

# ***The significance of microbiota in healthy aging among the elderly population***

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## **Abstract**

The human microbiota, a diverse ecosystem of microorganisms inhabiting various body niches, significantly impacts host health across the lifespan. In the elderly population, alterations in microbiota composition and diversity, known as dysbiosis, play a crucial role in age-related physiological changes and disease susceptibility. This review provides a comprehensive examination of the role of microbiota in healthy aging among the elderly, focusing on its influence on immune function, metabolism, neurological health and frailty. Through an analysis of current research findings, this article elucidates the complex interplay between microbiota and aging and highlights potential avenues for microbiota-based interventions to promote healthy aging. *Geriatrics* 2024;18:5-14. doi: 10.53139/G.20241808

*Keywords: microbiota, elderly, aging, dysbiosis, immune function, metabolism, neurological health, frailty*

## **Introduction**

The human microbiota, comprising a complex community of microorganisms including bacteria, viruses, fungi, and archaea, exists in symbiosis with the human body, exerting significant influences on various aspects of host physiology and health [1]. Over the past decade, research into these specimens has unveiled microbiota's critical role in modulating host immune responses, metabolism, neurodevelopment, and overall well-being. The gut microbiota, in particular, has emerged as a key player in our health, with its composition and diversity significantly impacting physiology and susceptibility to diseases.

Advancing age is accompanied by a myriad of physiological changes, including alterations in immune function, metabolic processes, and neurological function. These age-related changes, collectively referred to as senescence, are influenced by a variety of genetic, environmental, and lifestyle factors. In recent years, accumulating evidence has highlighted the impact of aging on the composition and function of the gut microbiota. Studies have shown that elderly individuals exhibit alterations in the gut microbiota composition, characterized by reduced microbial diversity, altered relative abundances of specific bacterial taxa, and increased variability between individuals [2].

These changes in the gut microbiota, collectively known as dysbiosis, have been linked to various factors, including dietary patterns, medication use, and comorbidities commonly seen in the elderly population. Dysbiosis-induced alterations in the gut microbiota composition have been associated with impaired immune function, metabolic dysfunction, and increased susceptibility to infections in older individuals [3]. Understanding the role of microbiota in healthy aging is essential for developing strategies to promote longevity and quality of life among the elderly.

In this review, we provide a comprehensive examination of the role of microbiota in health and disease among the aging population. Through an analysis of current research findings, we elucidate the relationship between microbiota and aging and highlight potential avenues for microbiota-based interventions to promote healthy aging.

## **Alterations in microbiota composition with aging**

As individuals age, they undergo significant changes in the composition and diversity of their gut microbiota, which play a pivotal role in maintaining overall health and well-being. This age-related shift in the gut microbiota, often referred to as dysbiosis, encompasses a multitude of alterations in microbial

community structure and function. These changes have been extensively documented in research studies and have profound implications for the health and vitality of aging individuals.

Research has consistently shown that elderly individuals exhibit a decline in microbial diversity within their gut microbiota compared to younger adults. This decline in diversity is characterized by a reduction in the number of distinct microbial species present in the gut ecosystem [2]. Moreover, the proportions of specific bacterial groups within the gut microbiota undergo significant changes with age, where some may prevail and others decline, leading to an overall imbalance in microbial community composition [4].

Several factors contribute to these age-related alterations in gut microbiota composition. Changes in dietary habits, such as reduced fiber intake and increased consumption of processed foods, can significantly impact the gut microbiota and contribute to dysbiosis [5]. Additionally, the use of medications, particularly antibiotics and proton pump inhibitors, can disrupt the delicate balance of the gut microbiota and promote the overgrowth of potentially pathogenic bacteria [6].

Furthermore, physiological changes caused by aging, such as alterations in gastrointestinal motility and secretion of digestive enzymes, can create an environment that is more conducive to the growth of certain microbial species over others [4]. Additionally, comorbidities commonly seen in the elderly population, such as diabetes, hypertension, and inflammatory bowel disease, can further exacerbate dysbiosis and contribute to changes in gut microbiota composition [7].

