

The gut microbiome and childhood growth: implications for microbiota-directed interventions

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Healthy childhood growth depends on complex interactions between nutrition, metabolism, immune function and the intestinal environment during the first 1 000 days of life. Increasing evidence indicates that the gut microbiome is an active contributor to these processes, providing a biological link between early-life nutrition and growth. While undernutrition has traditionally been attributed to inadequate dietary intake and recurrent infections, disruption of normal gut microbiome development is now recognised as an important factor contributing to growth faltering. Dysbiosis may impair nutrient utilisation, compromise intestinal barrier function, alter immune and endocrine signalling, and contribute to environmental enteric dysfunction (EED), thereby limiting the effectiveness of conventional nutritional rehabilitation.

This review synthesises current evidence on the role of the gut microbiome in childhood growth, with particular emphasis on microbiota-directed nutritional interventions during the first 1 000 days of life. The review describes the normal development and metabolic functions of the infant gut microbiome, examines the mechanisms through which dysbiosis contributes to impaired growth, and evaluates established and emerging nutritional strategies that influence the developing microbiome. Breastfeeding and appropriate complementary feeding remain the cornerstone of healthy infant nutrition and are increasingly recognised as the first microbiota-directed nutritional intervention. More recently, microbiota-directed complementary foods have shown promising effects on microbial maturation, restoration of microbial metabolic function and improvements in child growth. By contrast, although prebiotics, probiotics and synbiotics can beneficially modify the gut microbiome, current evidence supporting consistent improvements in childhood growth remains limited. Advances in microbiome research provide a stronger biological basis for established infant and young child feeding recommendations while identifying new opportunities to optimise nutritional rehabilitation. Although microbiota-directed complementary foods represent a promising development, further evidence from well-designed clinical trials conducted in diverse populations is required before these interventions can be incorporated into routine clinical practice. For dietitians and other clinicians, microbiome science provides a biological framework that strengthens and refines evidence-based nutritional strategies to support healthy childhood growth.

Keywords: gut microbiome, childhood growth, microbiota-directed complementary foods, breastfeeding, complementary feeding, undernutrition

Introduction

Childhood growth is a fundamental indicator of health, nutritional status and overall well-being. Despite substantial advances in maternal and child nutrition, growth faltering remains a major global public health challenge, particularly in low- and middle-income countries (LMICs).¹ Although the prevalence of childhood stunting has declined over recent decades, millions of children continue to experience impaired linear growth, while wasting remains an important contributor to childhood morbidity and mortality.¹ Growth faltering often begins during foetal life or early infancy, highlighting the first 1 000 days as a critical window during which nutrition and environmental exposures have profound effects on growth, development and long-term health.¹

The determinants of childhood growth extend beyond the provision of adequate nutrients. Linear growth reflects the interaction of nutritional, metabolic, endocrine, immunological and environmental factors, many of which are influenced by poverty, food insecurity, recurrent infections, poor water, sanitation and hygiene, environmental enteric dysfunction (EED) and chronic inflammation.^{1,2} Although established nutrition interventions have substantially improved child survival and nutritional outcomes, their effects on linear growth have

generally been more modest and less consistent than expected, suggesting that adequate nutrient intake alone may not fully explain healthy growth.² This has prompted increasing interest in the mechanisms through which nutrition influences growth, including the role of the gut microbiome.

The term gut microbiota refers to the microorganisms inhabiting the gastrointestinal tract, whereas the gut microbiome encompasses these microorganisms together with their collective genomes and functional activities (Table 1). One of the most important advances in paediatric nutrition research has been the recognition that the gut microbiome is an active contributor to childhood growth rather than simply a consequence of nutritional status. During early life, the gut microbiome undergoes rapid development in response to delivery mode, breastfeeding, complementary feeding, antibiotic exposure and environmental influences.^{3,4} As the microbiome develops, it acquires metabolic functions that support nutrient utilisation, intestinal development, immune regulation and metabolic homeostasis. Conversely, disruption of normal microbial development has been associated with growth faltering, undernutrition and EED.^{5,6} Increasing evidence further suggests that microbial metabolic activity may be more important than microbial composition alone, shifting attention from individual

