocally interconnected and potentially relevant to later allergic and inflammatory disease (Donald & Finlay, 2023).

This provides genuine biological support for the gut-immune axis. It does not, however, demonstrate that every product capable of changing microbiota composition improves immune health. A change in bacterial abundance, short-chain fatty acids, secretory IgA or cytokines can support a mechanism without establishing reduced infection burden.

5. Nutritional adequacy: the strongest foundation and the most frequently overextended narrative

Normal immune function requires adequate nutrition. The NIH Office of Dietary Supplements identifies **vitamins A, B6, B12, C, D, E and K together with folate, copper, iodine, iron, magnesium, selenium and zinc** among nutrients relevant to normal immune function. A major Annual Review of Nutrition analysis similarly highlights important interactions between vitamin A, vitamin D, iron, zinc and selenium status and host response to pathogens (Palmer et al., 2024).

The essential conceptual distinction is dose-response context: moving a deficient child toward adequacy can be physiologically important; moving an adequately nourished child from adequacy toward high exposure does not automatically create additional protection and may sometimes create risk. Nutritional necessity must therefore not be confused with proof of infection prevention.

5.1 Vitamin A: essential biology, population-specific supplementation

Vitamin A supports epithelial integrity, mucosal defence, lymphocyte development and antibody responses. Vitamin A deficiency is therefore clinically relevant. WHO evidence in children aged six months to five years demonstrates important reductions in mortality and diarrhoeal morbidity in populations where deficiency is endemic, but does not establish comparable prevention of respiratory disease across well-nourished populations.

This illustrates a recurring principle: nutritional interventions often produce their largest effects where deficiency is common. Extrapolating deficiency-focused public-health interventions to nutrient-replete children in high-income settings can therefore be scientifically inappropriate.

5.2 Vitamin D: mechanistic enthusiasm, heterogeneous clinical evidence

Vitamin D possesses a compelling immunological rationale. Vitamin D receptors are expressed by multiple immune-cell populations, and vitamin D signalling can affect macrophage function, antimicrobial peptide expression, dendritic-cell biology, T-cell differentiation and inflammatory regulation. Low vitamin D concentrations are observationally associated with increased respiratory morbidity, but association does not establish therapeutic causality.

A 2025 paediatric systematic review and meta-analysis included 17 randomized controlled trials and 18,372 participants. Overall vitamin D supplementation did not significantly reduce acute respiratory infection incidence (RR 0.82; 95% CI 0.64-1.06) and did not significantly improve hospitalisation duration, recovery time or all-cause mortality (Wang et al., 2025).

A larger updated meta-analysis incorporating 61,589 participants likewise found no statistically significant overall reduction in acute respiratory infections (OR 0.94; 95% CI 0.88-1.00; $p = 0.057$), with no convincing effect modification by age, baseline vitamin D status, dosing frequency or dose size (Jolliffe et al., 2025).

5.3 The 2026 vitamin-D network meta-analysis: a signal, not a universal mandate

In 2026, Xing and colleagues conducted a Bayesian network meta-analysis of 19 randomized trials involving 11,576 children. Direct comparisons did not demonstrate significant superiority of low-dose vitamin D, vitamin A, vitamin A plus zinc or zinc against placebo. The network analysis nevertheless produced a favourable estimate for the study-defined high-dose vitamin D category (OR 0.76; 95% credible interval 0.61-0.94), and this category achieved the highest SUCRA ranking.

The result is scientifically interesting but should not be overinterpreted. The analysis included substantial clinical heterogeneity, pragmatic dose categorisation, broad variation in dosing regimens, inconsistent respiratory-infection definitions and limited numbers of trials for several interventions. GRADE certainty ranged from moderate to very low depending upon the comparison (Xing et al., 2026).

Accordingly, the network result is best treated as a hypothesis-strengthening signal rather than a mandate for indiscriminate high-dose prophylaxis. A probabilistic ranking does not by itself establish universal clinical

superiority. Vitamin D remains nutritionally essential; deficiency should be prevented or corrected; current evidence does not justify presenting supplementation as universally proven respiratory-infection prophylaxis in otherwise healthy, replete children.

5.4 Zinc: essential, clinically useful and context-dependent

Zinc plays central roles in cellular metabolism, epithelial integrity, antioxidant defence, innate immunity, lymphocyte development, T-cell signalling and natural-killer-cell activity. Deficiency can therefore increase susceptibility to infection. Important paediatric evidence supports zinc supplementation in selected populations and conditions, particularly childhood diarrhoeal disease and deficiency-prone settings.

Those findings cannot simply be extrapolated to healthy, zinc-replete European or North American children. Excess is also not innocuous: chronic excessive zinc exposure can disrupt copper metabolism and eventually impair physiological function. The scientifically sophisticated zinc product is therefore not the one with the largest dose but the one with the correct dose for the intended age group, baseline nutritional context and total dietary exposure.

5.5 Vitamin C, iron and selenium: adequacy rather than maximalism

Vitamin C contributes to epithelial integrity, antioxidant defence, neutrophil and phagocyte function and lymphocyte biology. Severe deficiency clearly impairs host defence, yet evidence supporting large supplemental doses as universal prevention of childhood respiratory disease is substantially weaker than popular perception often suggests. Vitamin C is better understood as part of nutritional sufficiency architecture than as a stand-alone anti-infective intervention.

Iron exemplifies the complexity of nutritional immunity. Iron deficiency can impair immune function, yet iron is also required by many pathogens, and the body actively redistributes iron during infection. Selenium participates in antioxidant enzymes and immune regulation, but increasing selenium beyond adequacy does not imply progressively greater immune protection. Across micronutrients, adequacy is the target; excess is not an evidence-based synonym for optimisation.

6. Microbiome-directed and bioactive innovation platforms

6.1 Definitions matter: probiotic, prebiotic, synbiotic and postbiotic

The microbiome has created perhaps the most important conceptual expansion in paediatric immune nutrition. The contemporary field includes probiotics, prebiotics, synbiotics, postbiotics, human milk oligosaccharides, microbial metabolites, fermented preparations and emerging microbial consortia.

International Scientific Association for Probiotics and Prebiotics (ISAPP) consensus definitions are especially important because each concept includes an expectation of demonstrated host benefit. Probiotics are live microorganisms that, when administered in adequate amounts, confer a health benefit on the host (Hill et al., 2014). A prebiotic is a substrate selectively utilised by host microorganisms conferring a health benefit (Gibson et al., 2017). Synbiotics comprise live microorganisms and selectively utilised substrates producing a health benefit (Swanson et al., 2020). A postbiotic is a preparation of inanimate microorganisms and/or their components that confers a health benefit on the host (Salminen et al., 2021).

A material does not become an evidence-based probiotic, prebiotic or postbiotic solely because it satisfies a technological description. The health benefit itself remains part of the concept.