Specific microbial taxa have been identified as being particularly affected by aging. For example, there is evidence to suggest that the relative abundance of beneficial bacteria, such as Bifidobacteria and Lactobacilli, decreases with age, while potentially harmful bacteria, such as Proteobacteria and Firmicutes, increase in abundance [2,4]. Additionally, the ratio of Firmicutes to Bacteroidetes, a marker of gut microbiota dysbiosis, is often elevated in older adults, further highlighting the imbalance in microbial community composition [4].

These aging-related alterations in gut microbiota population have significant implications for overall health and disease susceptibility. Dysbiosis has been implicated in the pathogenesis of various conditions, including inflammatory bowel disease, cardiovascular disease, neurodegenerative disorders, and metabolic syndrome [2,4]. Moreover, dysbiosis-induced changes in

gut microbiota composition can compromise immune function, disrupt metabolic homeostasis, and contribute to chronic low-grade inflammation, all of which are hallmark features of aging and diseases associated with it [3,8].

Understanding these mechanisms is essential for developing strategies to promote healthy aging and prevent age-related diseases in the elderly population. By focusing on the relationship between aging and the gut microbiota, researchers can identify potential targets for intervention, such as dietary modifications, probiotic supplementation, and fecal microbiota transplantation, aimed at restoring microbial balance and promoting health and vitality in aging individuals.

### **Impact of microbiota on immune function in the elderly**

The human immune system is a complex network of cells, tissues, and molecules that protects the body against pathogens and maintains tissue homeostasis. The gut microbiota plays a crucial role in regulating immune system function and maintaining its balance. Aging is characterized by a decline in immune function, termed immunosenescence, which encompasses alterations in both innate and adaptive immune responses [9]. In the elderly population, dysbiosis has been implicated in age-related changes in immune function, contributing to increased susceptibility to infections and impaired immune responses.

One of the key functions of the gut microbiota is to educate and regulate the function of our immune system. The gut-associated lymphoid tissue (GALT), which comprises the largest component of the body's immune system, interacts closely with the microorganisms residing in the gastrointestinal tract through a complex network of correlations [3]. Commensal bacteria in the gut play a critical role in shaping the development and maturation of immune cells, including T cells, B cells, and antigen-presenting cells, during early life and throughout adulthood [3]. These interactions are essential for maintaining immune tolerance to harmless antigens while mounting effective immune responses against pathogens.

In elderly individuals, improper gut microbiota composition can disrupt the delicate balance between immune tolerance and immune activation, leading to dysregulated immune responses. Dysbiosis-induced alterations in the gut microbiota have been associated with impaired mucosal barrier function, increased

intestinal permeability, and translocation of microbial products into the systemic circulation [8].

### **Gut barrier function of microbiota in the elderly**

The gut barrier, consisting of a single layer of epithelial cells, mucus layer, and immune cells, serves as a critical interface between the gut microbiota and the host, playing a pivotal role in maintaining intestinal homeostasis and preventing the translocation of harmful pathogens and toxins to other organs and systems. In the elderly population, the changes in gut barrier function, coupled with alterations in the gut microbiota composition, can compromise barrier integrity and contribute to the development of various gastrointestinal disorders and systemic inflammation.

### ***Intestinal permeability***

The integrity of the gut barrier is primarily governed by the tight junctions between epithelial cells, which regulate the passage of molecules and ions across the intestinal epithelium. Age-related alterations in tight junction proteins, such as occludin and claudins, can impair barrier function and increase intestinal permeability, allowing the translocation of luminal antigens and microbial products into the systemic circulation [8]. Increased intestinal permeability, commonly referred to as “leaky gut,” has been implicated in the pathogenesis of various aging-related diseases, including inflammatory bowel disease, metabolic syndrome, and neurodegenerative disorders [10].

### ***Mucus layer integrity***

The mucus layer, composed of mucins produced by goblet cells, serves as a physical barrier that protects the intestinal epithelium from luminal microbes and abrasive particles. Age-related changes in mucus production and composition can compromise mucus layer integrity and alter microbial interactions with the gut epithelium [10]. Reductions in mucin production and alterations in mucin glycosylation have been observed in the elderly population, contributing to mucosal inflammation and susceptibility to gut dysbiosis [11].

