Life Sciences Student Journal
2025, Vol3, No2 pp 13-32

DOI:10.22034/LSSJ.2025.134

The Impact of Gut Microbiome Changes on Health and Disease in Older Adults

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Article Type:
Research article

Article Info:

Received: 30 January, 2025
Revised: 10 February. 2025
Accepted: 12 February. 2025
ePublished: 15 February. 2025
Key words: Gut microbiome, aging, gut brain axis, Probiotics, Exercise

Abstract

The aging process can make physiological and functional changes that boost the susceptibility of chronic diseases through alterations in the gut microbiome's composition and diversity. These alterations influence the immune system, metabolism, cognitive function, and other aspects of health. This review is designed to investigate how alterations in the gut microbiome are associated with aging-related conditions, including diabetes, cardiovascular diseases, Alzheimer's disease, and metabolic disorders. In this paper we also highlight the bidirectional gut-brain axis and the mechanisms that control gut health. In addition, it discusses effective strategies like balanced nutrition, probiotics, physical activity, and stress management that can help improve gut microbiome diversity and benefit the health of older adults. The findings aim to contribute in the development of targeted interventions to mitigate the effects of age-related changes in the gut microbiome.

1. Introduction

Aging is a natural process marked by physical challenges such as reduced energy, changes in appearance, and declining function. These changes arise from gradual deterioration of cells and physiological systems. While some consider aging as a disease-associated to decline and illness, others view it as a unique life stage with unique biological characteristics (1, 2). This process results in a gradual decline in body functions, increasing susceptibility to diseases and mortality. Key contributors in this regard include DNA instability, telomere shortening, and mitochondrial dysfunction. These biomarkers differentiate biological aging from chronological aging by linking cellular changes to age-related health issues.(3) is oxidative stress. Cisplatin therapy causes excess reactive oxygen dvascular diseases (1).

Table 1: List of abbreviations

Definition	Abbreviation
Short-chain fatty acids	SCFA
Colony-forming units	CFU
Irritable Bowel Syndrome	IBS
Lipopolysaccharides	LPS
Cardiovascular Diseases	CVD
Trimethylamine N-oxide	TMAO
Reactive Oxygen Species	ROS
Endoplasmic Reticulum	ER
Hypothalamic-Pituitary-Adrenal	HPA

body functions, increasing susceptibility to diseases and mortality. Key contributors in this regard include DNA instability, telomere shortening, and mitochondrial dysfunction. These biomarkers differentiate biological aging from chronological aging by linking cellular changes to age-related health issues.(3) Research have shown that aging significantly impacts various organs, particularly the brain, heart, kidneys, gastrointestinal system (intestines and stomach), and muscles.(4, 5) Among these, changes in the gut microbiome stand out particularly significant. These alterations can directly or indirectly influence the function of organs such as immune and digestive systems (6) Variations in gut microbiome diversity and balance are associated with chronic inflammation, metabolic disorders, and cognitive decline (7). The gut microbiome is a diverse community of microorganisms—bacteria, fungi, viruses, and other microbes—primarily located in the large intestine. It includes the collective genes and genetic products of these organisms and plays a crucial role in human health.(8, 9) The gut microbiome interacts bidirectionally with various organs, notably through the brain-gut, immune-gut, and muscle-gut axes, as well as in nutrient metabolism.(10, 11) The brain-gut axis can make mutual communication between gut and central nerve system. This system works through vagus nerve, chemical mediators, and inflammatory molecules. Mental and cognitive states are influenced directly by this interaction.(12)). Moreover research has been conducted during the past decade have demonstrated the significant role of gut microbiome in emotional wellbeing leading to the emergence of a new field is known as psychobioticst .(13)

The gut microbiome significantly influences the immune system by regulating immune responses through the production of biological molecules, such as short-chain fatty acids, which can either mitigate or enhance these responses, potentially amplifying systemic inflammation.(14) In addition, the microbiome impacts muscle function, with certain microbial metabolites enhancing performance and aiding muscle repair (15). Furthermore, microbiomes are essential in nutrient metabolism, fermenting carbohydrates, synthesizing vitamins, and regulating lipid metabolism, which directly affects energy supply and metabolic status.(16) Excessive use of antibiotic, poor dietary habits, or insufficient physical activity can potentially disrupt the balance of gut microbiome. This has been associated with conditions like obesity, type 2 diabetes, irritable bowel syndrome (IBS), and cardiovascular diseases.(17) The gut microbiome develops notably until about two to three years of age, influenced by delivery methods (vaginal or cesarean), feeding method (breast milk or formula), and environmental factors.(18) Microbial composition stabilizes with dietary diversification, after early childhood, usually resulting in Firmicutes and Bacteroidetes dominating by adolescence.(19, 20).

