



## Review

# Modulation of the Gut Microbiota through Precision Nutrition as a Physiological Countermeasure for Long-Duration Human Missions to Mars

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## SUMMARY

Long-duration human space missions present unique physiological challenges due to environmental stressors such as microgravity, ionizing radiation, confinement, and restricted dietary diversity. Among the biological systems affected by these conditions, the gut microbiota plays a critical role in regulating immune function, metabolic balance, and intestinal health. This systematic review evaluates current scientific evidence on alterations in gut microbiota during spaceflight and explores the potential of precision nutrition as a physiological countermeasure for long-duration human missions to Mars. Following PRISMA guidelines, studies published between 2000 and 2025 were analyzed from major scientific databases focusing on microbiome changes in astronauts and spaceflight analog environments. The results indicate that spaceflight conditions may alter microbial diversity and metabolic pathways, potentially affecting host immunity and nutrient metabolism. Evidence also suggests that targeted nutritional interventions, including prebiotics, probiotics, and personalized dietary strategies, may help maintain microbial stability and improve physiological resilience. These findings highlight the importance of microbiome-centered nutritional approaches for supporting astronaut health in future deep-space exploration missions.

## KEYWORDS

Gut Microbiota; Precision Nutrition; Microgravity; Astronaut Health; Mars Missions.

## INTRODUCTION

Human space exploration is entering a new phase characterized by the prospect of long-duration missions beyond low Earth orbit. Current exploration programs developed by organizations such as NASA and European Space Agency aim to enable crewed missions to Mars within the coming decades. These missions are expected to last between two and three years when considering travel, planetary surface operations, and return trajectories. The extreme duration of such missions introduces complex physiological and biomedical challenges that remain insufficiently understood.

One of the most critical concerns is the effect of the space environment on human biological systems. Microgravity alters fluid distribution, muscle mass, bone density, and immune responses, while cosmic radiation can induce DNA damage and oxidative stress (Garrett-Bakelman et al., 2019). These environmental stressors interact with other mission-related factors such as restricted diet diversity, confinement, psychological stress, and disrupted circadian rhythms.

Recent studies have highlighted the central role of the gut microbiota in maintaining physiological homeostasis under such conditions. The gut microbiome, composed of trillions of microorganisms including bacteria, archaea, and fungi, contributes to metabolic regulation, immune system maturation, and synthesis of essential metabolites such as short-chain fatty acids (SCFAs) (Turnbaugh et al., 2007). Alterations in microbiome composition, commonly referred to as dysbiosis, have been linked to inflammatory disorders, metabolic syndrome, and immune dysfunction.

Spaceflight has been shown to induce measurable shifts in microbial communities within the gastrointestinal tract. Experiments conducted aboard the International Space Station demonstrate that astronauts exhibit significant changes in microbial diversity during space missions (Voorhies et al., 2019). These alterations may influence nutrient absorption, immune competence, and susceptibility to opportunistic infections.

In response to these challenges, researchers have proposed precision nutrition as a promising countermeasure for main-





taining astronaut health. Precision nutrition integrates information from genomics, metabolomics, microbiome analysis, and physiological monitoring to design individualized dietary strategies that optimize metabolic and microbial balance (Ordovas et al., 2018).

This systematic review aims to synthesize current knowledge regarding the interaction between spaceflight conditions, gut microbiota dynamics, and nutritional interventions. The study specifically evaluates the potential of precision nutrition strategies as physiological countermeasures to support astronaut health during long-duration missions to Mars.

## LITERATURE BACKGROUND AND THEORETICAL FOUNDATIONS

The human gastrointestinal microbiota has emerged as a fundamental component of human physiology, influencing metabolic regulation, immune system development, and host–microbe interactions. Advances in microbiome research over the past two decades have significantly expanded our understanding of the complex ecosystem formed by trillions of microorganisms inhabiting the human digestive tract. These microbial communities contribute to essential biological processes, including nutrient metabolism, synthesis of vitamins, modulation of inflammatory responses, and maintenance of intestinal barrier integrity (Turnbaugh et al., 2007).