Table 1: Glossary of key terms

Term	Definition
Gut microbiota	The community of microorganisms, including bacteria, viruses, fungi and archaea, that inhabit the gastrointestinal tract ^{2–4}
Gut microbiome	The collective microorganisms, their genomes and their functional activities within the gastrointestinal tract ^{2–4}
Dysbiosis	A disruption in the composition and/or function of the gut microbiome that may impair normal host physiological processes and contribute to disease ²
Microbiome maturity	The degree to which the gut microbiome has developed the composition and functional characteristics expected for a child's age. Delayed microbial maturation (microbiome immaturity) has been associated with childhood growth faltering ^{5,7}
Short-chain fatty acids (SCFAs)	Microbial metabolites, mainly acetate, propionate and butyrate, produced through fermentation of dietary substrates. SCFAs support intestinal barrier function, immune regulation and host metabolism ¹³
Environmental enteric dysfunction (EED)	A chronic subclinical disorder of the small intestine characterised by impaired intestinal barrier function, inflammation and reduced nutrient absorption, commonly associated with poor sanitation and repeated enteric infections ^{1,2}
Human milk oligosaccharides (HMOs)	Complex carbohydrates found in human milk that are indigestible by the infant but selectively promote the growth of beneficial gut microorganisms, particularly <i>Bifidobacterium</i> species ^{11,12}
Microbiota-directed complementary foods (MDCFs)	Complementary foods formulated to restore gut microbiome development and microbial metabolic function while providing adequate nutrition for children with undernutrition ^{7–9}
Prebiotics	Non-digestible substrates that are selectively utilised by beneficial gut microorganisms, conferring a health benefit on the host ²²
Probiotics	Live microorganisms that, when administered in adequate amounts, confer a health benefit on the host ²³
Synbiotics	Combinations of probiotics and prebiotics designed to enhance the survival, colonisation and activity of beneficial microorganisms ²²

bacterial taxa towards the functional capacity of the developing gut microbiome.

These advances have also changed how early-life nutritional interventions are viewed. Breastfeeding is increasingly recognised as the first microbiota-directed nutritional strategy, while complementary feeding represents the next major opportunity to influence microbial development through diet. More recently, microbiota-directed complementary foods have emerged as a promising approach to restore microbial development alongside nutritional rehabilitation, with early clinical trials demonstrating improvements in microbial maturity, host metabolic pathways and child growth.^{7–9}

This narrative review was informed by a targeted search of the published literature using PubMed, supplemented by relevant reference lists. Priority was given to recent systematic reviews, clinical trials and landmark studies on gut microbiome development, childhood growth and microbiota-directed nutritional interventions, together with current international infant and young child feeding guidelines. It synthesises current evidence linking the gut microbiome with childhood growth, with particular emphasis on microbiota-directed nutritional interventions during the first 1 000 days of life. It begins by describing the normal development of the infant gut microbiome and its relationship with childhood growth before examining how dysbiosis contributes to growth faltering. Established and emerging microbiota-directed nutritional interventions, including breastfeeding, complementary feeding, microbiota-directed complementary foods, prebiotics, probiotics and synbiotics, are then critically evaluated. Finally, the implications of these advances for clinical practice and future research are discussed.

Early-life development of the gut microbiome

Nutritional regulation of gut microbiome development during early life

The first 1 000 days of life represent a critical period for the establishment and development of the gut microbiome. During this time, the intestinal microbial community develops from a relatively simple ecosystem into a diverse and metabolically active community that supports nutrient utilisation, immune development and healthy growth.^{2,5} Although microbial colonisation begins at or immediately after birth, its subsequent development is influenced by maternal, environmental and nutritional factors. Initial colonisation is affected by gestational age, mode of delivery, maternal health and antibiotic exposure, after which nutrition becomes the principal modifiable determinant of gut microbiome development.^{5,10}

Following birth, early colonising bacteria consume oxygen within the intestinal lumen, creating an anaerobic environment that allows obligate anaerobes, including *Bifidobacterium* and *Bacteroides*, to become established.² This orderly succession supports continued microbial development during infancy. Although factors such as prematurity, Caesarean delivery and antibiotic exposure influence the initial composition of the gut microbiome, nutrition is the major driver of its subsequent development.^{5,10}

Breastfeeding provides the first major nutritional stimulus for gut microbiome development by supplying nutrients and bioactive components that favour microbial communities adapted to the infant gut.^{11,12} Breastfeeding therefore supports not only infant nutrition but also immune and metabolic development through its effects on the gut microbiome. The mechanisms underlying these effects, together with the evidence supporting breastfeeding as a microbiota-directed nutritional strategy, are discussed under Nutritional interventions.

The introduction of complementary foods marks the next major stage of gut microbiome development. As the infant diet becomes more diverse, the gut microbiome adapts to utilise increasingly complex carbohydrates and other dietary substrates, resulting in greater microbial diversity and metabolic capacity.^{2,10} Appropriate complementary feeding therefore supports growth in two ways: by providing the nutrients required for rapid growth and by promoting continued development of the gut microbiome. The evidence supporting

complementary feeding as a microbiota-directed nutritional strategy is reviewed under Interventions.