6.2 Probiotics: strain specificity is not optional

Perhaps the greatest error in commercial probiotic communication is treating 'probiotics' as though they were a pharmacologically homogeneous ingredient. Effects can depend upon genus, species, strain, strain combination, dose, survival through storage, food matrix, age, clinical phenotype and endpoint. Evidence supporting one strain cannot automatically be transferred to another.

A 2025 systematic review and meta-analysis of prebiotic, probiotic, synbiotic and postbiotic supplementation in follow-on formula included 23 randomized trials and 6,984 children aged approximately six months to three years. For respiratory infections, pooled estimates were OR 0.22 (95% CI 0.05-1.09) for probiotics, OR 0.84 (95% CI 0.66-1.07) for prebiotics and OR 0.75 (95% CI 0.54-1.05) for synbiotics. The numerical direction is interesting, but each confidence interval includes the null. The authors therefore concluded that prebiotic and synbiotic supplementation may offer benefit while high-quality evidence remains sparse (Delcourt et al., 2025).

This is exactly how emerging nutritional science should be interpreted: promising is not synonymous with proven.

6.3 Postbiotics: high technological potential, preparation-specific evidence

Postbiotics may become especially valuable in children's products because they can potentially overcome several technological limitations associated with live organisms. Potential advantages include improved thermal stability, lower dependence on viability, greater shelf-life consistency, easier incorporation into challenging matrices and compatibility with manufacturing processes that would damage live probiotics.

ISAPP nevertheless emphasises that the health benefit must be demonstrated in the target host and that postbiotic identity involves the microorganism, matrix and inactivation process - not merely the statement that organisms have been killed (Salminen et al., 2021).

A double-blind randomized trial involving 256 healthy children aged 4-12 years evaluated 500 mg/day of a yeast-derived postbiotic over 84 days. The intervention produced lower overall cold/flu symptom severity, lower severity of selected symptoms and reduced use of cold/flu medication. However, the incidence of cold/flu symptoms itself was not significantly different between groups (Singh et al., 2024). This distinction supports a potential effect on symptom burden; it does not demonstrate prevention of infection.

6.4 Human-identical milk oligosaccharides: selective biomimicry, not breast-milk equivalence

Human milk contains a remarkable diversity of oligosaccharides. HMOs can selectively influence microbial ecology, interact with epithelial tissues, act as soluble decoys for some pathogens and influence immune signalling. Industrial biotechnology now permits production of defined structures such as 2'-fucosyllactose, 3-fucosyllactose, lacto-N-tetraose, lacto-N-neotetraose, 3'-sialyllactose and 6'-sialyllactose.

A 2026 systematic review identified only 12 randomized parallel-group clinical trials of human-identical milk oligosaccharides: eight in healthy infants, three in specific infant populations and one in young children. HiMO-containing formulations consistently demonstrated acceptable growth and tolerability. Several trials reported microbiota, inflammatory or gastrointestinal markers moving toward patterns observed in human-milk-fed infants, but clinical morbidity outcomes were mixed and the studies were generally underpowered for severe outcomes (Shivakoti et al., 2026).

The implication is not that HiMOs lack value. They represent one of the most scientifically sophisticated innovation platforms in early-life nutrition. But reproducing selected molecular components of human milk does not reproduce human milk, which remains a dynamic biological matrix containing hundreds of oligosaccharides together with immunoglobulins, lactoferrin, enzymes, lipids, phospholipids, cytokines, microorganisms and cells. The scientifically correct concept is selective biomimicry, not breast-milk equivalence.

6.5 Lactoferrin: promising but outcome-specific

Lactoferrin is a multifunctional iron-binding glycoprotein with antimicrobial, iron-sequestering, anti-inflammatory, immunoregulatory and epithelial effects. A 2025 systematic review and meta-analysis of 25 randomized paediatric trials found fewer cases of neonatal late-onset sepsis (OR 0.60; 95% CI 0.42-0.86) and fewer diarrhoeal outcomes (OR 0.56; 95% CI 0.41-0.75). For upper respiratory infection, however, the estimate was not statistically significant (OR 0.61; 95% CI 0.27-1.40) (Mayorga et al., 2025).

A generic statement that lactoferrin 'strengthens immunity' is therefore less informative than the evidence supports. The more defensible interpretation is that specific lactoferrin interventions show encouraging evidence in selected paediatric infectious contexts, while evidence for prevention of common upper respiratory infection remains inconclusive.

6.6 Milk fat globule membrane: from isolated nutrients to biological matrices

Milk fat globule membrane (MFGM) represents another conceptual shift: rather than administering a single purified molecule, MFGM provides a complex fraction containing phospholipids, sphingolipids, gangliosides, glycolipids, glycoproteins and other bioactive molecules.

A systematic review and meta-analysis identified 24 publications from 17 studies. MFGM-containing formulas showed acceptable safety and growth. Potential benefits including lower acute otitis-media incidence and improved cognitive development were observed, but the evidence base was considered insufficient for firm confirmation (Ambrozej et al., 2021).

The field also raises an important food-technology issue: commercial MFGM ingredients are not necessarily compositionally equivalent. Source material, processing, purification, thermal treatment and drying can alter the final biological fraction. Clinical evidence must therefore attach to a sufficiently characterised ingredient.

6.7 Beta-glucans: promising, structurally heterogeneous and product-specific

'Beta-glucan' describes a structural family rather than a single compound. Biological activity can depend upon source organism, linkage pattern, branching, molecular weight, solubility, purity and processing. Cereal beta-glucans should therefore not automatically be treated as clinically interchangeable with yeast or fungal beta-glucans.

Earlier randomized studies using pleuran from Pleurotus ostreatus reported favourable respiratory outcomes in children with recurrent respiratory infections. A 2025 international multicentre double-blind randomized trial enrolled 249 children with recurrent respiratory infections. The intervention contained pleuran together with vitamin D and zinc, while the active placebo contained vitamin D and zinc. Children receiving the pleuran-containing product experienced fewer total respiratory infections (2.35 +/- 1.25 versus 2.77 +/- 1.78; $p = 0.042$), representing an approximately 15.2% reduction over three months; common-cold episodes were reduced by approximately 18.6% (Jesenak et al., 2025).

Because both groups received vitamin D and zinc, the design provides stronger evidence that the pleuran-containing intervention contributed additional activity. Even here, however, the finding is product- and population-specific and cannot establish equivalent efficacy for all beta-glucans.

6.8 Omega-3 fatty acids: inflammatory-resolution biology, not a simple anti-infective claim

EPA and DHA participate in membrane composition and inflammatory-resolution pathways. Omega-3-derived specialised pro-resolving mediators provide an especially interesting mechanistic link between nutrition and inflammatory regulation. Their strongest paediatric rationale, however, should not automatically be framed as infection prevention.

Research involving respiratory and allergic outcomes is heterogeneous and influenced by maternal versus direct supplementation, developmental timing, dose, baseline diet and endpoint selection. Omega-3 therefore fits well within the broader immune-resilience framework because resolution of inflammation may be as biologically important as initial immune activation.