### ***Immune Regulation***

The gut-associated lymphoid tissue plays a crucial role in regulating gut barrier function and maintaining immune tolerance to luminal antigens. Age-related shifts in immune function, including alterations in T cell subsets and impaired mucosal immunity, can compromise

immune regulation, exacerbate gut barrier dysfunction and lead to chronic low-grade inflammation in the elderly patients [8,10].

### ***Microbiota-barrier interactions***

The gut microbiota plays a dynamic role in modulating gut barrier function through various mechanisms, including the production of short-chain fatty acids (SCFAs), antimicrobial peptides, and immunomodulatory molecules. Beneficial bacteria such as Bifidobacteria and Lactobacilli contribute to barrier integrity by enhancing mucin production, reinforcing tight junctions, and regulating immune responses [12]. Conversely, dysbiosis-induced alterations in gut microbiota composition can disrupt barrier function, promote inflammation, and exacerbate gut permeability in the elderly population [10].

In conclusion, maintaining gut barrier function is essential for preserving intestinal homeostasis and promoting overall health in the elderly population. Age-related changes in gut barrier function, coupled with alterations in the gut microbiota composition, can compromise barrier integrity and contribute to the development of gastrointestinal disorders and systemic inflammation. Understanding the interactions between microbiota and gut barrier function is crucial for developing targeted interventions to promote gastrointestinal health and mitigate age-related complications.

### **Dysbiosis-related immune impairment in elderly patients**

#### ***Impact on innate immunity***

Dysbiosis-related alterations in the gut microbiota composition can impair innate immune responses in elderly patients. The gut microbiota plays a critical role in educating the innate immune system and maintaining immune homeostasis through pattern recognition receptors (PRRs) such as Toll-like receptors (TLRs) and nucleotide-binding oligomerization domain-like receptors (NLRs) [13]. Dysbiosis-induced changes in microbial-associated molecular patterns (MAMPs) can dysregulate PRR signaling pathways, leading to impaired antimicrobial defense mechanisms and increased susceptibility to infections in elderly individuals [13].

#### ***Impact on adaptive immunity***

Dysbiosis can also impact adaptive immune responses in elderly patients, particularly T cell-mediated immunity. Age-related shifts in the gut microbiota

composition can influence T cell differentiation, function, and repertoire diversity, contributing to impaired immune surveillance and decreased responsiveness to antigens [8,9]. Dysbiosis-induced alterations in microbial metabolites, such as short-chain fatty acids and secondary bile acids, can modulate regulatory T cell (Treg) differentiation and effector T cell function, further exacerbating immune dysregulation in elderly individuals [14].

### ***Chronic inflammation and age-related diseases***

Dysbiosis-induced changes in the gut microbiota can affect the balance between pro-inflammatory and anti-inflammatory immune responses, contributing to chronic inflammation and immune dysfunction in the elderly population [3]. This phenomenon, termed inflammaging, is associated with increased risk of age-related diseases such as cardiovascular disease, neurodegenerative disorders, and cancer. Those contribute to accelerated tissue damage and organ dysfunction, further exacerbating age-related morbidity and mortality [15].

### ***Vaccination efficacy and dysbiosis in the elderly***

Elderly patients are at increased risk of severe infections due to aging-related shifts in immune function [16]. Vaccination plays a crucial role in protecting elderly individuals against infectious diseases and reducing morbidity and mortality associated with age-related complications. However, emerging evidence suggests that dysbiosis may impact vaccination efficacy in the elderly population. Understanding the correlation between dysbiosis and vaccination response is essential for optimizing immunization strategies and improving outcomes.

The gut microbiota influences vaccine efficacy through multiple mechanisms, including regulation of mucosal immunity, modulation of systemic inflammation, and enhancement of antigen-presenting cell function [17]. Dysbiosis can disrupt microbiota-immune interactions, impairing vaccine-induced immune responses in elderly individuals and leading to suboptimal vaccine outcomes in this population [13,17].