Although gut microbiome development follows a broadly predictable pattern, it remains susceptible to disruption during early life. Prematurity, recurrent infections, repeated antibiotic exposure and poor dietary quality may delay microbial development, reduce microbial diversity and change microbial metabolic activity during this critical period.^{2,5,10} These disturbances may have lasting consequences for intestinal function, immune development and childhood growth.

Functional development of the gut microbiome and implications for childhood growth

As the gut microbiome develops, it acquires metabolic functions that support infant growth and development. These include fermentation of dietary substrates, production of bioactive metabolites and interactions with host immune, endocrine and metabolic pathways.^{2,5} Functional development therefore provides the biological link between nutrition, the gut microbiome and childhood growth.

One of the most important metabolic functions of the developing gut microbiome is the production of short-chain fatty acids (SCFAs), primarily acetate, propionate and butyrate, through fermentation of human milk oligosaccharides (HMOs) during breastfeeding and dietary fibre after the introduction of complementary foods.^{2,11,12} These metabolites maintain intestinal barrier integrity, support epithelial cell turnover, regulate immune responses and enhance nutrient absorption, thereby creating an intestinal environment that supports healthy growth.^{2,5} The gut microbiome also contributes to amino acid metabolism, synthesis of selected B vitamins and vitamin K, and modification of bile acids involved in lipid digestion and energy homeostasis.⁵

Recent evidence indicates that microbial metabolic activity may be more closely associated with childhood growth than microbial composition alone. In a longitudinal birth cohort from rural Zimbabwe, functional metagenomic pathways involved in B-vitamin biosynthesis, nucleotide metabolism and amino acid metabolism predicted attained length and growth velocity more accurately than taxonomic composition.⁵ These findings suggest that healthy growth depends less on the presence of individual bacterial taxa than on the metabolic capacity of the developing gut microbiome.

The gut microbiome also interacts with host endocrine and immune pathways. Microbial metabolites influence immune maturation, energy metabolism and growth hormone-insulin-like growth factor-1 (GH-IGF-1) signalling, providing possible biological mechanisms through which the gut microbiome may influence linear growth.^{2,5} As microbial diversity and functional redundancy increase, the gut microbiome also becomes more resilient to short-term dietary and environmental disturbances, helping to maintain essential metabolic functions during early childhood.⁴

Healthy gut microbiome development provides an important biological foundation for childhood growth. An understanding of normal gut microbiome development provides the basis for interpreting how dysbiosis contributes to growth faltering, which is the focus of the following section.

Gut microbiome dysbiosis and childhood growth faltering

Healthy childhood growth depends on the coordinated development of a functionally competent gut microbiome. Although inadequate dietary intake, recurrent infections, poor sanitation and adverse socioeconomic conditions remain the primary determinants of undernutrition, they do not fully explain why some children continue to experience growth faltering despite nutritional rehabilitation.¹ Increasing evidence indicates that impaired growth should be viewed as a disorder of the host-microbiome ecosystem, in which disruption of normal gut microbiome development compromises the metabolic, immunological and physiological processes required to support healthy growth.^{2,5}

A consistent finding across studies is that children with growth faltering often exhibit microbiome immaturity, with delayed gut microbiome development relative to their chronological age.^{5,7} Rather than acquiring the microbial functions expected during infancy and early childhood, these children retain microbial communities that are developmentally immature and metabolically less efficient. A recent systematic review further showed that, although the specific bacterial taxa associated with stunting differ between populations, children with impaired growth consistently have altered gut microbial communities compared with healthy controls.⁶ These findings suggest that disruption of normal microbial development, rather than changes in individual bacterial taxa, is a common feature of childhood growth faltering.

Dysbiosis should not be viewed solely as a consequence of undernutrition. Poor dietary quality, recurrent infections, EED, antibiotic exposure and limited dietary diversity can all disrupt normal gut microbiome development. In turn, an immature or dysfunctional gut microbiome reduces the host's ability to digest and utilise nutrients efficiently, recover from infection and support normal growth.^{2,5,10} This bidirectional relationship helps explain why improving dietary intake alone does not always result in complete catch-up growth.