7. Botanicals: strong consumer affinity, demanding standardisation

Botanicals align strongly with parental preferences for natural products. But 'natural' is not an analytical specification. Botanical research requires control of species, cultivar, plant part, harvest conditions, extraction solvent, drug-to-extract ratio, marker compounds, active constituents, contaminants, pesticides, heavy metals, adulteration and batch consistency. Without that information, apparently similar botanical products may be pharmacologically different.

A 2025 systematic review and meta-analysis of Echinacea included nine randomized trials involving approximately 3,169 children. Pooled analyses suggested favourable effects on some upper-respiratory outcomes and antibiotic use, but the authors identified substantial heterogeneity in botanical preparations, plant parts, dosage forms and manufacturing approaches; safety information also remained insufficiently definitive (Pham et al., 2025). 'Echinacea

works' is therefore not a scientifically adequate formulation of the evidence. The relevant question is which chemically characterised preparation, at what dose, in which children, against which endpoint.

Elderberry remains a useful counterexample. It has substantial commercial recognition, yet systematic evidence remains sparse and uncertain regarding prevention of respiratory illness. Possible reductions in symptom duration or severity warrant further research, but available studies do not justify treating elderberry as an established paediatric infection-prevention intervention (Wieland et al., 2021).

8. Evidence map for contemporary paediatric immune-health ingredient platforms

Platform	Biological rationale	Current paediatric clinical position / principal limitation	R&D assessment
Micronutrient adequacy	Very strong	Strong where deficiency exists; benefit beyond adequacy often limited.	FOUNDATIONAL
Vitamin A	Very strong	Strong in deficiency-endemic settings for selected outcomes; limited generalisability to replete populations.	CONTEXT-SPECIFIC
Vitamin D	Very strong	Mixed respiratory-infection evidence; 2026 high-dose network signal requires cautious interpretation.	FOUNDATIONAL / NOT UNIVERSAL ARI PROPHYLAXIS
Zinc	Very strong	Strong for selected deficiency-related conditions; excess exposure can be harmful.	FOUNDATIONAL / CONTEXT-DEPENDENT
Vitamin C	Strong	Essential nutrient; limited evidence for universal infection prevention in replete children.	FOUNDATIONAL NUTRIENT
Specific probiotics	Strong	Positive signals for selected strains and outcomes; class-wide extrapolation invalid.	PROMISING / PRODUCT-SPECIFIC
Prebiotics	Strong	Emerging signals; substrate and responder heterogeneity remain.	PROMISING
Synbiotics	Strong	Emerging favourable signals; combination-specific evidence required.	PROMISING
Postbiotics	Strong emerging	Specific positive RCTs; preparation-specific evidence.	HIGH INNOVATION POTENTIAL
HiMOs	Very strong mechanistic	Strong safety/tolerability; biomarker effects; mixed clinical morbidity outcomes.	HIGH INNOVATION / EVIDENCE DEVELOPING
Lactoferrin	Strong	Positive in selected neonatal/diarrhoeal settings; URI evidence inconclusive.	PROMISING / SELECTIVE
MFGM	Strong	Safety established; encouraging signals; limited confirmation.	PROMISING PLATFORM
Beta-glucans	Moderate-strong	Increasing RCT evidence for defined preparations; structural heterogeneity critical.	PROMISING / PRODUCT-SPECIFIC
Omega-3	Strong inflammatory biology	Heterogeneous respiratory evidence; timing and phenotype matter.	SUPPORTIVE / NOT PRIMARY ANTI-INFECTIVE
Echinacea	Plausible	Some pooled positive evidence; major extract heterogeneity.	POTENTIALLY USEFUL / PREPARATION-SPECIFIC
Elderberry	Plausible	Sparse and inconclusive clinical evidence relative to commercial popularity.	EVIDENCE GAP
Generic immune blends	Variable	Frequently untested as final formulations; literature borrowed from components.	WEAK UNLESS FINISHED PRODUCT TESTED

Interpretative note: this table is a qualitative critical synthesis for R&D prioritisation, not a formal GRADE assessment.

9. Ingredient innovation is increasingly formulation innovation

A recurrent misconception in supplement development is that evidence belongs only to ingredients. It also belongs to the finished formulation. A product containing vitamin D, zinc, a probiotic and elderberry does not automatically inherit the clinical effects reported independently for each component. Formulation can change dissolution, absorption, microbial viability, chemical stability, oxidation, taste, adherence and actual exposure. Interactions may be additive, synergistic, neutral or antagonistic. The final formulation therefore becomes a new experimental entity.

Future differentiation will increasingly depend not only upon what is formulated but how it is delivered. Paediatric products must simultaneously achieve acceptable sensory characteristics, accurate low-dose delivery, active stability, microbiological safety, appropriate water activity, acceptable sugar exposure, suitable texture, manufacturing robustness and child-safe presentation. These constraints often conflict.

9.1 The gummy paradox

Gummies improve acceptance and routine adherence because children recognise them as familiar confectionery-like formats. The same advantage creates a safety and nutritional paradox: products may be perceived as candy, active payload is constrained, minerals can generate bitter or metallic notes, moisture can undermine stability, and accidental overconsumption becomes more plausible. Gummy dominance should therefore not be confused with technological superiority.

Advantages	Risks / limitations
High acceptability and easy administration	Sugar exposure and dental implications
No swallowing difficulty	Limited active payload
Strong routine adherence	Mineral taste masking challenges
Familiar sensory format	Moisture sensitivity and chemical incompatibility
Consumer convenience	Candy-like perception and accidental overconsumption

9.2 Reduced-sugar design

Demand for low-sugar and sugar-free children's products is increasing, but replacing sucrose is not technologically trivial. Polyols can create gastrointestinal intolerance at excessive exposures; high-intensity sweeteners can generate sensory challenges; and reducing soluble solids can affect texture, water activity, microbial stability, gel formation and shelf life. 'Sugar-free' is therefore a formulation-development objective, not merely a label change.

9.3 Powders and liquids

Powders permit larger active payloads, flexible serving size, incorporation of prebiotic fibres and reduced dependence on confectionery-style matrices. Their challenges include oxidation, hygroscopicity, agglomeration, flavour deterioration, moisture migration and dosing variability. Individual sachets can improve stability and dose control.

Liquids are particularly useful in younger children but require careful management of microbiological stability, preservation, oxidation, sedimentation, emulsion stability, flavour masking, container compatibility and dose accuracy. Human-factors engineering matters: validated syringes or calibrated droppers generally provide better dosing precision than household spoons.

9.4 Probiotic viability, postbiotic robustness and microencapsulation

For live microorganisms, the relevant dose is not simply the count introduced during manufacturing. It is the viable dose delivered through the labelled shelf life. Oxygen, humidity, temperature, acidity, minerals and food-matrix interactions can substantially reduce viability. A scientifically meaningful probiotic specification should therefore include strain identity, viable count, end-of-shelf-life specification and storage conditions.