Table 2: Changes in the gut microbiome in aging

Type of change	description	Consequences
Reduction in beneficial bacteria	Reduced diversity of beneficial bacteria such as Bifidobacterium and Lactobacillus	Increased inflammation and decreased immunity
Increase in pathogenic bacteria	Overgrowth of bacteria associated with inflammation, such as Clostridium and Enterococcus	Increased risk of chronic diseases
Metabolic disorder	Reduced production of short-chain fatty acids such as butyrate	Impaired nutrient absorption and increased systemic inflammation

method (breast milk or formula), and environmental factors.(18) Microbial composition stabilizes with dietary diversification, after early childhood, usually resulting in Firmicutes and Bacteroidetes dominating by adolescence.(19, 20) During this stage, the microbiome demonstrates significant resilience and recovery even when its balance or diversity is disrupted by antibiotics, stress, or lifestyle.(20)

It has been shown that as we age, the diversity of beneficial microbiota, such as Bifidobacteria decline while inflammation-associated bacteria increase. These changes are mostly linked to dietary modifications and the onset of chronic diseases.(21) Research have shown that age-related gut microbiome changes are associated with frailty, immune decline, and cognitive impairment (22) . Reduced microbial diversity during aging has also been linked to chronic inflammation and health disorders (23). Aging can also affect metabolism, leading to decreased basal metabolic rates, reduced activity of digestive enzymes, and impaired absorption of essential nutrients such as vitamins and amino acids.(24) (25) Beneficial bacteria such as Lactobacillus diminish, allowing pathogenic bacteria like Clostridium difficile and Enterococcus to flourish, it cause disrupting gut homeostasis and leading to digestive problems.(26) In the table 2, we can examine the changes in gut microbiomes during aging. In this paper, our main objective is to collect and analyze the changes in gut microbiomes due to aging and to review the bidirectional axis connection between the gut microbiome and various organs and systems in the body. This study aims to show how changes in the gut microbiome can impact body functions and to clarify the complex interactions between the microbiome and different systems in the body. Through this paper, we hope to provide new insights into the influence of gut microbiome on health outcomes at different ages.

2 Materials and Methods

In this study we use a comprehensive literature review to examine how changes in the gut microbiome can affect aging and age-related diseases. The primary sources include peer-reviewed articles, systematic reviews, and meta-analyses from reputable journals. Selection criteria include:

1) The relationship between gut microbiome changes and aging (2) Focus on age-related health outcomes including cognitive decline, metabolic disorders, and immune dysfunction; (3) publication within the last 20 years; and (4) availability in English. Databases like PubMed, Scopus, and Web of Science were searched using keywords such as "gut microbiome and aging," microbiome diversity in older adults, gut-brain axis, age-related diseases, and microbiome-targeted interventions. Only human studies were included to comprehensively understand the mechanisms and clinical implications. Articles without clear methodologies or irrelevant topics were excluded.

The review also investigated the effects of lifestyle factors such as diet, exercise, and probiotics on microbiome changes, as well as intervention strategies aimed at improving gut microbiome diversity and mitigating the negative effects of aging. The results offer a thorough understanding of the bidirectional relationship between gut microbiota and systemic health in older adults.

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3. Discussion

3.1 Understanding the Gut Microbiome: From Composition to Function

The composition of the gut microbiome can vary based on anatomical location, abiotic environmental conditions, and the distinct functions of various sections of the gut. The literature has shown that a healthy adult typically hosts between 500 and 1,000 bacterial species, with 10^12 to 10^14 colony-forming units (CFU) in the gut, amounting to an estimated weight of 1 to 2 kilograms (27, 28). During the fetal stage the transfer of gut microbiota started as the fetus was exposed to the maternal environment. immediately after birth, when the newborn comes into direct contact with the external environment. This process becomes more active and dynamic (29). It is believed that during vaginal delivery, the newborn will be passed through the birth canal and is exposed to microorganisms such as Lactobacillus, Bifidobacterium, Streptococcus, and other beneficial bacteria. This initial contact has a very important role in the development and maturation of the immune system and for establishing the infant's gut microbiota (30, 31) Lactobacilli have a vital role in producing lactic acid, which makes the acidic environment conducive to the growth of other beneficial bacteria (32). Bifidobacteria are one of the important bacteria for digesting breast milk and supporting immune system development (33). Streptococci and other bacterial species contribute to the formation of the gut microbiota, enhancing immunity and also improving digestive function (34). In cesarean delivery, the newborn bypasses the birth canal and is primarily exposed to the mother's skin microbiota and the surgical environment. This exposure leads to a different composition of microbiota for the infant (35). During this process, the newborn is typically exposed to various bacteria, including Staphylococcus (particularly Staphylococcus epidermidis and Staphylococcus aureus), Micrococcus species (notably Micrococcus luteus), and skin-related bacteria such as Corynebacterium and Propionibacterium (36). In cesarean delivery at first newborn is exposed to the mother's skin microbiota and hospital environment this is what causes different gut microbiome composition Compared to babies born vaginally. This exposure includes hospital-associated bacteria such as *Enterococcus* and *Acinetobacter* (37). After this stage, the gut microbiota gradually stabilizes until years of age. This issue forms the foundation for long-term health. This phase of microbiome stability effects immune system development and overall well-being (38). The gut microbiome can generally be divided into four main groups: bacteria, fungi, viruses, and protozoa (39). Among these microorganisms, bacteria is the largest population and most functional group, also playing an important role in maintaining body health. These microorganisms most of the time reside in the large intestine (40).