Repeated or prolonged antibiotic exposure during early life may disrupt gut microbiome development by reducing microbial diversity, delaying microbial maturation and depleting beneficial commensal bacteria, particularly during critical periods of immune and metabolic development. Although antibiotics remain essential for treating bacterial infections, unnecessary exposure should be avoided where possible. During and following antibiotic therapy, continued breastfeeding where appropriate, together with the provision of a diverse, nutrient-rich complementary diet containing microbiota-accessible substrates, may help support recovery of the gut microbiome, although further evidence is needed to define optimal dietary strategies.^{3,4,10,11}

Several biological mechanisms have been proposed to explain how dysbiosis contributes to growth faltering. As mentioned, a healthy gut microbiome produces metabolites that support intestinal integrity, immune regulation and nutrient utilisation. Dysbiosis disrupts these metabolic activities, reducing the production of SCFAs, particularly butyrate, together with other metabolites involved in amino acid metabolism, bile acid transformation and energy homeostasis.^{2,5} Because butyrate is the primary energy source for colonocytes, reduced production compromises epithelial renewal, weakens tight junction integrity and impairs mucus production, increasing intestinal permeability and reducing nutrient absorption.¹³

These changes contribute to the development of EED, a chronic subclinical condition characterised by villous blunting, crypt hyperplasia, impaired epithelial barrier function and persistent intestinal inflammation.² EED is common among children living in environments with poor sanitation and repeated exposure to enteric pathogens and has been consistently associated with impaired linear growth.¹ Current evidence suggests that gut microbiome dysbiosis contributes to the inflammatory processes underlying EED, further reducing nutrient absorption while increasing metabolic demands during a period of rapid growth.^{2,5}

Loss of intestinal barrier integrity also allows microbial products to cross the intestinal epithelium, resulting in chronic low-grade immune activation. Sustained inflammation diverts energy and nutrients away from growth and towards maintenance of the immune response. Inflammatory mediators also reduce tissue responsiveness to growth hormone and suppress insulin-like growth factor-1 (IGF-1), limiting chondrocyte proliferation at the growth plate and contributing to impaired linear growth.^{2,14} In addition, microbial metabolites influence endocrine pathways involved in appetite regulation, glucose metabolism and energy homeostasis, further supporting the role of the gut microbiome as an active regulator of host physiology.⁵

As discussed in the previous section, evidence from longitudinal birth cohort studies suggests that microbial metabolic activity is more closely associated with childhood growth than microbial composition alone.⁵ This observation supports the concept that dysbiosis impairs growth primarily through disruption of microbial function rather than changes in individual bacterial taxa. Similarly, a randomised trial in Zambia found that small-quantity lipid-based nutrient supplements improved child growth but produced only modest changes in gut microbial composition and biomarkers of EED.¹⁵ These findings suggest that nutritional interventions should aim to restore microbial function as well as address nutrient deficiencies.

These processes reinforce one another, creating a cycle in which poor diet and recurrent infections disrupt gut microbiome development, while dysbiosis further impairs nutrient utilisation, intestinal function and immune homeostasis. This cycle is particularly relevant in LMICs, where undernutrition frequently coexists with food insecurity, poor dietary diversity, recurrent enteric infections and EED.^{6,10}

These observations have important implications for nutritional practice. Established interventions, including breastfeeding, appropriate complementary feeding and the prevention and treatment of undernutrition, remain the foundation of child nutrition programmes. However, current evidence suggests that successful nutritional rehabilitation depends not only on correcting nutrient deficiencies but also on restoring the microbial functions that support nutrient utilisation, intestinal integrity and healthy growth. The following section examines microbiota-directed nutritional interventions that aim to achieve these complementary goals.

Microbiota-directed nutritional interventions

The microbiota-directed nutritional interventions discussed in this review are summarised in Table 2.

Breastfeeding

Breastfeeding is widely recognised as the biological norm for infant feeding and remains one of the most effective strategies

for promoting child survival, healthy growth and development.¹⁶ The World Health Organization (WHO) recommends initiation of breastfeeding within the first hour after birth, exclusive breastfeeding for the first six months of life and continued breastfeeding alongside appropriate complementary feeding until two years of age or beyond.^{16,17} These recommendations are supported by extensive evidence demonstrating that breastfeeding reduces infant morbidity and mortality, promotes optimal growth and neurodevelopment, and protects against infectious and chronic diseases throughout the life course.¹⁸

Advances in microbiome research have provided additional biological insight into these well-established benefits. Human milk is a complex biological fluid that not only provides the nutrients required for rapid infant growth but also contains bioactive components that shape the establishment and development of the infant gut microbiome.^{11,12} Breastfeeding is therefore increasingly recognised as the first microbiota-directed nutritional strategy, supporting microbial development during one of the most critical periods of physiological growth.