Microencapsulation may improve taste masking, protect oxidation-sensitive actives, increase probiotic survival, separate incompatible ingredients, alter intestinal release or improve bioavailability. But encapsulation changes the intervention itself. Bioavailability demonstrated for an unencapsulated material cannot automatically be assumed for a differently encapsulated commercial formulation. Validation must follow the final technology.

10. Safety: a competitive advantage, not an afterthought

Children have lower body mass, age-dependent physiological requirements, different metabolic capacities and narrower exposure margins for some nutrients. Product safety must therefore consider total exposure from habitual diet, fortified foods, other supplements and the proposed product. Product stacking can unintentionally create excessive exposure, particularly for vitamins A and D, zinc, iron, iodine and selenium.

The American Academy of Pediatrics states that most healthy children eating a balanced diet do not require supplemental vitamins above recommended intakes and warns that megadoses of certain vitamins can produce toxicity. This does not mean supplements have no role; it means the indication for supplementation should be rational and age-appropriate.

Safety domain	Key questions for paediatric product development
Chemical	Heavy metals, pesticides, residual solvents, process contaminants, oxidation products?
Microbiological	Pathogens, yeasts/moulds, stability, microbial identity, contamination controls?
Nutritional	Upper intake levels, age appropriateness, cumulative exposure, nutrient duplication?
Physical	Choking risk, dosage-form size, packaging, child-resistant storage?
Behavioural	Candy-like perception, accidental overconsumption, caregiver instructions?
Allergen	Milk, egg, soy, nuts or source-derived proteins adequately controlled and labelled?
Interaction	Relevant nutrient-drug or botanical-drug interactions considered?

11. Regulatory reality: Europe and the United States

11.1 Europe: "nutraceutical" is not a legal category

The European Commission has explicitly indicated that 'nutraceutical' is not defined as a specific legal category in EU legislation. Products described commercially as nutraceuticals must ultimately be classified under the relevant legal framework, for example as foods, food supplements or, depending upon their characteristics and presentation, medicinal products.

Food supplements are regulated principally under Directive 2002/46/EC together with general food-law requirements. The Directive defines food supplements as concentrated sources of nutrients or other substances with a nutritional or physiological effect, marketed in dose form. It also prohibits labelling, presentation and advertising from attributing properties of preventing, treating or curing human disease.

11.2 EU health claims and claims concerning children

Regulation (EC) No 1924/2006 establishes the EU framework for nutrition and health claims. Claims must not be false, ambiguous or misleading and must comply with the applicable authorisation and substantiation requirements. Several micronutrients have authorised claims concerning normal immune function. For example, zinc and vitamin C may, when the conditions of use are fulfilled, be described as contributing to the normal function of the immune system under Commission Regulation (EU) No 432/2012.

Such authorised wording does not mean that a product has demonstrated prevention of colds, influenza or other infections. 'Contributes to normal immune function' and 'prevents respiratory infection' are scientifically and legally different propositions.

Claims referring specifically to children's development or health fall under Article 14(1)(b) of Regulation 1924/2006 and are subject to the corresponding scientific assessment and authorisation pathway. Innovation involving children therefore carries a higher claims-substantiation burden than generic adult wellness communication.

11.3 Infant formula: an especially restrictive environment

Commission Delegated Regulation (EU) 2016/127 expressly prohibits nutrition and health claims on infant formula. This is crucial when discussing HMOs, MFGM, probiotics, lactoferrin or other infant-formula innovations. Compositional authorisation or lawful use of an ingredient is not equivalent to permission to communicate a health effect.

11.4 United States: structure/function claims do not permit disguised disease claims

The US framework differs substantially. Dietary supplements may carry certain structure/function claims where legal requirements and substantiation standards are satisfied. FDA describes such claims as statements concerning the role of a nutrient or dietary ingredient in affecting normal structure or function.

However, a structure/function claim cannot become a disguised disease claim. FDA guidance treats language suggesting that a supplement helps the body resist infection or has antiviral capabilities as disease-related. Thus, although the regulatory vocabulary differs between Europe and the United States, neither system supports scientifically unsubstantiated disease-prevention positioning for ordinary dietary supplements.

12. Clinical evidence: parents do not buy biomarkers

Paediatric immune trials frequently report secretory IgA, cytokines, natural-killer-cell activity, inflammatory proteins, microbial abundance, short-chain fatty acids or gene-expression changes. These outcomes are valuable for mechanistic research but are not intrinsically equivalent to better health.

Parents do not purchase an 18% increase in secretory IgA. They seek fewer illnesses, less severe illness, faster recovery, fewer antibiotics, fewer doctor visits and fewer missed school days. A mature clinical-development programme must therefore distinguish mechanistic endpoints, potential surrogate endpoints and clinically meaningful outcomes.

Endpoint tier	Examples	Interpretive value
Tier 1 - clinically strongest	Laboratory-/physician-confirmed infection; hospitalisation; antibiotic requirement; healthcare utilisation	Directly relevant to morbidity and resource use.
Tier 2 - clinically meaningful	Number of episodes; episode duration; symptomatic days; validated severity score; school/daycare absenteeism; medication use	Highly relevant to families and daily function.
Tier 3 - supportive	Microbiome composition; secretory IgA; cytokines; immune-cell populations; metabolites	Useful for mechanism; should not substitute for clinical benefit.

13. From ingredient stacking to systems formulation

Traditional supplement formulation frequently operates through additive storytelling: vitamin C supports immunity, vitamin D supports immunity, zinc supports immunity, elderberry is associated with colds and a probiotic affects the microbiome; therefore the combination is assumed to provide superior immune protection. The conclusion does not logically follow from the premises.

Clinical efficacy cannot generally be calculated by summing unrelated literature. The combination may generate additive effects, antagonism, redundant mechanisms, altered bioavailability, insufficient individual doses or no measurable clinical effect. The alternative is systems formulation: product development begins with the desired biological and clinical outcome rather than with a shopping list of ingredients.

Clinical objective -> mechanism -> ingredient identity -> dose -> formulation -> validation -> lawful claim.

For example, a product designed for healthy school-age children during high seasonal exposure could define its objective as reducing symptom burden and illness-related disruption while supporting nutritional adequacy. The biological architecture might then combine nutrient sufficiency, epithelial/mucosal support, microbiome modulation and inflammatory regulation. Only after that model is established should ingredients be selected, and the finished commercial formulation must subsequently be validated as the intervention.