3.2 Functions and Importance of Bacteria in the Gut Microbiome

Digestion and breakdown of food

Some bacteria like Lactobacillus and Bifidobacterium play a crucial role in breaking down sugars and dietary fibers and facilitates the production of short-chain fatty acids (SCFAs), such as acetate, propionate, and butyrate. In addition to producing energy, these fatty acids not only produce energy but also play a significant role in maintaining overall health (41, 42).

The gut microbiome contains specific bacteria that can produce certain vitamins. Research showed that Escherichia and Bacteroides bacteria can make vitamin K, and also Lactobacillus and Bifidobacterium can produce vitamin B9 (folate) (43). These processes highlight a close and complex relationship between diet and gut microbiome. When diets contain healthy and nutritious food, gut microbiomes can produce essential ingredients optimally, such as vitamins (44).The use of antibiotics not only destroys pathogenic bacteria but also affects beneficial bacteria (45). Antibiotic use can disrupt the diversity of the gut microbiome, leading to reduced production of certain vitamins (46). The overuse of antibiotics can disrupt the balance of the gut microbiome, promoting the overgrowth of harmful bacteria such as Clostridioides difficile, Enterococcus faecium, Escherichia coli, Klebsiella pneumoniae, and Proteus mirabilis. This overgrowth can inhibit the proliferation of beneficial bacteria, further compromising gut health (47-49).

3.3 The Role of Microbiome Changes in Aging and Their Impact on the Development of Related Diseases

Aging leads to changes in gut microbiome composition, characterized by a decline in beneficial bacteria like Bifidobacterium and Lactobacillus, and an increase in pathogenic microorganisms. These changes impair intestinal barrier integrity, frequently leading to "leaky gut" syndrome. Increased intestinal permeability disrupts the gut barrier, which in turn heightens susceptibility to various diseases. Antibiotic use significantly contributes to gut microbiome dysbiosis, promoting the growth of harmful pathogens such as Clostridioides difficile (50, 51).

3.4 Gut microbiome and Alzheimer

Alzheimer's is an irreversible brain disorder that is usually common in people over 65 years of age and is one of the most prevalent cause of dementia in these group of people (52). Alzheimer's disease is a neurodegenerative disorder characterized by the gradual degeneration and loss of function of brain cells, leading to declines in memory and cognitive abilities (53). Recent research has revealed a complex neural connection between the central nervous system and the enteric nervous system, referred to as the gut-brain axis (54). This bidirectional communication network utilizes neural and hormonal pathways to play a crucial role in maintaining homeostasis and cognitive function (55). The vagus nerve plays a central role in transmitting signals between the gut and the brain, conveying mechanical and chemical messages bidirectionally (56). Several hormones produced by the gut, including serotonin, ghrelin, and leptin, play a key role in regulating mood, appetite, and cognitive function, thus influencing brain health (57).

3.5 Serotonin

About 90 to 95 percent of the body's serotonin is produced in the enterochromaffin cells of the gut. This hormone plays a key role in regulating mood, appetite, and sleep (58). A reduction in gut serotonin can lead to psychological disorders such as depression and anxiety (59).

- Ghrelin:
  Secreted by the gut and stomach, ghrelin affects the hypothalamus through neural pathways, stimulating and regulating appetite (60).
- Leptin:
  Produced by fat cells, leptin travels through the bloodstream to the brain and, like ghrelin, helps regulate appetite (61).

Changes in the diversity or ratio of beneficial versus harmful gut microbiota—commonly referred to as dysbiosis—can lead to the production of inflammatory metabolites, such as lipopolysaccharides (LPS) (62). This change can result from factors such as an unbalanced diet, stress, antibiotic use, or gastrointestinal diseases (63). In dysbiosis conditions, the production of beneficial metabolites (such as short-chain fatty acids) decreases, while the production of inflammatory metabolites increases (64). Once LPS enters the bloodstream, it can activate the innate immune system, triggering a cascade of inflammatory cytokines such as TNF-α, IL-6, and IL-1β (65).