### ***Immune system and gut microbiota senescence in elderly patients with Inflammatory Bowel Disease (IBD)***

Inflammatory bowel disease (IBD), encompassing conditions such as Crohn's disease and ulcerative

colitis, represents chronic inflammatory disorders of the gastrointestinal tract with increasing prevalence in older populations. Aging is associated with alterations in both the immune system and gut microbiota, which can impact the pathogenesis and clinical course of IBD in elderly patients. This relationship may be essential for optimizing therapeutic strategies and improving outcomes in this vulnerable population.

Immunosenescence contributes to the pathogenesis of IBD by impairing mucosal immunity, altering gut barrier function, and promoting inflammation in the gastrointestinal tract. Dysbiosis in the gut microbiota is associated with increased risk of IBD onset, disease severity, and treatment resistance in elderly patients [15]. The interplay between immune senescence and gut microbiota dysbiosis plays a critical role in the pathogenesis of IBD in this population. Age-related differences in mucosal immunity and gut barrier function create an environment conducive to dysbiosis and microbial translocation, exacerbating inflammation and tissue damage in the gastrointestinal tract. Dysbiosis-induced alterations in the gut microbiota composition can further drive immune dysregulation, perpetuating a cycle of chronic inflammation and exacerbating IBD symptoms in elderly individuals [15].

### **Role of microbiota in metabolism and nutrient absorption**

The gut microorganisms play a vital role in regulating metabolism and nutrient absorption, which are essential for maintaining overall health and well-being, especially in the elderly population. Through participating in the interactions between the host and dietary components, the gut microbiota influences various metabolic processes and nutrient utilization.

#### **Metabolism regulation**

The gut microbiota contributes significantly to the metabolism of dietary components and endogenous molecules, influencing energy homeostasis and metabolic health. In the elderly, the changes in the microbiome composition, can disrupt metabolic pathways, leading to metabolic dysfunction and increased susceptibility to metabolic disorders such as obesity, type 2 diabetes, and cardiovascular disease [4].

#### **Short-Chain Fatty Acid production**

One of the key metabolic activities of the gut microbiota is the fermentation of dietary fibers and complex

carbohydrates, producing short-chain fatty acids such as acetate, propionate, and butyrate. SCFAs serve as an energy source for colonic epithelial cells, regulate host energy metabolism, and modulate immune and inflammatory responses [12]. In the elderly, dysbiosis can affect SCFA production, potentially impacting metabolic health and immune function [4].

### **Nutrient absorption**

The gut microbiota plays a crucial role in nutrient absorption by metabolizing dietary components and synthesizing essential nutrients. Bacterial enzymes produced by gut microbiota facilitate the breakdown of complex carbohydrates, proteins, and fats into absorbable nutrients, enhancing nutrient availability to the host [12]. Age-related changes in the gut microbiota can impair nutrient absorption and utilization, leading to nutritional deficiencies and compromised metabolic health in the elderly [2].

### **Vitamin production**

Certain members of the gut microbiota are capable of synthesizing vitamins and cofactors that are essential for human health, such as vitamin K, B vitamins, and folate. These microbial-derived vitamins contribute to various physiological processes, including blood clotting, energy metabolism, and DNA synthesis [12]. Dysbiosis-induced shifts in the gut microbiota composition may affect the production of these essential vitamins, potentially impacting metabolic and immune function in the elderly [2].

### **Influence of microbiota on neurological health**

The gut microbiome exerts a profound influence on neurological health, including cognition, mood regulation, and brain function. Emerging research suggests that the gut-brain axis, a bidirectional communication pathway between the gut and the brain, plays a critical role in mediating the effects of the gut microbiota on neurological function. In the elderly population, alterations in the gut microbiota composition and function have been implicated in age-related cognitive decline, neurodegenerative diseases, and mood disorders.