Among these bioactive components, HMOs are the best characterised. Although indigestible by the infant, HMOs selectively promote the growth of infant-associated *Bifidobacterium* species that possess specialised pathways for HMO utilisation.^{11,12} Fermentation of HMOs produces SCFAs and other metabolites that support epithelial integrity, modulate immune responses and protect against enteric pathogens, thereby creating an intestinal environment that supports healthy microbial development.^{11,12}

Breast milk also contains viable microorganisms together with numerous immunologically active compounds, including immunoglobulins, antimicrobial proteins, cytokines, growth factors and extracellular vesicles, which interact with the developing microbiome and immature immune system to promote intestinal and immune maturation.^{19,20} Rather than acting independently, these components function synergistically to support microbial succession, protect against infection and optimise nutrient utilisation during a period of rapid growth.

Although the contribution of individual breast milk components continues to be investigated, accumulating evidence indicates that many of the recognised benefits of breastfeeding are mediated, at least in part, through their influence on the developing gut microbiome.^{11,12} Microbiome research therefore complements rather than replaces the established nutritional rationale for breastfeeding by providing a biological explanation for many of its recognised effects. This evidence further reinforces international recommendations promoting breastfeeding as the optimal method of infant feeding.^{16–18}

As breastfeeding gradually transitions to complementary feeding, the gut microbiome must adapt to an increasingly diverse range of dietary substrates while continuing to support rapid growth and development. The complementary feeding period therefore represents the next major opportunity to influence the developing gut microbiome through nutrition.

Complementary feeding and microbiota-directed complementary foods

The transition from exclusive milk feeding to complementary feeding represents one of the most important nutritional milestones during early childhood. From around six months of age, breast milk alone is no longer sufficient to meet the increasing nutritional requirements associated with rapid growth and

Table 2: Summary of microbiota-directed nutritional interventions to support childhood growth

Intervention	Primary mechanism	Evidence for gut microbiome	Evidence for growth	Current clinical role
Breastfeeding ^{11,12,16–20}	HMOs, bioactive compounds and breast milk microbiota promote healthy microbial maturation	Strong	Strong	First-line recommendation for all infants
Complementary feeding ^{2,10,17}	Diverse foods support microbial succession and metabolic maturation	Strong	Strong	Essential component of infant feeding
Microbiota-directed complementary foods ^{7–9,21}	Designed to restore microbial function and anabolic pathways	Strong	Promising clinical evidence	Emerging intervention requiring further validation
Prebiotics ^{11,12,22}	Selectively stimulate beneficial bacteria and SCFA production	Strong	Limited/inconsistent	May support gut health; insufficient evidence for growth promotion
Probiotics ^{22,23}	Introduce selected beneficial microorganisms	Moderate	Limited/inconsistent	Indicated for selected gastrointestinal conditions; not recommended solely for growth promotion
Synbiotics ^{22,23}	Combine probiotics with prebiotic substrates	Moderate	Limited/inconsistent	Potential adjunct; further evidence required

development, necessitating the introduction of safe, nutritionally adequate complementary foods while breastfeeding continues.¹⁷ This dietary transition also coincides with a period of rapid development of the gut microbiome, during which microbial communities shift from utilising predominantly milk-derived substrates to metabolising more diverse dietary carbohydrates, proteins and lipids.^{3,10} Complementary feeding therefore provides an opportunity not only to support growth through adequate nutrient intake but also to influence the development of the intestinal microbial ecosystem during a critical window of physiological plasticity.

The WHO provides comprehensive evidence-based recommendations regarding the timing, composition and quality of complementary feeding, including dietary diversity, meal frequency, food consistency, responsive feeding and food safety.¹⁷ These recommendations, which are comprehensively addressed in the WHO guideline, are beyond the scope of this review. Instead, this section considers complementary feeding from the perspective of gut microbiome development and its implications for childhood growth.

The introduction of diverse complementary foods supplies substrates that support microbial succession, promote fermentation and increase the production of metabolites that contribute to intestinal barrier integrity, immune regulation and host metabolism.^{2,10} These observations provide a biological explanation for why diverse, nutrient-rich complementary diets consistently support healthy growth and reinforce existing infant and young child feeding recommendations.

Recent advances in microbiome research have expanded this concept by demonstrating that complementary foods can be deliberately designed to restore microbial development in children with undernutrition.^{7–9} Rather than replacing conventional complementary feeding recommendations, microbiota-directed complementary foods build upon established dietary principles by selecting ingredients according to both their nutritional value and their ability to promote microbial functions associated with healthy growth.

