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Review Article

The Significance of Gut Microbiome Health Axis: Exploring the Synbiotic Role of GOS and Lactobacillus Reuteri in Supporting Brain, Skeletal and Muscular Development

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Abstract

The human gut microbiome is a complex ecological community that plays an important role in physiological development, immune maturation, metabolic homeostasis, and organ function, particularly during early life. The first years after birth represent a critical developmental window when microbial colonization and dietary interactions can influence long-term health. Emerging evidence indicates that the gut microbiome extends beyond digestion and functions as a communication network connecting intestinal health with distant organs through the gut microbiome health axis. This axis integrates microbial metabolites, immune signaling, endocrine regulation, and neural pathways to influence brain, skeletal, and muscular development. Disruption of early-life microbial balance has been associated with impaired gut comfort, altered immune responses, metabolic disturbances, and developmental challenges. Synbiotics, defined as combinations of beneficial microorganisms and selectively utilized substrates that provide synergistic health effects, have gained attention as nutritional strategies for supporting healthy microbiome development. Among these, galacto-oligosaccharides (GOS), a well-characterized prebiotic carbohydrate, and Lactobacillus reuteri, a probiotic species associated with gastrointestinal health, represent a promising combination. GOS selectively stimulates beneficial bacteria, particularly Bifidobacterium species, supporting short-chain fatty acid (SCFA) production, intestinal barrier integrity, and microbial diversity. Meanwhile, L. reuteri may contribute through competitive exclusion of potentially harmful microorganisms, immune modulation, enhancement of intestinal tolerance, and production of bioactive compounds that influence host physiology. Recent randomized clinical evidence suggests that young-child nutritional formulations containing L. reuteri and GOS may modulate gut microbial composition and support musculoskeletal developmental parameters, highlighting the potential value of targeted microbiome interventions during early growth. The gut-brain axis is among the most extensively studied microbiome-mediated pathways. Microbial metabolites, including SCFAs, neurotransmitter-related compounds, and immune mediators, may influence neuronal development, cognitive function, and neuroinflammatory regulation. The gut-bone axis illustrates how microbial metabolites can influence mineral absorption, osteoblast activity, vitamin metabolism, and skeletal remodeling. Improved nutrient utilization and SCFA production may support calcium availability and help regulate inflammatory

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processes. Emerging evidence also supports a gut-muscle axis, through which microbial composition may influence muscle metabolism, nutrient utilization, protein synthesis, and physical development. This review examines the gut microbiome health axis and the mechanistic role of the GOS and L. reuteri synbiotic combination in supporting early-life gut comfort and development, with particular emphasis on brain, skeletal, and muscular outcomes.

Keywords

Gut Microbiome, Gut-brain Axis, Synbiotics, Galacto-oligosaccharides, Lactobacillus Reuteri, Early-life Nutrition, Skeletal Development, Muscle Development

1. Introduction

The human gastrointestinal tract contains trillions of microorganisms collectively known as the gut microbiota, consisting of bacteria, archaea, viruses, fungi, and other microorganisms that interact continuously with the host. Once considered passive inhabitants of the digestive system, these microbial communities are now recognized as essential regulators of human biology. The gut microbiome contributes to nutrient metabolism, protection against pathogens, immune system education, maintenance of intestinal barrier function, and regulation of systemic physiological processes [1].

Early life represents one of the most important periods for microbiome establishment. Immediately after birth, microbial colonization begins through exposure to maternal microbiota, feeding patterns, environmental factors, and dietary components. During infancy and early childhood, the gut microbiome undergoes rapid maturation, gradually developing into a more stable ecosystem. The composition of microorganisms during this developmental stage can influence immune programming, metabolic pathways, and growth-related processes.

A healthy early-life microbiome is characterized by microbial diversity, abundance of beneficial bacteria, efficient production of microbial metabolites, and effective interaction between microorganisms and host tissues. Conversely, dysbiosis, defined as an imbalance in microbial composition or function, has been associated with gastrointestinal discomfort, increased inflammation, impaired immune regulation, and altered developmental outcomes.