LPS and the mentioned cytokines reach the brain and activate microglia. The persistent activation of microglia leads to neuroinflammation, which results in the reduction of neural synapses and neuronal death, ultimately causing impairments in cognitive function.(66, 67)

Chronic neuroinflammation can affect critical regions of the hippocampus in the brain, leading to the development and progression of neurodegenerative diseases such as Alzheimer’s and Parkinson’s.(68, 69)

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3.6 Gut microbiome and Diabetes

The intestinal environment and the microbes in it can cause immune disorders such as diabetes. In addition, a decrease in microbial diversity in the intestine can cause inflammation and immune system dysfunction (70). Type 1 diabetes causes a malfunction in the immune system, which causes immune cells to attack the cells in the pancreas where insulin is produced. A reduction in gut microbial diversity can exacerbate this autoimmune process (71). Recent research has shown that changes in the composition and diversity of the gut microbiome can play a fundamental role in the development of diseases such as type 1 diabetes (72). A reduction in microbial diversity or changes in the composition of gut bacteria can disrupt immune response regulation, thereby exacerbating autoimmune processes (73). In type 1 diabetes, these microbial changes may result in the immune system attacking the insulin-producing cells in the pancreas. In other words, an imbalance in the gut microbiome can pave the way for abnormal immune reactions and, consequently, the development of autoimmune diseases such as diabetes (74, 75). While type 1 diabetes involves autoimmune processes driven by microbial imbalances, type 2 diabetes is primarily a metabolic disorder linked to chronic inflammation and insulin resistance, both of which can also be influenced by gut microbiome health. Type 2 diabetes is a chronic metabolic disorder characterized by elevated blood glucose levels due to reduced insulin sensitivity or inadequate insulin production (76).

Reduction in microbial diversity or an overgrowth of specific bacteria (such as Firmicutes and Proteobacteria) can lead to the production of inflammatory molecules (such as lipopolysaccharides). These molecules can cross the intestinal barrier and enter the bloodstream (77). This process triggers chronic inflammation, a key factor contributing to insulin resistance in peripheral tissues like muscles and the liver (78). Healthy microbiome produces short-chain fatty acids (SCFAs) like butyrate. These fatty acids can regulate insulin sensitivity and reduce inflammation. A reduction in SCFA production due to microbiome dysbiosis can decrease insulin sensitivity and impair glucose metabolism (79). One of the essential roles of the gut microbiome is the regulation of gut hormones that play a key role in controlling appetite and metabolism (80). Changes in gut microbiome composition and diversity can disrupt the production and function of these hormones. For example, some gut bacteria may reduce the production of GLP-1 and PYY, which can result in overeating, weight gain, and ultimately increase the risk of developing type 2 diabetes (81, 82). Additionally, the gut microbiome can affect metabolic processes such as insulin resistance and blood sugar regulation, which are significant factors in the development of type 2 diabetes (83). Therefore, any alterations in the composition of the gut microbiome can lead to metabolic disorders and an increased risk of diseases like type 2 diabetes.

Imbalance in the gut microbiome can trigger the production of specific metabolic products that lead to increased oxidative stress and inflammation in the body, including the pancreas (84). These free radicals and chronic inflammation can damage the beta cells in the pancreas and reduce insulin production (85). The reduced function of these cells makes it more difficult to control blood sugar and increases the risk of developing type 2 diabetes. Therefore, an unhealthy microbiome can directly impact pancreatic function and blood sugar regulation, contributing to metabolic disorders like diabetes.(86)

An imbalance in the gut microbiome can stimulate the production of harmful metabolites, leading to oxidative stress and chronic inflammation(87). Reactive oxygen species (ROS), which are highly reactive molecules, can accumulate in pancreatic beta cells, leading to oxidative stress. Due to the high metabolic activity of these cells and their limited antioxidant defenses, they are particularly vulnerable to ROS-induced damage, impairing their functes (86).

An imbalance in the gut microbiome can stimulate the production of harmful metabolites, leading to oxidative stress and chronic inflammation (87). Reactive oxygen species (ROS), which are highly reactive molecules, can accumulate in pancreatic beta cells, leading to oxidative stress. Due to the high metabolic activity of these cells and their limited antioxidant defenses, they are particularly vulnerable to ROS-induced damage, impairing their function and further contributing to insulin resistance (88). Chronic inflammation caused by microbial products increases intestinal permeability and triggers inflammatory pathways through cytokines such as IL-6, TNF-α, and IL-1β, leading to beta-cell destruction (71). These two key processes, by activating apoptotic pathways and endoplasmic reticulum (ER) stress, disrupt beta-cell function and reduce insulin production. Consequently, blood glucose regulation becomes more challenging, increasing the risk of developing type 2 diabetes (89, 90).

3.7 Gut microbiome and cardiovascular disease

In older adults, changes in diet, reduced physical activity, medication use, and alterations in the immune system can disrupt the balance of the gut microbiome. These disruptions are increasingly linked to the development of cardiovascular diseases (CVD) (91). Research indicates that aging leads to a decrease in the diversity and abundance of beneficial bacteria such as Faecalibacterium and Bifidobacterium. This reduction contributes to systemic chronic inflammation, commonly referred to as inflammaging, which is a significant risk factor for cardiovascular diseases (6, 92). Defining a purely pathogenic bacterial community is challenging; however, the term dysbiosis is commonly used to describe an imbalance in the gut microbiota composition associated with specific diseases or phenotypes. Numerous studies have reported correlations between cardiovascular disease (CVD) phenotypes and alterations in the relative abundance of certain microbial species, as well as changes in the richness and diversity of gut bacteria (93, 94). The relationship between specific dietary components and the production of harmful metabolites by the microbiome underscores the importance of nutritional choices in preventing cardiovascular diseases (95). Trimethylamine