The pioneering work of Gordon and colleagues provides the strongest evidence supporting this concept. Initial longitudinal studies in Bangladeshi children demonstrated that

undernutrition was characterised by persistent gut microbiome immaturity, with depletion of age-discriminatory bacterial taxa and microbial functions that normally emerge during the complementary feeding period despite conventional nutritional rehabilitation. These observations led to the hypothesis that successful nutritional rehabilitation would require restoration of microbiome development in addition to correction of nutrient deficiencies. To test this hypothesis, the investigators combined longitudinal human microbiome data with gnotobiotic mouse and piglet models colonised with microbiota obtained from undernourished children. Candidate complementary food ingredients were systematically evaluated according to their capacity to restore growth-associated microbial taxa and metabolic pathways. Combinations of chickpea flour, peanut flour, soy flour and green banana consistently promoted microbial communities associated with healthy development, stimulated anabolic metabolic pathways and activated host signalling pathways involved in bone formation, neurodevelopment and immune function, providing the biological rationale for microbiota-directed complementary foods.⁷

The investigators focused on restoring microbial function rather than simply altering microbial composition. The selected formulations promoted recovery of members of the healthy weaning-phase microbial network, increasing bacterial taxa associated with normal microbiome development while reducing the persistence of microorganisms that typically dominate during exclusive milk feeding. These changes were accompanied by enhanced microbial pathways involved in amino acid metabolism, carbohydrate utilisation and other anabolic processes that support tissue accretion and growth.⁷

The preclinical findings were subsequently translated into a series of clinical studies in Bangladeshi children with moderate acute malnutrition. Chen and colleagues conducted a randomised controlled trial comparing the optimised microbiota-directed complementary food formulation with a conventional ready-to-use supplementary food (RUSF) in children aged 12–18 months with moderate acute malnutrition. Although both interventions provided comparable nutritional support, children receiving microbiota-directed complementary foods showed greater improvements in weight-for-length and weight-for-age together with marked changes in almost 5 000 circulating plasma proteins involved in bone growth, neurodevelopment,

immune function and metabolism. Microbiota-directed complementary foods also promoted recovery of bacterial taxa belonging to the healthy weaning-phase microbial network, with enrichment of taxa associated with normal microbial development. The investigators concluded that these improvements reflected restoration of microbial metabolic activity and host physiological pathways rather than increased nutrient intake alone.⁸

Mostafa and colleagues subsequently evaluated prolonged microbiota-directed complementary foods supplementation in Bangladeshi children aged 12–18 months. The intervention resulted in significant improvements in linear growth, providing some of the first direct clinical evidence that restoring microbial development may contribute not only to recovery from wasting but also to sustained skeletal growth. These improvements were accompanied by recovery of microbial pathways involved in amino acid metabolism, B-vitamin biosynthesis and other anabolic processes considered important for tissue growth.⁹

More recently, Hartman et al. extended this work to Bangladeshi children recovering from severe acute malnutrition. Children receiving a microbiome-directed therapeutic food showed faster recovery in weight-for-length than those receiving a conventional ready-to-use supplementary food, together with favourable changes in microbial pathways and circulating proteins associated with musculoskeletal and neurodevelopment.²¹ Evidence from Zambia further illustrates the limitations of conventional complementary food interventions. Although small-quantity lipid-based nutrient supplements improved child growth, they had only modest effects on gut microbial composition and biomarkers of EED.¹⁵

Complementary feeding is therefore entering a new phase in which nutritional adequacy and support of the developing gut microbiome are increasingly viewed as complementary objectives rather than independent goals. Microbiome-directed complementary foods should not be regarded as replacing established infant and young child feeding recommendations, but rather as refining them through a better understanding of the biological mechanisms linking diet, the gut microbiome and childhood growth. Whether similar approaches can be developed using locally available, culturally acceptable foods in African settings remains an important priority for future research.

Prebiotics, probiotics and synbiotics

The growing recognition that the gut microbiome contributes to nutrient metabolism, immune development and intestinal homeostasis has stimulated considerable interest in nutritional strategies that selectively modify microbial communities. Among these, prebiotics, probiotics and synbiotics have received the greatest attention. Unlike microbiota-directed complementary foods, which aim to restore healthy microbial development through whole foods and dietary patterns, these interventions target specific microorganisms or microbial metabolic pathways through the administration of selected substrates, live microorganisms or combinations of both. Their potential to improve gut health and support childhood growth has therefore been investigated in a wide range of clinical settings.