The concept of the gut microbiome health axis describes the interconnected communication network between intestinal microorganisms and distant organs. Through microbial metabolites, immune mediators, and neural pathways, the gut communicates with the brain, skeletal system, and muscular tissues. This multidirectional relationship explains why alterations in gut microbial composition may influence cognitive development, bone formation, and muscle growth.

One of the most promising approaches for improving microbiome function is the use of synbiotics. Unlike isolated probiotics or prebiotics, synbiotics combine beneficial microorganisms with specific substrates that support their survival and activity. The International Scientific Association for Probiotics and Prebiotics defines synbiotics as combinations designed to provide synergistic health benefits by improving the survival and activity of beneficial microorganisms [2].

Galacto-oligosaccharides (GOS) are among the most extensively studied prebiotics used in infant and young child nutrition. Structurally similar to human milk oligosaccharides, GOS resist digestion in the upper gastrointestinal tract and reach the colon, where they serve as selective substrates for beneficial bacteria. Through fermentation, GOS promotes production of SCFAs such as acetate, propionate, and butyrate, which contribute to intestinal barrier function, immune regulation, and metabolic health.

Lactobacillus reuteri is a probiotic bacterium naturally found in the gastrointestinal tract and human breast milk. Specific strains, particularly *L. reuteri* DSM 17938, have been widely studied for their effects on intestinal comfort, microbial balance, immune modulation, and gastrointestinal function. Research has demonstrated potential benefits of *L. reuteri* in reducing digestive discomfort, supporting intestinal maturation, and maintaining microbial stability [3].

The combination of GOS and *L. reuteri* represents a biologically rational synbiotic strategy because GOS provides nutritional support for beneficial microorganisms while *L. reuteri* contributes functional probiotic effects. Recent evidence from randomized trials suggests that this combination may influence microbiome composition and support musculoskeletal development in young children.

Therefore, understanding the mechanisms through which GOS and *L. reuteri* influence the gut microbiome health axis may provide valuable insights into nutritional approaches that support optimal development during early life. This review discusses the role of this synbiotic combination in maintaining gut comfort and explores its potential contribution to brain, skeletal, and muscular development.

2. Gut Microbiome Health Axis: A Central Regulator of Early-Life Development

The gut microbiome health axis represents a complex biological communication system through which intestinal microorganisms influence multiple physiological processes beyond digestion. During early life, the establishment of a balanced gut microbial ecosystem is essential because microbial signals contribute to maturation of the immune system, metabolic programming, intestinal barrier development, and communication with developing organs. The interaction between microorganisms and host tissues occurs through several mechanisms, including microbial metabolites, immune modulation, endocrine pathways, and neural signaling [4].

A major mechanism underlying the gut microbiome health axis is the production of microbial-derived metabolites. Dietary components that escape digestion, particularly complex carbohydrates and prebiotic fibers, are fermented by intestinal bacteria to produce short-chain fatty acids (SCFAs), including acetate, propionate, and butyrate. These metabolites serve as energy sources for intestinal epithelial cells, enhance tight junction integrity, regulate inflammatory responses, and influence systemic metabolism. Butyrate, in particular, plays an important role in maintaining intestinal barrier function by promoting epithelial cell differentiation and reducing excessive inflammatory signaling.

During infancy, microbial colonization strongly influences immune system development. Beneficial bacteria such as *Bifidobacterium* and *Lactobacillus* species contribute to immune tolerance by regulating regulatory T-cell activity, balancing pro-inflammatory and anti-inflammatory cytokine production, and preventing excessive immune activation. A disrupted microbiome during this critical developmental period may increase susceptibility to allergic diseases, gastrointestinal disorders, metabolic abnormalities, and impaired growth patterns [4].

The gut microbiome health axis can be categorized into multiple interconnected pathways:

Gut-brain axis: Communication between intestinal microorganisms and the nervous system through microbial metabolites, vagal nerve signaling, immune mediators, and neurotransmitter-related compounds.

Gut-bone axis: Interaction between gut microorganisms and skeletal tissues through regulation of mineral absorption, inflammatory pathways, vitamin metabolism, and osteoblast activity.

Gut-muscle axis: Communication between gut microorganisms and skeletal muscles through regulation of protein metabolism, energy utilization, amino acid availability, and inflammatory control [5].