### **Communication via the gut-brain axis**

The gut-brain axis serves as a communication network linking the gut microbiota to the central nervous system (CNS) through neural, endocrine,

and immune pathways. Bidirectional communication between the gut and the brain occurs via the vagus nerve, neuroendocrine signaling molecules, and immune mediators, allowing the gut microbiota to influence neurological function and behavior [18]. Dysbiosis-induced alterations in gut microbiota composition can disrupt the microbiota-brain axis, impairing neurobehavioral responses and contributing to cognitive decline in elderly individuals [19].

### **Impact on cognitive function and association with neurodegenerative diseases**

Cognitive decline is a common feature of aging and is associated with increased risk of neurodegenerative disorders. Growing evidence suggests that the gut microbiota plays a crucial role in regulating cognitive function and age-related cognitive decline. Alterations in gut microbiota composition can trigger systemic inflammation, neuroinflammation, oxidative stress, synaptic dysfunction, and amyloid-beta accumulation, contributing to neurodegeneration and cognitive decline in the elderly [20]. Inflammaging can impair neuronal function and promote neurodegenerative processes [8], leading to cognitive impairment, memory deficits, and increased risk of neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease [4,6]. Dysbiosis-induced inflammation and gut barrier dysfunction may also contribute to blood-brain barrier disruption and neuroinvasion of microbial metabolites, further exacerbating neurodegenerative processes and disease progression in elderly individuals [20].

### **Modulation of neurotransmitter production**

Microbial-derived metabolites, such as short-chain fatty acids, neurotransmitters, and neuroactive compounds, can influence neuronal activity, neurotransmission, and synaptic plasticity in the brain, impacting cognitive function and behavior in aging [19]. The gut microbiota produces various neurotransmitters and neuromodulators, including serotonin, dopamine, and gamma-aminobutyric acid (GABA), which play essential roles in mood regulation and brain function. Alterations in gut microbiota composition can affect the production of these neurotransmitters, influencing mood, stress responses, and cognitive function in the elderly [21].

In conclusion, the gut microbiota plays a crucial role in influencing neurological health and cognitive function in the elderly population. Dysbiosis-induced alterations in gut microbiota composition can disrupt

the gut-brain axis communication, leading to cognitive impairment, mood disorders, and neurodegenerative diseases.

### **The role of microbiota in frailty**

Frailty, characterized by reduced physiological reserve and increased vulnerability to stressors, is a common syndrome associated with aging and is a significant predictor of adverse health outcomes, such as disability, hospitalization, and mortality, in the elderly population. Changes in the microbiome composition may contribute to the development and progression of frailty in elderly individuals.

### **Microbiota composition in frailty**

Age-related changes in the gut microbiota composition have been observed in frail elderly individuals, with alterations in microbial diversity and functional metabolic pathways [22]. Dysbiosis resulting in systemic inflammation, immune dysregulation, and metabolic dysfunction, contributing to the pathophysiology of frailty [22]. Other effects of microbial dysregulation may also contribute to frailty-related complications, such as infections, cognitive decline, and functional decline [2,23].

Frailty-impacted dysbiosis may contribute to the pathogenesis of age-related diseases, including cardiovascular disease, neurodegenerative disorders, metabolic syndrome, and musculoskeletal disorders. The induced pro-inflammatory status can exacerbate comorbidities like sarcopenia and osteoporosis, further complicating the frailty phenotype in aging [24].

### **Nutritional status and sarcopenia**

Sarcopenia, characterized by progressive loss of skeletal muscle mass, strength, and function, is associated with increased risk of falls, fractures, functional decline, and mortality in elderly individuals. Our microbiota plays a critical role in nutrient metabolism and absorption, which are essential for maintaining muscle mass and function. Impaired nutrient absorption, leading to malnutrition and sarcopenia, a key component of frailty syndrome [10]. Additionally, microbial-derived metabolites such as short-chain fatty acids and amino acids play important roles in regulating muscle protein synthesis and energy metabolism [22]. The incidence of dysbiosis has been correlated with muscle wasting in elderly individuals [25]. The induced inflammation and oxidative stress can promote muscle protein breakdown,

impair muscle regeneration, and exacerbate sarcopenic phenotype in aging [26].