Prebiotics are non-digestible food components that are selectively utilised by beneficial intestinal microorganisms, thereby conferring a health benefit on the host.¹¹ HMOs are the best-

characterised naturally occurring prebiotics and play a central role in establishing the *Bifidobacterium*-dominated microbiome of healthy breastfed infants.^{11,12} Following the introduction of complementary foods, dietary fibres, resistant starches and other fermentable carbohydrates continue to provide substrates for microbial fermentation, supporting the production of metabolites that contribute to intestinal barrier integrity, immune regulation and host metabolism.²

Probiotics are defined as live microorganisms that, when administered in adequate amounts, confer a health benefit on the host. Proposed mechanisms include competitive exclusion of pathogenic microorganisms, enhancement of epithelial barrier integrity, modulation of innate and adaptive immune responses, and production of microbial metabolites that influence host physiology.² Importantly, probiotic effects are highly strain-specific, and clinical benefits demonstrated for one strain cannot be assumed for another.

Synbiotics combine probiotics with complementary prebiotic substrates to improve the survival, colonisation and metabolic activity of microorganisms. By providing both beneficial microorganisms and the substrates required to support their growth, synbiotics aim to achieve more sustained modulation of the gut microbiome than either component alone.²²

Among the three approaches, prebiotics have perhaps the strongest physiological rationale because they build upon mechanisms that occur naturally during breastfeeding. Clinical studies evaluating galacto-oligosaccharides (GOS), fructo-oligosaccharides (FOS) and related prebiotic mixtures have consistently demonstrated increases in *Bifidobacterium* and *Lactobacillus* species, reductions in faecal pH and increased production of SCFAs. Several studies have also shown that prebiotic-supplemented infant formulas promote gut microbial communities that more closely resemble those of breastfed infants, together with favourable changes in stool characteristics and microbial metabolism.^{4,11} More recently, formulas supplemented with selected HMOs have similarly been shown to support normal infant growth while selectively enriching *Bifidobacterium* species.¹²

Despite these favourable microbiological effects, improvements in childhood growth have been far less consistent. Although prebiotic supplementation clearly modifies the intestinal microbiome, these changes have generally not translated into clinically meaningful improvements in weight gain, linear growth or other anthropometric outcomes.²² Current evidence therefore suggests that prebiotics support the establishment of a healthier intestinal ecosystem, but their independent contribution to childhood growth remains uncertain.

Evidence supporting probiotics and synbiotics for promoting childhood growth is similarly inconsistent. A major limitation is the considerable heterogeneity among published studies. Trials have evaluated different probiotic strains, prebiotic substrates and synbiotic formulations across diverse populations, ranging from healthy infants to children with moderate or severe acute malnutrition, using varying doses, intervention durations and outcome measures. Consequently, direct comparisons are difficult, and no single probiotic or synbiotic intervention has consistently improved growth across different settings.^{2,22}

Studies in children with acute malnutrition illustrate both the potential and the limitations of these approaches. A large

randomised controlled trial in Malawi evaluated a synbiotic consisting of selected probiotic strains combined with prebiotic substrates as an adjunct to ready-to-use therapeutic food. Although the intervention altered selected features of the gut microbiome, it did not improve nutritional recovery or reduce mortality compared with standard treatment, suggesting that modifying microbial communities alone may be insufficient to restore healthy growth.²

More encouraging findings have emerged from Bangladesh, where supplementation with *Bifidobacterium longum* subsp. *infantis* EVC001, administered with and without an HMO, promoted colonisation by the administered strain, reduced intestinal inflammation and was associated with improvements in weight-for-age z-scores and mid-upper arm circumference.² The investigators proposed that these benefits reflected restoration of specific microbial activities important for host metabolism and immune function rather than simply increasing bacterial abundance. However, these findings were obtained in a relatively small pilot study and require confirmation in larger clinical trials before routine clinical application can be recommended.

Current clinical guidance reflects the uncertainty of the available evidence. The 2023 ESPGHAN position paper emphasises that probiotic efficacy is strain-specific, with recommendations restricted to individual strains that have demonstrated benefit for specific paediatric gastrointestinal conditions in high-quality clinical trials.²³ These include selected probiotics for the management of acute gastroenteritis, prevention of antibiotic-associated diarrhoea and, in carefully defined clinical settings, prevention of necrotising enterocolitis in preterm infants. However, ESPGHAN does not recommend probiotics as growth-promoting interventions because current evidence is insufficient to demonstrate consistent improvements in anthropometric outcomes. Any effects on growth are likely to be indirect, mediated through reductions in infection burden, improvements in intestinal integrity and modulation of inflammatory responses rather than direct stimulation of growth.²³

Overall, prebiotics, probiotics and synbiotics have established roles in selected paediatric gastrointestinal conditions and remain valuable tools for modulating the gut microbiome. However, unlike microbiota-directed complementary foods, they have not consistently demonstrated clinically significant improvements in childhood growth. Future research should therefore focus on identifying interventions that restore microbial metabolic capacity and determining how these approaches can best complement established nutritional strategies to support healthy growth.