Early-life nutrition plays a decisive role in shaping these pathways. Breast milk naturally contains human milk oligosaccharides (HMOs), which selectively promote beneficial microbial populations. GOS has been developed as a functional prebiotic that mimics some microbiome-supporting effects of HMOs by promoting beneficial bacteria and enhancing microbial metabolite production.

When combined with specific probiotics such as *Lactobacillus reuteri*, GOS may create a favorable microbial environment by supporting probiotic survival, increasing beneficial bacterial activity, and enhancing host-microbial interactions. This synbiotic relationship provides a foundation for improving intestinal comfort while potentially supporting broader developmental processes [6].

2.1. Significance of the Synbiotic Role of GOS and *Lactobacillus reuteri* in Early-Life Gut Comfort

Early-life gastrointestinal discomfort is a common concern due to the immaturity of digestive function, developing intestinal motility, and incomplete microbial stabilization. Symptoms such as excessive crying, abdominal discomfort, irregular bowel patterns, and digestive intolerance are frequently associated with microbial imbalance and immature gut function. Nutritional strategies targeting microbiome development have therefore gained significant attention.

GOS functions as a selective substrate that promotes the growth of beneficial bacteria, particularly *Bifidobacterium* species. Because GOS is resistant to digestion in the small intestine, it reaches the colon where it undergoes bacterial fermentation. This process increases SCFA production, lowers intestinal pH, suppresses growth of potentially harmful microorganisms, and supports intestinal ecosystem stability [7].

Lactobacillus reuteri contributes additional probiotic benefits through several mechanisms:

1) Competitive exclusion of pathogenic microorganisms by occupying ecological niches.
2) Production of antimicrobial compounds such as reuterin.
3) Enhancement of intestinal epithelial integrity.
4) Modulation of immune responses.
5) Regulation of inflammatory pathways.
6) Improvement of intestinal microbial diversity.

The combination of GOS and *L. reuteri* demonstrates a synergistic mechanism because GOS provides a favorable environment for beneficial bacteria, while *L. reuteri* actively contributes to microbial balance and host interaction. This relationship represents more than simple coexistence; rather, it reflects a functional partnership between dietary components and microorganisms [8].

Recent clinical investigations have explored the effect of young child nutritional products containing *L. reuteri* and GOS on microbiome composition and developmental outcomes. Findings indicate that synbiotic supplementation may increase beneficial microbial populations, improve microbial metabolic activity, and influence markers associated with musculoskeletal development. Such evidence supports the

concept that early nutritional interventions targeting microbiome function may have effects extending beyond digestive health.

2.2. Supporting Brain Development: The Gut-Brain Axis

The gut-brain axis represents one of the most extensively studied microbiome-mediated communication pathways. It describes the bidirectional relationship between intestinal microorganisms and the central nervous system, involving neural, immune, metabolic, and endocrine mechanisms [9].

During early childhood, brain development requires precise regulation of neuronal growth, synapse formation, neurotransmitter balance, and immune signaling. The gut microbiome contributes to these processes through production of bioactive metabolites and regulation of systemic inflammation.

SCFAs produced through GOS fermentation influence brain function through several mechanisms. Butyrate can cross biological barriers and regulate gene expression through epigenetic mechanisms, potentially influencing neuronal maturation and synaptic plasticity. Acetate and propionate participate in metabolic regulation and communication between peripheral tissues and the brain.