### **Gut-muscle axis**

The gut microbiota communicates bidirectionally with skeletal muscle through various signaling pathways, collectively referred to as the gut-muscle axis. Microbial-derived metabolites, such as short-chain fatty acids, secondary bile acids, and trimethylamine-N-oxide (TMAO), can modulate muscle metabolism and mitochondrial function, influencing muscle mass and function in aging. Dysbiosis can impair muscle homeostasis and contribute to sarcopenic phenotype in elderly individuals [27].

### **Impact of medications and polypharmacy**

Polypharmacy, defined as the simultaneous use of multiple medications by an individual, is prevalent among elderly populations and is associated with increased risk of adverse drug reactions, drug-drug interactions, and medication-related complications. Polypharmacy may also impact the composition and function of the gut microbiota.

### **Impact of polypharmacy on gut microbiota**

Polypharmacy can disrupt the balance of the gut microbiota, leading to dysbiosis and alterations in microbial diversity, composition, and function. The use of multiple medications, particularly antibiotics, proton pump inhibitors (PPIs), nonsteroidal anti-inflammatory drugs (NSAIDs), and laxatives, can directly affect gut microbiota composition by altering microbial growth, metabolism, and community structure [6,28]. Additionally, polypharmacy-induced changes in one's physiology, such as changes in gastrointestinal motility, acidity, and nutrient absorption, can indirectly influence gut microbiota dynamics in elderly individuals [28].

### **Association with age-related diseases**

Medication-induced alterations in gut microbiota composition may exacerbate frailty-related symptoms and complicate management strategies in older patients. Dysbiosis induced by polypharmacy may contribute to the pathogenesis of age-related diseases, including cardiovascular disease, neurodegenerative disorders, metabolic syndrome, and gastrointestinal disorders or exacerbate underlying chronic conditions and increase the risk of disease progression in elderly individuals. Dysbiosis-associated inflammation and gut barrier

dysfunction may also contribute to medication-related complications, such as antibiotic-associated diarrhea, *Clostridium difficile* infection, and drug-induced enteropathy [28].

### ***Impact on medication efficacy and safety***

Dysbiosis induced by polypharmacy may affect the efficacy and safety of medications in elderly individuals. Alterations in gut microbiota composition can influence drug metabolism, pharmacokinetics, and bioavailability, potentially altering therapeutic outcomes and increasing the risk of adverse drug reactions. Furthermore, dysbiosis-associated changes in gastrointestinal physiology and gut barrier function may impact drug absorption, distribution, and elimination, further complicating medication management in elderly populations [29].

### **Therapeutic strategies targeting microbiota for healthy aging**

As our understanding of the gut microbiota's influence on aging and age-related diseases deepens, therapeutic strategies targeting the microbiota have emerged as promising approaches for promoting healthy aging and improving quality of life in the elderly population. By modulating the composition and function of the gut microbiota, these interventions aim to restore microbial balance, enhance immune function, and mitigate age-related metabolic and neurological changes. Several therapeutic strategies targeting the microbiota have shown potential for promoting healthy aging in elderly individuals.

### **Dietary interventions and probiotic supplementation**

Dietary interventions represent one of the most accessible and effective strategies for modulating the gut microbiota composition and promoting healthy aging. Increasing dietary fiber intake, consuming prebiotic-rich foods (e.g., onions, garlic, leeks), and incorporating fermented foods (e.g., yogurt, kefir, sauerkraut) into the diet can promote the growth of beneficial bacteria and enhance microbial diversity in the gut [5]. Additionally, adhering to a Mediterranean-style diet rich in fruits, vegetables, whole grains, and healthy fats has been associated with a diverse and resilient gut microbiota composition, as well as reduced risk of age-related diseases [30].

On the contrary, patterns characterized by low fiber intake, high saturated fat consumption, and processed food consumption have been associated with dysbiosis

and increased frailty risk in elderly populations [31]. Additionally, dietary interventions aimed at promoting mucosal healing, such as increased fiber intake and consumption of polyphenol-rich foods, can support gut barrier function and improve intestinal health in the elderly [10].