N-oxide (TMAO) and phenylacetylglutamine (PAG) are metabolites produced by the gut microbiota. These metabolites are derived from dietary components such as choline and carnitine, commonly found in Western diets. They have been associated with adverse effects in the body, including increased inflammation, platelet activation, and the development of atherosclerosis (89, 96). Scientific studies have demonstrated that TMAO and PAG are directly and indirectly linked to cardiovascular diseases due to their specific physiological effects on various bodily systems. These metabolites increase the risk of heart diseases by influencing various bodily systems, including inflammatory pathways, lipid metabolism, and platelet function (97). Trimethylamine N-oxide (TMAO), produced from the metabolism of choline, carnitine, and phosphatidylcholine by the gut microbiome, has the capacity to inhibit natural cholesterol metabolism processes (98). TMAO impairs the normal cholesterol metabolism by inhibiting the liver's ability to excrete cholesterol and by promoting the accumulation of cholesterol in the arterial walls, a hallmark of atherosclerosis (99). Phenylacetylglutamine (PAG), produced from the metabolism of phenylalanine by the gut microbiome, significantly impacts platelet activation. Research has shown that this metabolite can increase platelet sensitivity to activating stimuli, accelerating thrombosis formation. This characteristic elevates the risk of cardiovascular events such as heart attack and stroke in individuals (100). Both metabolites contribute to oxidative stress—a key factor in the progression of cardiovascular diseases—by increasing the production of reactive oxygen species (ROS) and reducing the body's antioxidant capacity. Additionally, their amplifying effects on inflammatory pathways can lead to fibrosis and vascular stiffness.(92)

Activation of pathways such as the NLRP3 inflammasome by TMAO and other metabolites leads to increased oxidative stress and vascular inflammation, which are key factors in the progression of their amplifying effects on inflammatory pathways can lead to fibrosis and vascular stiffness (92).

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3.8 Strategies to improve microbiomes in elderly people

Research shows that implementing various strategies to maintain a balanced and healthy gut microbiome plays a crucial and significant role in health during aging. To this end, we highlight some of these strategies.

3.9 Consume a healthy and balanced diet

High fiber intake plays an important role in gut health and increases the diversity of beneficial bacteria. Certain fiber-rich foods, such as vegetables, fruits, whole grains, and legumes, contain prebiotic fibers that act as nourishment for beneficial gut bacteria. Prebiotics are a source of nutrition for beneficial gut bacteria and help their growth and proliferation (102). when these bacteria ferment fiber, they produce metabolites called short-chain fatty acids (SCFAs), such as butyrate, acetate, and propionate. These compounds have beneficial effects on the body, including:

- Strengthening gut wall health and preventing leaky gut
- Reducing inflammation
- Boosting the immune system (103, 104)

3.10 Probiotic Consumption

Foods containing probiotics, such as yogurt, kefir, sauerkraut, kimchi, and other fermented products, play an important role in improving gut microbiota balance. Probiotics include live microorganisms, especially beneficial bacteria and yeasts, which, when consumed in adequate amounts, can have positive effects on the health of the host (105). These foods contribute to maintaining gut microbiome homeostasis by enhancing the abundance of beneficial bacteria, such as Lactobacillus and Bifidobacterium, while suppressing the proliferation of pathogenic microorganisms (106). Additionally, probiotics stimulate the production of bioactive metabolites such as lactic acid and other organic acids, which can make the gut environment unfavorable for the growth of harmful microorganisms (107). Regular consumption of probiotics can help strengthen immune function, reduce inflammation, improve digestion, and maintain overall gut health. These effects are especially important in older age when the diversity of microbiomes may decline (105).

3.11 Reduction of Sugar and Saturated Fats Consumption

Excessive consumption of sugar and saturated fats can negatively impact the composition and diversity of the gut microbiome. These foods lead to negative changes in the gut bacterial population, promoting the growth of harmful bacteria while reducing the growth of beneficial bacteria (108). Evidence from recent studies suggests that diets high in fat and sugar can disrupt gut microbiota and impair the function of Th17 immune cells, which play a critical role in preserving gut health and defending against pathogenic bacteria. For example, research conducted by Columbia University Irving Medical Center demonstrated that dietary sugar disrupts gut microbiota homeostasis, resulting in the depletion of protective Th17 cells and an increased risk of obesity and diabetes (109). Furthermore, it has been found that dietary sugar increases the population of harmful bacteria and decreases Th17 cells (110). Studies also indicated that diets high in sugar and saturated fats can reduce the diversity of gut microbiota and create conditions in which inflammatory and pathogenic bacteria, such as Clostridium and weakened Bifidobacterium species, are increased (111). As a result, these microbial changes can increase the risk of metabolic diseases, cardiovascular diseases, and digestive issues. Therefore, reducing the intake of sugar and saturated fats helps maintain a healthy gut microbiome balance and improves overall body health. (112)

bial changes can increase the risk of metabolic diseases, cardiovascular diseases, and digestive issues. Therefore, reducing the intake of sugar and saturated fats helps maintain a healthy gut microbiome balance and improves overall body health (112).