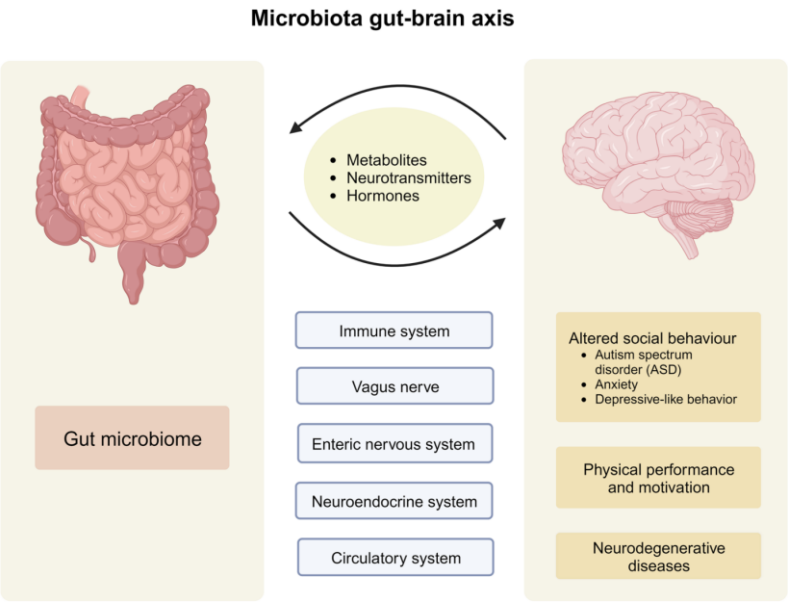

Figure 1. *Microbiota-gut-brain axis and its therapeutic applications in neurodegenerative changes [11].*

Gut microorganisms also influence neurotransmitter pathways. Several bacterial species are capable of producing or regulating molecules associated with neurological function, including gamma-aminobutyric acid (GABA), serotonin precursors, and dopamine-related metabolites. Although the direct contribution of microbial neurotransmitter production to human brain development remains under investigation, evidence strongly supports the importance of microbiome-mediated signaling [10].

L. reuteri has demonstrated potential neurodevelopmental effects through modulation of immune responses and microbial signaling pathways. Experimental studies suggest that certain strains may influence social behavior, stress response, and neural communication through the vagus nerve pathway.

One proposed mechanism involves reduction of excessive inflammatory signaling. Chronic low-grade inflammation can negatively affect brain development by altering neuronal growth and immune balance. By maintaining intestinal barrier integrity and regulating cytokine production, *L. reuteri* may contribute indirectly to a healthier neurodevelopmental environment [12].

The combination of GOS and *L. reuteri* may support brain development by:

1) Increasing beneficial microbial populations.
2) Enhancing SCFA production.
3) Maintaining intestinal barrier integrity.
4) Reducing systemic inflammation.
5) Supporting balanced immune-neural communication.

Although further long-term human studies are required, current evidence suggests that microbiome-targeted nutrition represents a promising approach for supporting optimal brain development during early life.

2.3. Supporting Skeletal Development: The Gut-Bone Axis

Bone development during childhood depends on adequate nutrient availability, hormonal regulation, immune balance, and mechanical stimulation. Recent research has identified the

gut microbiome as an important regulator of skeletal health through the gut-bone axis [13].

The gut microbiome influences bone development through several mechanisms:

Beneficial bacteria enhance intestinal absorption of minerals required for skeletal growth, particularly calcium, magnesium, and phosphorus. SCFAs produced from GOS fermentation reduce intestinal pH, which increases mineral solubility and improves absorption.