Supplementation with probiotics and prebiotics has been shown to improve gut microbiota composition, enhance immune function, improve antibody production and alleviate age-related inflammation in elderly individuals [6,32]. Specific strains of probiotics, such as *Lactobacillus* and *Bifidobacterium*, have been investigated for their potential to promote gut health and improve age-related outcomes [33]. Probiotic supplementation with beneficial bacteria has been shown to enhance gut barrier integrity, reduce intestinal permeability, and alleviate gastrointestinal symptoms in elderly individuals [6]. Targeted immunomodulatory therapies aimed at restoring immune function and suppressing inflammation may be beneficial in elderly patients with IBD [15].

Modulating the gut microbiota through dietary interventions, probiotics, and prebiotics represents a promising approach for promoting neurological health and cognitive function in the elderly population. Probiotic supplementation has been shown to modulate gut microbiota composition, reduce neuroinflammation, and improve mood, reduce anxiety and depression, and enhance cognitive function in elderly individuals [6,33,34].

Therapeutic interventions targeting the gut microbiota may also improve recovery in sarcopenic patients and preserve muscle health in aging population. Probiotic supplementation with beneficial bacteria has been shown to improve muscle function and modulate gut microbiota composition, reduce inflammation, and improve gastrointestinal function in frail elderly individuals [6,26]. Additionally, dietary interventions aimed at promoting gut microbiota diversity and resilience may support muscle health and attenuate age-related muscle loss and reduce the risk of frailty [2,10].

### **Fecal microbiota transplantation (FMT)**

FMT involves the transfer of fecal matter from a healthy donor to a recipient with the aim of restoring microbial balance and treating dysbiosis-associated conditions. While primarily used for the treatment of recurrent *Clostridioides difficile* infection, appears to be a promising therapeutic intervention for modulating the gut microbiota and improving health outcomes

in elderly patients [35]. Clinical trials investigating the efficacy of FMT in the management of age-related conditions such as frailty and cognitive decline deliver results showing potential benefits for gut microbiota restoration and immune function [6].

Transferring fecal microbiota from healthy donors to recipients, holds promise for restoring gut microbiota balance and promoting immune health and may also enhance vaccination efficacy in elderly individuals with dysbiosis [36]. Moreover, fecal microbiota transplantation may improve microbial composition and promote mucosal healing in patients with IBD [37].

### **Lifestyle modifications**

Lifestyle factors such as physical activity, stress management, and sleep hygiene can significantly impact the gut microbiota composition and promote healthy aging. Regular exercise has been shown to modulate gut microbiota diversity, reduce inflammation, and improve metabolic health in elderly patients [30]. Stress reduction techniques such as mindfulness meditation and relaxation exercises may also positively influence gut microbiota composition and alleviate age-related symptoms. Prioritizing adequate sleep duration and quality is essential for maintaining gut microbiota balance and supporting overall health among the elderly [21].

Lifestyle modifications, including cognitive stimulation, social engagement, and stress reduction, may also influence gut microbiota composition and cognitive function in elderly individuals [34]. Exercise-induced changes in gut microbiota composition, such as increases in beneficial bacteria and microbial diversity, have been also associated with improvements in muscle mass, strength, and function in older patients. The gut microbiota may mediate the beneficial effects of exercise on muscle health through modulation of inflammation, oxidative stress, and mitochondrial function [38].

### **Pharmacological interventions**

Pharmacological interventions targeting the gut microbiota, such as antibiotics, prebiotics, and microbial metabolites, are being explored for their potential to modulate microbial composition and improve health outcomes. However, caution must be exercised when using antibiotics, as indiscriminate use can disrupt the gut microbiota and exacerbate dysbiotic complications [6]. Novel therapeutics targeting specific microbial pathways and metabolites are also being developed, with the aim of restoring microbial balance and promoting healthy aging.