3.12 Water and microbial diversity in the elderly

The elderly often experience a reduction in gut microbiome diversity, which is associated with age-related diseases such as chronic inflammation, metabolic syndrome, and weakened immune function (113). Research indicates that older adults often experience dehydration due to factors such as diminished thirst sensation, the use of certain medications like diuretics (e.g., furosemide or hydrochlorothiazide) or nonsteroidal anti-inflammatory drugs (NSAIDs) (e.g., ibuprofen or naproxen), and chronic illnesses (114). Insufficient water in the body leads to alterations in the intestinal mucus layer, which plays a crucial role in protecting the gut and providing an environment conducive to the growth and activity of beneficial bacteria such as Lactobacillus and Bifidobacterium. Disruption of this layer can allow harmful bacteria like Clostridium difficile and pathogenic strains of Escherichia coli to proliferate, resulting in reduced gut microbial diversity (115, 116). Chronic dehydration not only reduces the viscosity of the intestinal mucus but also significantly slows bowel movements, leading to constipation, accumulation of harmful metabolites, and alterations in the gut microbial ecosystem (117). Chronic dehydration not only reduces the viscosity of the intestinal mucus but also significantly slows bowel movements, leading to constipation, accumulation of harmful metabolites, and alterations in the gut microbial ecosystem (117, 118). Research conducted in this field highlight that adequate water intake in old age is of great importance and plays a vital role in maintaining individuals' health. In addition, following a healthy and scientific diet that includes sufficient consumption of water-rich foods, fruits, and vegetables can serve as an effective method for enhancing health and preventing diseases in older age (119).

3.13 The Impact of Exercise on Gut Microbiome in the Elderly

Aging represents a distinct and critical phase of life, during which the lack of a healthy lifestyle can exacerbate various health challenges and significantly worsen existing conditions. Conversely, adopting appropriate nutrition and engaging in age-specific exercises can profoundly influence various bodily systems, including the gut microbiome, which plays a pivotal role in overall health (120, 121).

It has been proven that certain types of exercise have a greater impact on gut microbiota in older adults compared to other types. These include endurance (aerobic) exercises, resistance training, and yoga (122, 123).

Aerobic (endurance) training, such as walking, running, cycling, and swimming, are activities that increase heart rate and improve respiratory capacity. Scientific research has shown that these types of exercises can positively impact on the gut microbiome. The exercise intensity should range from 50 to 70 percent of the individual's maximum heart rate, and the total duration should be at least 150 minutes per week (124). Research indicated that regular aerobic exercises can lead to an increase in beneficial bacteria such as Bifidobacterium and Lactobacillus, which play a key role in digestive and immune processes (125). Aerobic exercises, such as walking, running, cycling, and swimming, can increase the abundance of beneficial bacteria like Akkermansia muciniphila, which play a crucial role in gut health. These bacteria are involved in producing anti-inflammatory substances and maintaining the integrity of the intestinal wall (126). It has been highlighted that aerobic exercises not only enhance the immune system function by increasing the number and functionality of immune cells such as T cells and B cells but also positively influence the composition and diversity of the gut microbiome. These changes in the microbiome can play a crucial role in maintaining overall health and preventing diseases(127)

Resistance training has been shown to have positive effects on gut microbiota composition and tion by increasing the number and functionality of immune cells such as T cells and B cells but also positively influence the composition and diversity of the gut microbiome. These changes in the microbiome can play a crucial role in maintaining overall health and preventing diseases (127).

Resistance training has been shown to have positive effects on gut microbiota composition and function, potentially leading to significant changes in metabolic health and microbial diversity. According to a recent study, RT significantly increased microbial diversity, measured by the Chao1 index Higher microbial diversity is generally associated with better health outcomes and indicates optimal gut microbiota function (128). Analysis of bacterial community structure (β-Diversity) revealed that resistance training induced significant changes in the microbial community composition These changes lead to a reduction in the relative abundance of Pseudomonas, Serratia, and Comamonas, which are commonly associated with inflammatory conditions and diseases. Conversely, an increase in the abundance of Coprococcus_1 was observed, which is linked to the production of short-chain fatty acids (SCFAs) and improved metabolism (15, 129).

RT also has beneficial metabolic effects. These exercises can reduce visceral fat tissue and an improvement in glucose tolerance, while no changes were observed in food intake or triglyceride levels. Furthermore, functional microbiome pathways related to lipid and amino acid metabolism, as well as cellular signaling, were improved in the exercise group (130). Overall, resistance training was able to increase microbial diversity by remodeling the gut microbiome's structure and function, guiding bacterial communities toward a healthier pattern (131). These changes not only contributed to improved gut health but also helped reduce inflammation and enhance overall metabolism. The results suggest that RT could serve as an effective intervention for improving general health, particularly in older adults (15, 132).