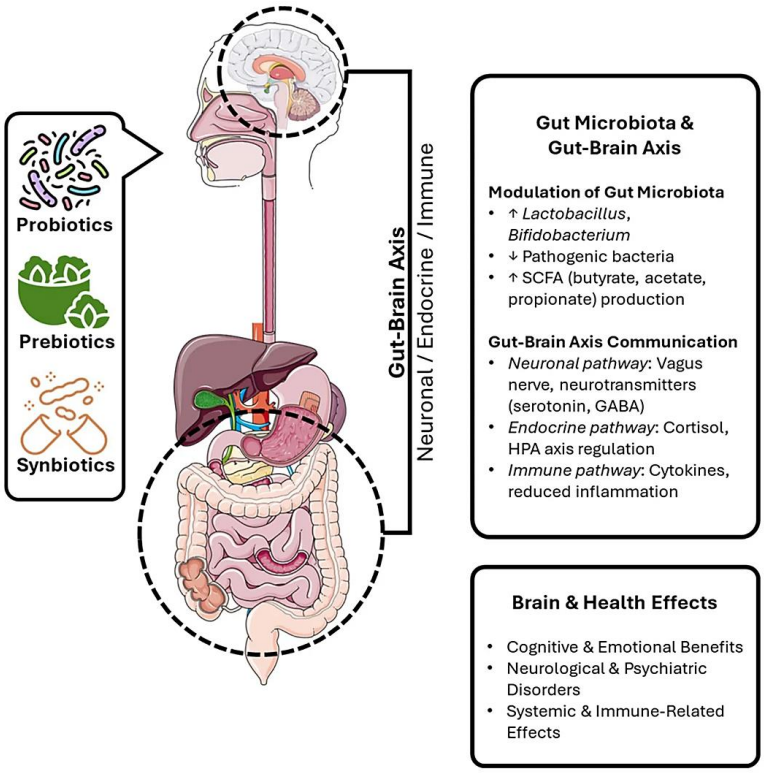

Figure 2. *Significance of the Synbiotic Role of GOS and L. reuteri in Early-Life Gut Comfort [15].*

Table 1. *Gut Microbiome Health Axis and Developmental Functions [14].*

Axis	Major Mechanism	Important Microbial Factors	Developmental Effect
Gut-brain axis	Neural signaling, SCFA production, immune regulation	*Bifidobacterium*, *Lactobacillus*, *L. reuteri*	Cognitive development and neurological maturation
Gut-bone axis	Mineral absorption, inflammatory control	SCFAs, beneficial bacteria	Bone mineralization and skeletal growth
Gut-muscle axis	Protein metabolism, energy regulation	Microbial metabolites	Muscle growth and physical development

Calcium availability is essential for:

1) Bone mineralization.
2) Osteoblast activity.
3) Growth plate development.
4) Skeletal strength.

Bone formation and degradation are controlled by osteoblasts and osteoclasts. Microbial metabolites influence signaling molecules involved in this balance. SCFAs can promote osteoblast differentiation while reducing excessive inflammatory activation of osteoclast pathways [16, 17].

Chronic inflammation can negatively affect bone formation by increasing inflammatory cytokines that stimulate bone resorption. By improving microbial balance, GOS and *L. reuteri* may contribute to reduced inflammatory pressure on skeletal tissues.

A randomized clinical study investigating young child formula supplemented with *L. reuteri* and GOS demonstrated

modulation of gut microbiota composition and improvements in developmental parameters related to bone and muscle growth. These findings suggest that microbiome-directed nutritional strategies may contribute to supporting physical development during childhood [18, 19].

Table 2. *Functional Role of GOS and L. reuteri as a Synbiotic Combination [20].*

Component	Primary Function	Mechanism	Health Benefit
GOS	Prebiotic substrate	Selective stimulation of beneficial bacteria	Improved microbial balance
L. reuteri	Probiotic microorganism	Immune modulation and pathogen inhibition	Improved gut comfort
GOS + L. reuteri	Synbiotic action	Enhanced microbial survival and activity	Support of systemic development

2.4. Supporting Muscular Development: The Gut-Muscle Axis

The relationship between intestinal microorganisms and skeletal muscle has recently emerged as an important area of research. The gut-muscle axis describes how microbial composition and microbial metabolites influence muscle metabolism, growth, and function.

Skeletal muscle requires continuous supply of amino acids, energy substrates, and regulatory signals. The gut microbiome contributes to these processes by affecting nutrient absorption, metabolism, and inflammatory regulation [21, 22].

Beneficial gut microorganisms may support muscle development through:

1) Improved nutrient utilization.
2) Enhanced amino acid metabolism.
3) Regulation of energy availability.
4) Reduction of chronic inflammation.

SCFAs produced from GOS fermentation serve as metabolic substrates and signaling molecules that influence energy homeostasis. These metabolites may improve mitochondrial function and support efficient energy production required for muscle development [23, 24].

L. reuteri may contribute to muscle development indirectly through improved intestinal health. A healthier intestinal environment allows better nutrient absorption and reduces inflammatory stress. Inflammation is a major factor that can impair muscle protein synthesis and negatively influence growth [25].

By maintaining microbial balance and supporting digestive comfort, *L. reuteri* may create favorable conditions for normal muscular development [26].