The concept of the human microbiome as a functional organ has been widely discussed in contemporary biomedical research. Microbial populations within the gastrointestinal tract interact dynamically with host metabolic pathways, producing bioactive metabolites such as short-chain fatty acids (SCFAs), neurotransmitter precursors, and immune-modulating compounds. These interactions are essential for maintaining physiological homeostasis and regulating host responses to environmental stressors (Koh et al., 2016).

In terrestrial environments, alterations in microbiome composition—commonly referred to as dysbiosis—have been associated with a wide range of health conditions, including inflammatory bowel disease, metabolic disorders, and immune dysregulation. Increasing evidence suggests that environmental conditions can significantly influence microbial composition, indicating that extreme environments such as spaceflight may also affect microbiome stability.

Human spaceflight introduces a unique set of environmental stressors that differ significantly from conditions on Earth. Microgravity, ionizing radiation, confinement, altered circadian rhythms, and restricted dietary diversity collectively create a complex physiological environment that can affect multiple biological systems. Research conducted during missions aboard the International Space Station has demonstrated that astronauts experience measurable physiological changes, including bone density loss, muscle atrophy, immune alterations, and metabolic shifts (Garrett-Bakelman et al., 2019).

Recent studies have also begun to investigate how these environmental stressors influence the gut microbiome. Preliminary findings indicate that spaceflight can alter microbial diversity and metabolic activity, potentially affecting nutrient absorption and immune regulation (Voorhies et al., 2019). These observations suggest that the gut microbiota may play an important role in mediating the physiological adaptation of humans to space environments.

The theoretical framework underlying microbiome research in space medicine is based on the concept of host–microbe co-adaptation. According to this perspective, the microbiota and the human host form an integrated biological system in which microbial metabolism influences host physiology and vice versa. Environmental changes affecting the host may therefore indirectly influence microbial populations, creating feedback mechanisms that can either stabilize or destabilize the microbiome ecosystem.

In the context of long-duration missions, these host–microbe interactions may become particularly important. Missions planned by organizations such as NASA and European Space Agency envision human exploration beyond low Earth orbit, including crewed missions to Mars that may last multiple years. Maintaining astronaut health under such conditions will require effective strategies to mitigate physiological risks associated with prolonged exposure to the space environment.

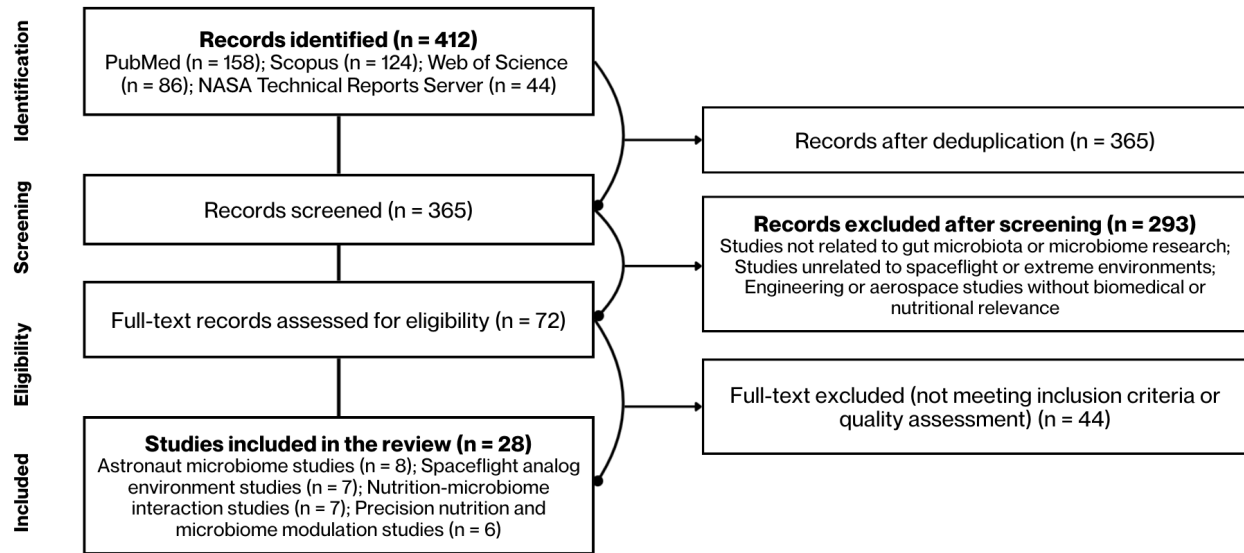
Nutrition represents one of the most powerful environmental modulators of the gut microbiome. Dietary substrates provide the primary energy sources for microbial metabolism, and variations in diet composition can lead to rapid changes in microbial community structure. Diets rich in fermentable fibers promote the growth of beneficial bacteria that produce short-chain fatty acids, which are essential for maintaining intestinal barrier function and regulating immune responses (Koh et al., 2016).