Implications for clinical nutrition and future research

One of the most important advances in the field has been the recognition that restoring microbial metabolic function, rather than simply altering microbial composition, may be the key to improving childhood growth.^{5,8} While numerous interventions have successfully modified the abundance of individual bacterial taxa, relatively few have consistently translated these microbiological changes into clinically meaningful improvements in growth.^{2,22} In contrast, microbiota-directed complementary foods have demonstrated that carefully selected dietary ingredients can restore microbial metabolic activity, improve circulating biomarkers associated with bone growth,

neurodevelopment and immune function, and, in several studies, improve weight gain and linear growth.^{7–9}

Despite these encouraging advances, important knowledge gaps remain before microbiota-directed nutritional interventions can be incorporated into routine clinical practice. Current evidence is derived largely from relatively small studies conducted in limited geographical settings using heterogeneous methodologies, making comparisons between studies difficult and limiting translation across populations.^{5,10} Larger multicentre randomised controlled trials applying harmonised microbiome methodologies together with clinically meaningful growth outcomes are now required to establish the effectiveness, safety and generalisability of these interventions.

Future research should also move beyond describing microbial communities towards understanding the metabolic pathways through which the gut microbiome influences growth. Integrating metagenomics with metabolomics, metatranscriptomics and other systems biology approaches will improve understanding of host–microbiome interactions and allow the identification of microbial and metabolic biomarkers capable of predicting growth trajectories, identifying children at greatest risk of growth faltering and monitoring responses to microbiota-directed nutritional interventions.^{5,10}

Well-designed longitudinal birth cohort studies will be essential for understanding how maternal nutrition, breastfeeding, complementary feeding, microbiome development and child growth interact throughout early life.¹⁰ Continued follow-up beyond infancy will also be necessary to determine whether early modulation of the gut microbiome results in sustained benefits for growth, neurodevelopment and long-term health.

These priorities are particularly relevant in LMICs, where childhood undernutrition frequently coexists with recurrent infections, EED, poor dietary diversity and food insecurity.⁵ The successful development of microbiota-directed complementary foods using locally available ingredients in Bangladesh demonstrates that microbiome science can be translated into culturally appropriate nutritional interventions.^{7–9} More recently, a multicentre study in India showed that microbiota-directed complementary foods were well accepted by caregivers, achieved high compliance and could be delivered safely in community settings.²⁴ An important next step will be to determine how region-specific foods and traditional dietary practices can be harnessed to promote healthy microbiome maturation while remaining affordable, sustainable and culturally acceptable. Traditional African fermented foods may represent one such opportunity because they provide diverse microbial communities and bioactive metabolites that could inform future microbiota-directed complementary foods adapted to African settings.²⁵

Ultimately, the greatest contribution of microbiome science may not be the development of entirely new nutritional therapies, but a deeper understanding of how nutrition supports microbial development during early life to support healthy growth. Rather than replacing established infant and young child feeding recommendations, microbiome research provides a biological framework that strengthens them and offers opportunities to refine future nutritional strategies. As the evidence base continues to grow, integrating microbiome science into

clinical nutrition has the potential to strengthen evidence-based practice and improve growth outcomes among children most vulnerable to undernutrition.

Conclusion

The gut microbiome is increasingly recognised as an important contributor to childhood growth, providing a biological link between nutrition, intestinal function, immune development and metabolism during the first 1 000 days of life. Growing evidence suggests that healthy growth depends not only on adequate nutrient intake but also on the establishment of a functionally competent gut microbiome capable of supporting these physiological processes. This evolving understanding helps explain why nutritional rehabilitation alone may not consistently restore normal growth in children experiencing undernutrition.

For dietitians and other clinicians, these advances support the importance of established infant and young child feeding practices, including breastfeeding and appropriate complementary feeding, while providing new insights into the biological mechanisms through which they support healthy growth. Emerging microbiota-directed nutritional interventions, particularly microbiota-directed complementary foods, offer promising opportunities to complement existing strategies by restoring microbial function alongside improving nutritional status. However, further evidence from well-designed clinical trials conducted in diverse populations is required before these approaches can be widely incorporated into routine practice.

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