Table 3. *Evidence Supporting the Role of GOS and L. reuteri in Brain, Skeletal and Muscular Development [27, 28].*

Developmental System	Proposed Mechanism	Role of GOS	Role of *L. reuteri*	Potential Developmental Outcome
Brain development	Gut-brain communication through SCFAs, immune regulation and microbial signaling	Enhances beneficial bacteria and increases production of neuroactive metabolites	Modulates inflammatory responses and supports microbial stability	Improved neurodevelopmental environment and cognitive support
Skeletal development	Gut-bone axis through mineral absorption, osteoblast regulation and immune control	Enhances SCFA production and improves mineral availability	Supports intestinal health and reduces inflammatory imbalance	Improved bone mineralization and skeletal growth
Muscular development	Gut-muscle axis through nutrient utilization, metabolism and inflammation regulation	Promotes microbial fermentation and metabolic efficiency	Improves gut function and nutrient absorption	Supports muscle growth, energy metabolism and physical development

3. Conclusion

The gut microbiome has emerged as a critical regulator of early-life development, extending far beyond its traditional role in digestion. The concept of the gut microbiome health axis demonstrates that intestinal microorganisms actively communicate with multiple organ systems, including the brain, skeletal system, and muscular tissues. Through microbial metabolites, immune regulation, and metabolic signaling, the gut microbiome contributes to establishing physiological conditions required for healthy growth and long-term health.

Early childhood represents a particularly sensitive period because microbial colonization and maturation occur simultaneously with rapid neurological, skeletal, and muscular development. Therefore, nutritional approaches capable of supporting beneficial microbial communities during this developmental window may provide important advantages in maintaining gut comfort and optimizing growth outcomes.

The combination of galacto-oligosaccharides (GOS) and *Lactobacillus reuteri* represents a scientifically promising synbiotic strategy because these components provide complementary functions. GOS acts as a selective nutritional substrate that promotes beneficial bacteria, particularly bifidobacteria, while supporting the production of short-chain fatty acids that contribute to intestinal barrier integrity, immune regulation, and metabolic health. Meanwhile, *L. reuteri* provides probiotic activity through competitive exclusion of undesirable microorganisms, production of antimicrobial compounds, modulation of immune pathways, and enhancement of microbial stability.

The gut-brain axis highlights the importance of microbiome-derived signals in supporting neurological development. Through SCFA production, immune regulation, and microbial communication pathways, GOS and *L. reuteri* may contribute to a favorable environment for brain maturation. Although direct causal relationships between specific synbiotic interventions and cognitive outcomes require further investigation, current evidence supports the importance of maintaining a balanced microbiome during early neurodevelopment.

Similarly, the gut-bone axis provides evidence that microbial activity influences skeletal development through improved mineral absorption, regulation of inflammatory pathways, and modulation of bone remodeling processes. By enhancing intestinal function and nutrient availability, synbiotic interventions may support optimal bone formation during childhood.

The emerging gut-muscle axis further expands understanding of microbiome-mediated development. Muscle growth depends on efficient nutrient utilization, energy metabolism, and controlled inflammatory responses. By improving intestinal health and microbial metabolic activity, GOS and *L. reuteri* may indirectly support muscular development and physical growth.

However, despite promising findings, several limitations remain. Many mechanistic studies are based on animal models or short-term human trials, and the long-term developmental effects of specific synbiotic combinations require further investigation. Future research should focus on large-scale longitudinal clinical trials, strain-specific probiotic effects, personalized microbiome responses, and the interaction between genetic, environmental, and nutritional factors.

Overall, current evidence supports the concept that targeted microbiome modulation through synbiotic combinations such as GOS and *L. reuteri* represents a promising nutritional approach for promoting early-life gut comfort and supporting integrated development of the brain, skeletal system, and muscles. Understanding these complex microbiome-host interactions may contribute to the development of future precision nutrition strategies aimed at improving lifelong health outcomes.

Author Contributions

Nayema Sadia: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Project administration, Supervision, Validation, Visualization, Writing – original draft

Khan Lamia Nahid: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Supervision, Visualization, Writing – original draft

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Shuma Riam: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Project administration, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing

Shahana Begum: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Project administration

Rebecca Akhter: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Project administration, Supervision, Validation

Saiful Alam: Conceptualization, Data curation, Formal Analysis, Investigation, Project administration

Conflicts of Interest

The authors declare no conflicts of interest.

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