Figure 2. Seven-Layer Evidence Architecture for Paediatric Immune Products

A translational pathway from biological plausibility to lawful consumer communication

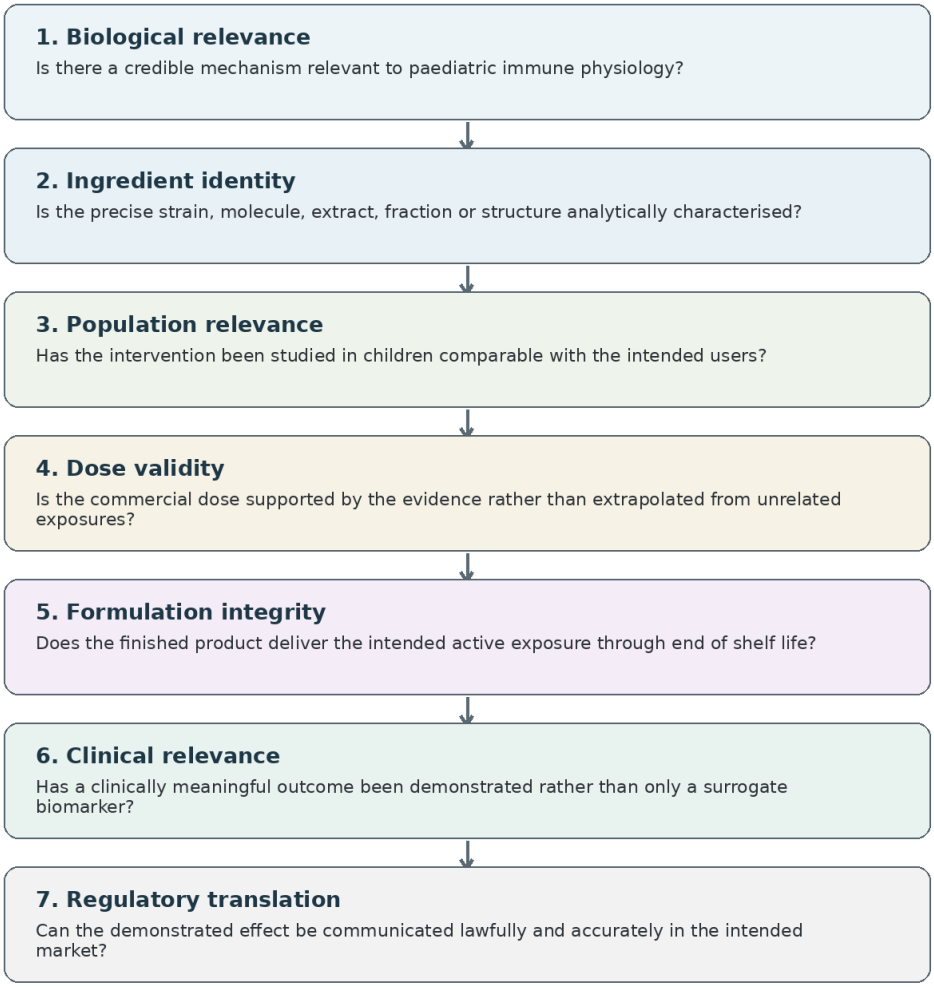

Figure 2. Seven-Layer Evidence Architecture for Paediatric Immune Products. Evidence must remain vertically coherent from biological rationale to lawful communication. Original conceptual framework developed for this review.

A product may fail despite containing a scientifically interesting ingredient. Strong mechanism plus poorly characterised ingredient remains weak evidence. A clinically studied ingredient used at one-tenth of the research dose remains weak evidence. A correct dose in an unstable formulation remains weak evidence. A biomarker effect without clinical benefit remains incomplete evidence. A positive clinical result attached to a prohibited consumer claim remains a regulatory-commercial failure.

Evidence must therefore be vertically coherent through all seven levels. This architecture provides a practical method for separating genuine innovation from science-washing.

14. Transparency, precision nutrition and responder biology

14.1 Consumer transparency as an R&D parameter

Parents increasingly want to understand why an ingredient is included, how much is present, what evidence supports it, whether it contains sugar and whether the formulation is safe and appropriate for children. Demand for transparency can improve science by encouraging manufacturers to specify strain, extract standardisation, ingredient form, active dose, source, allergen status and quality controls.

The movement from vague proprietary blends toward transparent quantitative formulas should therefore be viewed as a positive development. Consumer simplicity should be met with scientific simplicity, not scientific simplification: a concise proposition may sit on top of sophisticated R&D.

14.2 The next frontier: precision paediatric nutrition

Perhaps the most interesting future opportunity is not discovering one universally effective immune ingredient but identifying responders. Average effects in clinical trials may be diluted because children differ substantially in baseline nutritional status, microbiome composition, previous antibiotic exposure, diet, age, daycare attendance, allergic phenotype, previous infection history, vaccination status and genetics.

A prebiotic that depends upon particular microbial pathways may have little effect where the relevant organisms are absent. A micronutrient intervention may have much stronger effects in deficient than replete children. A probiotic may behave differently after antibiotic-mediated ecosystem disruption. These considerations naturally lead toward stratified nutrition.

14.3 Multi-omics should identify causal responders, not decorate trials

Future studies can integrate metagenomics, metabolomics, proteomics, transcriptomics, immunophenotyping and nutritional biomarkers. The objective should not be to create the largest possible dataset, but to identify baseline variables and biological pathways that predict clinically meaningful response.

At present, however, the enthusiasm surrounding personalised microbiome testing requires restraint. Current science does not justify routine prescription of paediatric immune supplements based solely upon consumer stool-microbiome profiles. Taxonomic composition alone may not reliably predict functional capacity, immune phenotype or treatment response. Precision nutrition is therefore a legitimate research frontier but remains a premature universal consumer claim.

15. Designing the next generation of paediatric immune-health trials

A credible clinical-development programme should predefine the population, intervention, comparator, primary endpoint, safety framework, modifiers and statistical success criteria before recruitment begins.

Design domain	Recommended minimum specification
Population	Age range narrow enough to reflect comparable developmental biology; healthy vs recurrent-infection phenotype; baseline nutritional status; relevant comorbidities.
Intervention	Exact ingredient identity; analytical specification; dose; formulation; administration schedule; shelf-life exposure.
Comparator	Placebo, usual diet or justified active comparator.
Primary endpoint	One prospectively defined clinically interpretable endpoint with appropriate power.
Secondary endpoints	Severity, duration, medication use, absenteeism, healthcare utilisation.
Mechanistic endpoints	Microbiome, IgA, cytokines, metabolomics, immunophenotype - supportive rather than substitutive.
Modifiers/confounders	Vaccination, antibiotics, seasonality, diet, sleep, environmental exposure, daycare/school attendance, nutritional status.
Safety	Prospective adverse-event capture, allergenicity, excessive exposure, relevant laboratory abnormalities and discontinuations.

15.1 Trial duration, recurrence phenotypes and replication

Many respiratory interventions are evaluated during a single season. This is understandable but creates limitations: one season may be unusually mild or severe, circulating pathogens vary, school exposure changes and vaccination patterns evolve. Robust programmes should consider multicentre recruitment, adequate seasonal coverage, predefined infection definitions, prospective symptom recording and replication where feasible.

Children described as experiencing recurrent respiratory infections are attractive trial populations because event rates are high, improving statistical power. But recurrent infection is not a single biological phenotype. Normal high-exposure childhood, daycare attendance, allergic disease, asthma, anatomical factors, nutritional deficiencies, sleep disturbance, tobacco exposure and, less commonly, immunodeficiency may all contribute. Trials should avoid treating recurrent infection as a homogeneous disease entity.