Rational medication management strategies, such as deprescribing unnecessary medications, reducing polypharmacy burden, and optimizing drug selection and dosing, can minimize the risk of medication-related complications and preserve gut microbiota homeostasis [39]. Additionally, dietary interventions aimed at promoting gut microbiota diversity, may counterbalance the impact of polypharmacy on the gut microbiota [28].

### **Future perspectives**

As research into the gut microbiota's influence age-related diseases continues to evolve, there are certain directions for future research aimed at understanding and harnessing the therapeutic potential of microbiota in the elderly population.

#### **Personalized medicine and precision nutrition**

Advancements in high-throughput sequencing technologies and computational analyses have enabled the characterization of individualized gut microbiota profiles, paving the way for personalized interventions targeting microbiota composition and function [40]. Integrating microbiota data into personalized medicine approaches and precision nutrition strategies may optimize therapeutic outcomes and improve healthspan in aging populations.

Tailored vaccination strategies, incorporating microbiota-modulating interventions, may improve vaccine efficacy and promote immune health [36]. Moreover, healthcare providers should consider the gut microbiota status of elderly patients when designing vaccination schedules and recommending adjuvant therapies to optimize vaccine responses in this vulnerable population.

Incorporating microbiota assessment into routine clinical practice may help identify individuals at increased risk of medication-related complications and guide personalized interventions to preserve gut microbiota homeostasis [39]. Additionally, healthcare providers should consider the potential effects of polypharmacy on gut microbiota health when prescribing medications to elderly individuals and prioritize strategies to minimize medication-related adverse effects and preserve host-microbiota symbiosis in clinical practice [29].

#### **Microbiota-based therapeutics**

The development of microbiota-based therapeutics, including probiotics, prebiotics, postbiotics, and fecal microbiota transplantation, offers novel opportuni-



ties for modulating gut microbiota composition and promoting healthy aging [41]. Engineered probiotics and microbial consortia designed to target specific age-related pathways and dysbiotic states may hold promise for mitigating complications of aging and enhancing resilience to stressors.

### Multi-omics integration and systems biology approaches

Integrating multi-omics data, including metagenomics, metabolomics, transcriptomics, and proteomics, with clinical phenotypes and health outcomes may provide comprehensive insights into the complex interactions between the gut microbiota and patient's physiology in aging [42]. Systems biology approaches, coupled with machine learning algorithms, can help identify predictive biomarkers of healthy aging and actionable targets for therapeutic intervention.

### Lifestyle interventions and health promotion

Lifestyle interventions targeting modifiable factors such as diet, physical activity, sleep, and stress management represent cost-effective strategies for promoting gut microbiota diversity and resilience in elderly individuals [32]. Public health initiatives aimed at promoting healthy aging and preventing age-related diseases should prioritize gut health and microbiota-targeted interventions as integral components of comprehensive wellness programs.

### Longitudinal Studies and Aging Cohort Analyses

Longitudinal studies tracking changes in gut microbiota composition and function across the aging continuum are essential for describing age-related trajectories of microbial dynamics and their associations with health outcomes [4]. Large-scale aging cohort analyses, such as the Human Microbiome Project (HMP) and the Elderly Microbiome Project (EMP), can provide valuable

insights into the role of microbiota in the processes of aging and inform the development of personalized interventions.

### Conclusion

The gut microbiota plays a crucial role in shaping health and aging trajectories in the elderly population [43]. Dysbiosis-induced alterations in microbiota composition have been implicated in the pathogenesis of age-related diseases and conditions, highlighting the importance of microbiota-mediated mechanisms in aging [5]. Future research should focus on discovering the underlying mechanisms of microbiota-host interactions and developing targeted interventions to improve the quality of life for aging individuals. Leveraging advances in microbiota research, personalized medicine, and systems biology approaches provide opportunities for developing innovative strategies to promote healthy aging, mitigate age-related diseases, and improve quality of life in elderly individuals. Embracing a holistic view of aging that recognizes the relationship between the gut microbiota, patient physiology, and environmental factors is essential for realizing the full potential of microbiota-targeted interventions in research and clinical practice.

### Conflict of interest

None

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