Yoga is a comprehensive physical, mental, and spiritual system with ancient roots in India, aiming to harmonize the body, mind, and spirit. This practice encompasses physical postures (asanas), breathing techniques (pranayama), and meditation (mindfulness), contributing to enhanced flexibility, strength, balance, and stress reduction, thereby promoting overall health (133). Scientists suggests that stress, anxiety, and depression can alter neurotransmitter release, which in turn affects the gut microbiota profile (134). Stress can also disrupt epithelial homeostasis by blocking the protective effects of the vagus nerve barrier. Reduced vagal tone has been implicated in inflammatory bowel disease (IBD) and irritable bowel syndrome (IBS), and gut microbiome changes can affect gut motility, integrity, secretion, and brain function through the impact on neurotransmission and behavior (135). These effects are bidirectional. Cyclic meditation (CM) and yoga may help improve stress-induced gut microbiota dysbiosis, and several studies have shown that these practices enhance vagal tone and cognitive functions (136).

The vagus nerve plays a crucial role in the gut-brain axis by regulating the parasympathetic nervous system (56). Yoga have been shown to enhance vagal tone, which leads to improved gastrointestinal motility, secretion of digestive enzymes, and anti-inflammatory effects. These changes help restore a healthy gut microbiome composition. (137). Yoga reduces nuclear factor kappa B (NF-κB), a regulator of inflammation, and decreases inflammatory markers such as IL-6, TNF-α, IL-1a, IL-17A, CTLA4, ESR, CRP, and cortisol, exerting anti-inflammatory effects (47, 137, 138). Additionally, it increases transforming growth factor-beta (TGF-β), supporting the survival of regulatory T cells, thereby preventing excessive immune system activity and autoimmunity (139). Vagus nerve stimulation, in addition to reducing inflammation by inhibiting cytokine production, plays a crucial role in maintaining intestinal homeostasis. Yoga practices can enhance vagal activity, helping to prevent the transition from symbiosis to dysbiosis or facilitate the reversal from dysbiosis to symbiosis. This process can support intestinal balance and reduce the progression of arthritis.(140) Studies suggest that regular yoga and meditation practices

Table 3: Suggested strategies for improving microbiomes in the elderly

Strategy	description	Scientific evidence
High fiber intake	Increase dietary fiber intake to feed beneficial bacteria	Improving microbiome diversity and reducing inflammation
Taking probiotics	Consume yogurt, kefir, and fermented foods to increase beneficial bacteria.	Strengthening the immune system and reducing the risk of disease
Regular physical activity	Aerobic and resistance training to improve microbiome composition and diversity	Increase beneficial bacteria such as Acremancy and Bifidobacterium
Stress and sleep management	Reducing stress and improving sleep quality to reduce gut-brain axis disorders	Improve cognitive function and reduce inflammation

role in maintaining intestinal homeostasis. Yoga practices can enhance vagal activity, helping to prevent the transition from symbiosis to dysbiosis or facilitate the reversal from dysbiosis to symbiosis. This process can support intestinal balance and reduce the progression of arthritis.(140) Studies suggest that regular yoga and meditation practices increase the diversity of the gut microbiome. Greater microbial diversity is associated with resilience to stress and a lower risk of gut-related disorders.(141) Gut microbes are essential for producing neurotransmitters such as serotonin, dopamine, and GABA. Yoga enhance vagal tone and reduce stress, indirectly promoting neurotransmitter production, which improves mood, cognition, and gut health (142).

3.14 Sleep Quality and gut microbiome

Sleep is an essential part of the circadian rhythm, which is regulated by the body's biological clock and is dependent on the natural cycles of light and darkness. This rhythm is controlled by the suprachiasmatic nucleus (SCN) in the hypothalamus of the brain (143). Research has shown that gut microbiomes possess their own circadian rhythms, characterized by fluctuations in composition, metabolic activity, and the secretion of signaling molecules.