15.2 Safety monitoring and pre-registered failure criteria

Safety assessment should not consist merely of reporting that no serious adverse events occurred. Trials should prospectively assess gastrointestinal symptoms, allergic reactions, excessive nutrient exposure, laboratory abnormalities where relevant, interactions, adherence, accidental overdose and discontinuation. This is especially important for botanicals, novel microbial preparations, high-dose nutrients and multi-ingredient formulas.

Nutraceutical R&D also suffers from post hoc reinterpretation: a primary endpoint fails, a secondary biomarker moves and marketing subsequently focuses on the biomarker. Before a study begins, researchers should define the primary endpoint, expected effect size, minimum clinically important difference, statistical analysis and criteria for success. A failed trial can generate valuable mechanistic knowledge, but a failed primary endpoint should not be retroactively converted into a successful efficacy trial by selecting favourable secondary outcomes.

16. Strategic implications for manufacturers and product portfolios

The market is moving toward greater differentiation. Competitive advantage will increasingly shift from number of ingredients toward quality of evidence. A premium paediatric immune-health product should be able to answer six questions: why this ingredient, why this dose, why this age group, does it remain active through shelf life, what clinically meaningful outcome has been demonstrated, and what are we legally entitled to say about that evidence?

Manufacturers should stop asking 'What immune ingredients can we add?' and begin asking 'What paediatric immune-health outcome are we attempting to influence, and what formulation gives us the strongest biological and clinical probability of achieving it?' That shift transforms ingredient selection, formulation, dose, clinical design, claim strategy, safety assessment and commercial differentiation.

16.1 Four generations of paediatric immune products

Generation	Product logic	Typical evidence position
Generation 1 - Nutritional insurance	Multivitamin/mineral formulations aimed primarily at dietary adequacy.	Nutritional requirement framework; limited product-specific immune efficacy.
Generation 2 - Ingredient-led immune products	Vitamin C, vitamin D, zinc, elderberry, echinacea and similar combinations assembled from individual ingredient narratives.	Evidence often borrowed from components.
Generation 3 - Mechanistically integrated products	Formulations combining nutritional sufficiency, microbiome modulation, barrier support and/or inflammatory regulation around a coherent biological model.	Requires formulation-level validation.
Generation 4 - Evidence-defined precision products	Age- and phenotype-specific interventions supported by formulation-level trials and potentially responder biomarkers.	Highest scientific ambition; still emerging.

16.2 Strategic innovation territories

1. Nutritional sufficiency without megadosing - correct doses rather than maximum doses.
2. Microbiome-targeted interventions based on specific strains, substrates, synbiotics and postbiotics with defined evidence.
3. Human-milk-inspired bioactives such as HiMOs, MFGM and lactoferrin, while avoiding breast-milk-equivalence narratives.
4. Defined beta-glucan structures where product-specific paediatric evidence is available.
5. Low-sugar delivery without sacrificing stability, palatability or dosing accuracy.
6. Clinically validated combinations rather than literature-based ingredient stacking.
7. Age-specific formulation rather than identical architectures across toddlers, preschool children, school-age children and adolescents.
8. Transparent evidence communication that makes science understandable without distorting it.

17. Limitations of the current evidence base

- Small trials and limited statistical power for clinically important outcomes.
- Frequent industry sponsorship, which does not invalidate evidence but increases the importance of protocol transparency and independent replication.
- Heterogeneous age groups and baseline nutritional status.
- Non-equivalent probiotic strains, botanical extracts, MFGM fractions, beta-glucans and multi-ingredient products.
- Inconsistent definitions of respiratory infection, ranging from parent-reported symptoms to physician-confirmed disease.
- Short follow-up, often limited to a single season.
- Potential publication bias favouring positive nutritional trials.
- Overreliance on surrogate biomarkers without clinically meaningful benefit.
- Insufficient product-level replication and weak transferability from ingredient evidence to final commercial formulations.

These limitations do not imply failure of the field. They indicate that paediatric immune nutrition is progressing from a first generation of biological plausibility toward a second generation of clinical precision.

18. Research agenda for 2027-2035

1. Large multicentre paediatric trials with prospectively defined clinical endpoints.
2. Narrower and biologically rational age stratification.
3. Baseline nutritional phenotyping and deficiency-aware subgroup analysis.
4. Better standardisation of respiratory-infection definitions.
5. Product-specific rather than category-level validation.
6. Full analytical characterisation of botanicals and complex biological fractions.
7. End-of-shelf-life probiotic specifications and formulation stability data.
8. Integrated microbiome, metabolomic and immunophenotypic studies where mechanistically justified.
9. Responder versus non-responder analysis with prospectively defined hypotheses.
10. Longer-term paediatric safety data.
11. Replication independent of original commercial sponsors.
12. Clinical trials of final combination formulas rather than inference from component literature.
13. Low-sugar and child-appropriate delivery technology research.

14. Real-world adherence and human-factors studies.
15. Greater use of clinically meaningful effect sizes rather than statistical significance alone.
16. Transparent publication of negative and neutral trials.

Future research should seek not merely statistical significance, but clinically meaningful effect sizes.

19. Discussion

The children's immune-health supplement market presents an unusual contrast. The biological rationale for nutrition-immune interactions is exceptionally strong, yet the evidence supporting many commercial interventions remains fragmented. There is high-confidence evidence that nutritional deficiency compromises immunity; there is substantially less certainty that increasing nutrient intake beyond adequacy protects healthy children from common infections.

There is convincing evidence that microbiota participate in immune development; there is far less evidence that any arbitrary microbiome-modulating supplement creates clinically meaningful respiratory protection. There is sophisticated mechanistic evidence surrounding HiMOs and MFGM; clinical outcomes remain less established than mechanistic narratives sometimes imply. There are promising data for specific postbiotics, probiotics, lactoferrin preparations, beta-glucans and botanical extracts; product specificity prevents easy generalisation.

These findings are not contradictory. They reflect a field moving from biological plausibility to clinical precision. Nutritional adequacy remains the strongest foundation. Microbiome and bioactive platforms create genuine innovation opportunities. But clinical endpoints must become more important than mechanistic storytelling, and final formulations must increasingly become the unit of evidence.

The central scientific paradox is therefore clear: nutrition undeniably affects immunity, yet this does not demonstrate that every product sold for immune support works. The category contains both excellent biological science and considerable commercial over-extrapolation. The future of the field depends on separating the two.

20. Conclusions

Children's immune-health nutrition is moving into a substantially more sophisticated phase. The old model - vitamin C plus vitamin D plus zinc plus a botanical equals immune support - is being replaced by a systems model in which nutritional status, epithelial barriers, microbial ecosystems, innate defence, adaptive immunity, immune tolerance, inflammatory regulation and environmental exposure interact continuously.

Micronutrient adequacy remains foundational. Vitamin D demonstrates why biological plausibility does not guarantee universal infection prevention: contemporary meta-analyses remain mixed, and the favourable 2026 network-meta-analysis signal for higher-dose regimens should be treated as a research stimulus rather than a mandate for indiscriminate high-dose supplementation. Zinc is important but context-dependent. Vitamin C is an essential nutrient, not a universal respiratory shield.

Probiotics require strain-specific evidence. Prebiotics require substrate-specific and responder-aware interpretation. Synbiotics must be evaluated as combinations. Postbiotics represent one of the most attractive technological frontiers but require validation of the exact preparation. HiMOs constitute a sophisticated biomimetic platform but should not be confused with replication of human milk. Lactoferrin demonstrates promising but outcome-specific evidence. MFGM exemplifies the movement toward complex biological matrices. Beta-glucans are increasingly interesting where structurally characterised preparations have been subjected to paediatric randomized trials. Botanicals such as echinacea and elderberry demonstrate why standardisation and clinical specificity are indispensable.

The strategic conclusion is therefore straightforward: the next generation of paediatric immune-health nutraceuticals should not be assembled around ingredients. They should be engineered around evidence. The relevant objective is not indiscriminate immune stimulation but nutrition-enabled paediatric immune resilience - maintaining adequate nutritional substrate, preserving epithelial and microbial homeostasis, enabling proportionate defence against

biological challenge, maintaining tolerance, controlling inflammation and facilitating efficient recovery during normal immune maturation.

That construct is biologically more defensible than 'immune boosting', clinically more testable, better aligned with modern developmental immunology and ultimately a stronger foundation for genuine innovation in paediatric nutrition.

Key take-home principles

1. Children are not small adults; immune ontogeny and developmental stage matter.
2. Deficiency correction and supra-adequate supplementation are biologically different interventions.
3. Normal immune function should not be confused with prevention of infection.
4. Mechanistic plausibility is not clinical efficacy.
5. Biomarker modulation is not necessarily clinical benefit.
6. Probiotic evidence is strain-specific.
7. Postbiotic evidence is preparation-specific.
8. HiMO effects are structure- and combination-dependent.
9. Botanical evidence is extract-specific.
10. Beta-glucans are structurally heterogeneous and should not be treated as interchangeable.
11. Ingredient evidence cannot simply be added together to validate a multi-ingredient formula.
12. The commercial formulation itself must ultimately become the clinical intervention.
13. Paediatric safety requires total-exposure assessment rather than evaluation of each product in isolation.
14. Consumer convenience must be balanced against sugar exposure, stability and dosing accuracy.
15. Future competitive advantage will come from evidence quality rather than ingredient count.

References

Ambrożej, D., Dumycz, K., Dziechciarz, P., & Ruszczyński, M. (2021). Milk fat globule membrane supplementation in children: Systematic review with meta-analysis. Nutrients, 13(3), 714. https://doi.org/10.3390/nu13030714

American Academy of Pediatrics. (2026). Nutritional supplements, vitamins and boosting your child's immunity. HealthyChildren.org. https://www.healthychildren.org/English/healthy-living/nutrition/Pages/Do-Kids-Really-Need-Vitamins-or-Supplements-to-Stay-Healthy-and-Boost-Immunity.aspx

Delcourt, H., Verbrugghe, L., Vandenplas, Y., & Huysentruyt, K. (2025). Systematic review and meta-analysis of randomized controlled trials on pre-, pro-, post- and synbiotic supplementation in follow-on formula. Clinical Nutrition, 51, 101-114. https://doi.org/10.1016/j.clnu.2025.05.022

Donald, K., & Finlay, B. B. (2023). Early-life interactions between the microbiota and immune system: Impact on immune system development and atopic disease. Nature Reviews Immunology, 23, 735-748.

European Commission. (2011). Answer to Parliamentary Question E-000065/2011 concerning the regulatory status of nutraceuticals. European Parliament. https://www.europarl.europa.eu/doceo/document/E-7-2011-000065-ASW_EN.html

European Commission. (2012). Commission Regulation (EU) No 432/2012 establishing a list of permitted health claims made on foods. EUR-Lex. https://eur-lex.europa.eu/eli/reg/2012/432/oj/eng

European Commission. (2016). Commission Delegated Regulation (EU) 2016/127 concerning infant formula and follow-on formula. EUR-Lex. https://eur-lex.europa.eu/eli/reg/2016/127/oj/eng

European Food Safety Authority. (2026). Health claims on disease risk reduction and children's development or health under Article 14. https://www.efsa.europa.eu/en/topics/health-claims-art-14

European Parliament and Council. (2002). Directive 2002/46/EC on the approximation of the laws of the Member States relating to food supplements (consolidated version). EUR-Lex. https://eur-lex.europa.eu/eli/dir/2002/46/2024-02-06/eng

European Parliament and Council. (2006). Regulation (EC) No 1924/2006 on nutrition and health claims made on foods. EUR-Lex. https://eur-lex.europa.eu/eli/reg/2006/1924/oj/eng

Food and Drug Administration. (n.d.). Small entity compliance guide: Structure/function claims. U.S. Department of Health and Human Services. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/small-entity-compliance-guide-structurefunction-claims

Food and Drug Administration. (n.d.). Structure/function claims. U.S. Department of Health and Human Services. https://www.fda.gov/food/nutrition-food-labeling-and-critical-foods/structurefunction-claims

Gibson, G. R., Hutkins, R., Sanders, M. E., Prescott, S. L., Reimer, R. A., Salminen, S. J., Scott, K., Stanton, C., Swanson, K. S., Cani, P. D., Verbeke, K., & Reid, G. (2017). The International Scientific Association for Probiotics and Prebiotics consensus statement on the definition and scope of prebiotics. Nature Reviews Gastroenterology & Hepatology, 14, 491-502. https://doi.org/10.1038/nrgastro.2017.75

Hill, C., Guarner, F., Reid, G., Gibson, G. R., Merenstein, D. J., Pot, B., Morelli, L., Berni Canani, R., Flint, H. J., Salminen, S., Calder, P. C., & Sanders, M. E. (2014). The International Scientific Association for Probiotics and Prebiotics consensus statement on the scope and appropriate use of the term probiotic. Nature Reviews Gastroenterology & Hepatology, 11, 506-514. https://doi.org/10.1038/nrgastro.2014.66

Iliev, I. D., Blander, J. M., Collins, N., Guo, C.-J., Longman, R. S., Sonnenberg, G. F., Zeng, M. Y., & Artis, D. (2025). Microbiota-mediated mechanisms of mucosal immunity across the lifespan. Nature Immunology, 26, 1645-1659. https://doi.org/10.1038/s41590-025-02281-w

Innova Market Insights. (2026). Functional gummies trends: Global market overview. https://www.innovamarketinsights.com/trends/functional-gummies-trends-global-market-overview/