Studies indicated that sleep quality directly influence the diversity and stability of the gut microbiome.(144) Sleep disturbances, such as fragmented or short-term sleep, can lead to maladaptive changes in the composition of the microbiome, resulting in dysbiosis (microbial imbalance). These changes often occur due to the activation of the hypothalamic-pituitary-adrenal (HPA) axis (145). Conversely, the gut microbiome also reciprocally influences sleep quality. Metabolic products of gut bacteria, such as short-chain fatty acids (SCFAs) like butyrate, have a direct impact on the body's clock genes and sleep patterns (146, 147). For instance, butyrate can improve sleep quality and plays a significant role in regulating the sleep-wake cycle. This indicates a cyclical relationship between sleep and the microbiome, where each affects the other (148). In addition, insufficient sleep, increases inflammation in the body, which can be explained through the gut microbiome. Poor or inadequate sleep raises levels of inflammatory markers such as TNFα and IL-6, which can negatively affect the immune system and overall body health (144). Insufficient or poor-quality sleep increases stress levels. Stress can disrupt the microbiome balance through the hypothalamic-pituitary-adrenal (HPA) axis. Specifically, elevated cortisol levels resulting from chronic stress may be associated with a reduction in beneficial bacteria such as Lactobacillus and Bifidobacterium (149). As we age, the diversity of the gut microbiome decreases, and the number of beneficial bacteria diminishes. These changes can lead to increased inflammation in the body, a phenomenon known as inflammaging.(150) Older adults commonly experience changes in circadian rhythms (such as lighter sleep and nighttime a phenomenon known as inflammaging (150). Older adults commonly experience changes in circadian rhythms (such as lighter sleep and nighttime awakenings). These changes can negatively affect the activity patterns of microbiomes. Reduced exposure to natural light and alterations in melatonin levels are also common in the elderly, affecting both sleep and microbiomes (151). Age-related diseases such as diabetes and cardiovascular diseases can have significant effects on the gut microbiome and sleep quality. In diabetes, metabolic disorders, including elevated blood sugar levels and insulin resistance, can alter the composition and diversity of the gut microbiome (152). This dysbiosis can lead to increased intestinal permeability (referred to as "leaky gut"), allowing harmful microbial components to enter the bloodstream, potentially triggering systemic inflammation and affecting sleep patterns. Furthermore, changes in the microbiome can exacerbate metabolic disturbances, creating a negative feedback loop that impacts overall health (153, 154). Sleep deprivation or poor-quality in older adults can increase stress hormones like cortisol, which leads to changes in the microbiome and an increase in systemic inflammation. These changes may increase the risk of developing gut-related diseases, such as Irritable Bowel Syndrome (IBS) and Inflammatory Bowel Disease (IBD) (155, 156). Research indicates that in older adults, short-term sleep is associated with an increase in inflammation-related bacteria such as Blautia and a decrease in beneficial bacteria, including Verrucomicrobia and Lentisphaerae. In contrast, the effect of sleep disturbances on the microbiome in younger individuals is inconsistent and requires further evidence (145). Microbial changes caused by poor sleep reduce the production of short-chain fatty acids (SCFAs), such as butyrate. These compounds play a key role in reducing inflammation and maintaining muscle health. Moreover, the increase in pro-inflammatory bacteria activates inflammatory pathways, leading to muscle degradation through anabolic resistance and enhanced catabolic processes. These processes, particularly in older adults, result in reduced muscle quality and volume, ultimately contributing to sarcopenia (157, 158). Researchers believe that investigating microbial changes caused by sleep disturbances over a lifetime and identifying intervention methods, such as dietary modifications or sleep management, can help improve muscle health and reduce chronic inflammation (159).

4. Conclusion

Aging causes significant changes in the gut microbiome. marked by reduced beneficial bacterial diversity and increased pathogenic microorganisms. These changes impact essential physiological systems, resulting in chronic inflammation, cognitive decline, metabolic disorders, and immune dysfunction. The gut-brain axis, immune-gut interactions, and nutrient metabolism pathways are crucial mechanisms linking microbiome changes to health outcomes in older adults. Targeted interventions can reduce the negative impacts of microbiome changes. Maintaining a fiber- and probiotic-rich diet, exercising regularly, and managing stress effectively enhance gut microbiome diversity and overall health. Some sports, such as yoga and tai chi, which combine physical movement with mental focus, show potential for regulating the gut-brain axis and enhancing microbiome composition. Proper hydration and quality sleep promote gut health by reducing inflammation and maintaining microbial balance. This review highlights the need for a holistic approach to health in aging, stressing the connection between the gut microbiome and overall well-being. Further research should prioritize personalized interventions and longitudinal studies to enhance microbiome-targeted strategies for aging populations. Understanding the gut microbiome allows us to create effective tools. that improves quality of life and lessens the impact of age-related diseases.

This study shows that there are the following research gaps regarding changes in the gut microbiome during aging:

1)It is essential to investigate the impact of lifestyle-based interventions such as genetics and microbiome composition to improve gut health

2) The impact of factors such as air pollution, climate and geographical changes on the gut microbi-

ome during aging:

1) It is essential to investigate the impact of lifestyle-based interventions such as genetics and microbiome composition to improve gut health

2) The impact of factors such as air pollution, climate and geographical changes on the gut microbiome has been less studied.

3) The exact mechanism by which adequate sleep and water intake affect the gut microbiome remains unclear and requires further research.

4) It is recommended that further research be conducted on the mechanism of effectiveness of functional exercises such as yoga and tai chi, which can simultaneously activate the body and mind.

5. Acknowledgements

We are grateful to all the participants in this study.

6. Conflicts of Interest:

The authors declare no conflict of interest

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