Jesenak, M., Prokopova, E., Bozensky, J., Bonaci-Nikolic, B., Milosevic, K., Stankovic, K., Ostojic, O., Zivkovic, Z., Diamant, Z., Kunc, P., Janeczek, K., & Majtan, J. (2025). Novel chewable pleuran-based supplement decreases respiratory tract infections in children: A randomised controlled trial. Advances in Therapy, 42, 6132-6149. https://doi.org/10.1007/s12325-025-03393-3

Jolliffe, D. A., Camargo, C. A., Jr., Sluyter, J. D., Aglipay, M., Aloia, J. F., Bergman, P., Bischoff-Ferrari, H. A., Borzutzky, A., Bubes, V. Y., Damsgaard, C. T., Ducharme, F. M., Dubnov-Raz, G., Esposito, S., Ganmaa, D., Gilham, C., Ginde, A. A., Golan-Tripto, I., Goodall, E. C., Grant, C. C., ... Martineau, A. R. (2025). Vitamin D supplementation to prevent acute respiratory infections: Systematic review and meta-analysis of stratified aggregate data. The Lancet Diabetes & Endocrinology, 13(4), 307-320. https://doi.org/10.1016/S2213-8587(24)00348-6

Marco, M. L., Cunningham, M., Bischoff, S. C., Clarke, G., Delzenne, N., Lewis, J. D., Meisel, M., Merenstein, D., O'Toole, P. W., Staudacher, H. M., Szajewska, H., Wells, J. M., & Quigley, E. M. M. (2026). The International Scientific Association for Probiotics and Prebiotics consensus statement on the definition and scope of gut health. Nature Reviews Gastroenterology & Hepatology, 23(5), 432-448. https://doi.org/10.1038/s41575-026-01176-x

Mayorga, V. S., Navarro, R., Torres Roldan, V. D., Urtecho, M., Tipe, S., Calvert, B., Wright, L. A., & Ochoa, T. J. (2025). Efficacy of lactoferrin supplementation in pediatric infections: A systematic review and meta-analysis. Biochemistry and Cell Biology, 103, 1-23. https://doi.org/10.1139/bcb-2024-0181

National Institutes of Health, Office of Dietary Supplements. (2026). Dietary supplements for immune function and infectious diseases: Health professional fact sheet. https://ods.od.nih.gov/factsheets/ImmuneFunction-HealthProfessional/

NutraIngredients. (2026, April 16). Global research: What parents want and where brands miss the mark. https://www.nutraingredients.com/Article/2026/04/16/global-research-what-parents-want-and-where-brands-miss-the-mark/

NutraIngredients. (2026, August 19). Targeted health support drives new era of children's supplements. https://www.nutraingredients.com/Article/2026/08/19/targeted-health-support-drives-new-era-of-childrens-supplements/

Palma, P., Farber, D. L., Konnikova, L., & Levy, O. (2026). Immune development in early life. Nature Immunology, 27, 1119-1129. https://doi.org/10.1038/s41590-026-02523-5

Palmer, A. C., Bedsaul-Fryer, J. R., & Stephensen, C. B. (2024). Interactions of nutrition and infection: The role of micronutrient deficiencies in the immune response to pathogens and implications for child health. Annual Review of Nutrition, 44, 99-124. https://doi.org/10.1146/annurev-nutr-062122-014910

Pham, T.-P.-T., Vu, T.-M.-H., Doan, P.-M.-K., Nguyen, T.-T.-D., Bui, T.-T.-T., Ha, T.-H.-L., Hoang, T.-K.-Q., Taufani, I. P., & Ha, H.-A. (2025). Efficacy and safety of Echinacea purpurea in treating upper respiratory infections and complications of otitis media in children: Systematic review and meta-analysis. Clinical Nutrition ESPEN, 67, 702-713. https://doi.org/10.1016/j.clnesp.2025.04.025

Salminen, S., Collado, M. C., Endo, A., Hill, C., Lebeer, S., Quigley, E. M. M., Sanders, M. E., Shamir, R., Swann, J. R., Szajewska, H., & Vinderola, G. (2021). The International Scientific Association of Probiotics and Prebiotics consensus statement on the definition and scope of postbiotics. Nature Reviews Gastroenterology & Hepatology, 18, 649-667. https://doi.org/10.1038/s41575-021-00440-6

Shivakoti, R., Laughton, B., Mandell, J., Barrios-Tascon, A., Rajendran, R., Glashoff, R., Bode, L., Aldrovandi, G., & Kuhn, L. (2026). Limited evidence of benefits from clinical trials of human-identical milk oligosaccharides for infants. Advances in Nutrition, 17(3), 100593. https://doi.org/10.1016/j.advnut.2026.100593

Singh, R. G., Garcia-Campayo, V., Green, J. B., Paton, N., Saunders, J. D., Al-Wahsh, H., Crowley, D. C., Lewis, E. D., Evans, M., & Moulin, M. (2024). Efficacy of a yeast postbiotic on cold/flu symptoms in healthy children: A randomized-controlled trial. Pediatric Research, 96(7), 1739-1748. https://doi.org/10.1038/s41390-024-03331-z

Swanson, K. S., Gibson, G. R., Hutkins, R., Reimer, R. A., Reid, G., Verbeke, K., Scott, K. P., Holscher, H. D., Azad, M. B., Delzenne, N. M., & Sanders, M. E. (2020). The International Scientific Association for Probiotics and Prebiotics consensus statement on the definition and scope of synbiotics. Nature Reviews Gastroenterology & Hepatology, 17, 687-701. https://doi.org/10.1038/s41575-020-0344-2

Wang, L., Yu, Y., Liu, K., Yu, X., & Li, Y. (2025). The role of vitamin D in the prevention and treatment of acute respiratory infections in pediatric populations: A systematic review and meta-analysis of randomized controlled trials. BMC Pediatrics, 25, 985. https://doi.org/10.1186/s12887-025-06361-6

Wieland, L. S., Piechotta, V., Feinberg, T., Ludeman, E., Hutton, B., Kanji, S., Seely, D., & Garritty, C. (2021). Elderberry for prevention and treatment of viral respiratory illnesses: A systematic review. BMC Complementary Medicine and Therapies, 21, 112. https://doi.org/10.1186/s12906-021-03283-5

World Health Organization. (n.d.). Vitamin A supplementation for preventing morbidity and mortality in children from six months to five years of age. https://www.who.int/tools/elena/review-summaries/vitamina-children--vitamin-a-supplementation-for-preventing-morbidity-and-mortality-in-children-from-six-months-to-five-years-of-age

Xing, Y., Huang, D., Niu, L., & Liu, Y. (2026). Comparative efficacy of nutritional supplements for the prevention of respiratory tract infections in children: A systematic review and network meta-analysis. BMC Infectious Diseases, 26, 1293. https://doi.org/10.1186/s12879-026-13567-1

Editorial note. This article is a structured critical review and conceptual synthesis. The evidence maps and two framework figures are interpretative R&D tools and should not be represented as formal GRADE assessments or clinical guidelines.