Building on these insights, the field of precision nutrition has emerged as a promising approach for optimizing diet based on individual biological characteristics. Precision nutrition integrates data from genomics, metabolomics, microbiome profiling, and physiological monitoring to design personalized dietary interventions. This approach recognizes that individuals may respond differently to the same dietary components due to variations in genetic background, metabolic pathways, and microbiome composition (Ordovas et al., 2018).

In the context of space exploration, precision nutrition may offer a novel strategy for maintaining microbiome stability and reducing health risks associated with long-duration missions. By tailoring dietary interventions to the unique biological profiles of astronauts, it may be possible to modulate microbial communities in ways that enhance metabolic resilience and immune function.

Moreover, advances in systems biology and computational modeling have made it possible to analyze complex interactions between diet, microbiota, and host physiology. These interdisciplinary approaches provide a theoretical foundation





**Figure 1. PRISMA flow diagram illustrating the study selection process for the systematic review**

A total of 412 records were identified through database searches in PubMed (n = 158), Scopus (n = 124), Web of Science (n = 86), and the NASA Technical Reports Server (n = 44). After removal of duplicates, 365 records remained for title and abstract screening. Following the screening process, 72 full-text articles were assessed for eligibility. Based on the predefined inclusion and exclusion criteria, 28 studies were included in the final qualitative synthesis examining gut microbiota modulation through precision nutrition in the context of long-duration human space missions to Mars.

for developing microbiome-targeted countermeasures that could support astronaut health during extended missions.

Taken together, current literature suggests that the gut microbiota represents a critical component of the human adaptive response to environmental stress. Understanding how microbial communities respond to the unique conditions of spaceflight is therefore essential for developing effective strategies to support human exploration of deep space..

## METHODS

### Review Design and Research Framework

This systematic review followed the guidelines established by the PRISMA 2020 statement, which provides a structured framework for identifying, screening, and synthesizing scientific evidence.

A comprehensive literature search was conducted across four major scientific databases: PubMed, Web of Science, Scopus, and the NASA Technical Reports Server. The search strategy included combinations of keywords related to spaceflight, microbiome research, and nutrition science. Terms such as spaceflight microbiome, gut microbiota astronaut, precision nutrition, space nutrition, and Mars mission human health were combined using Boolean operators.

The search covered publications from January 2000 to March 2025. This time range was selected because microbiome research began expanding significantly after the early

2000s with advances in next-generation sequencing technologies.

Studies were included if they investigated changes in gut microbiota during spaceflight or simulated spaceflight environments, or if they evaluated dietary interventions capable of modulating microbial composition in contexts relevant to human space exploration.

Articles were excluded if they lacked microbiome data, focused exclusively on unrelated animal models, or did not include nutritional or metabolic outcomes.

### PRISMA Study Selection

The initial search identified 412 records across the selected databases. After removing duplicates, 365 unique articles remained. Titles and abstracts were screened to identify potentially relevant studies, resulting in 72 articles selected for full-text analysis. Following application of inclusion and exclusion criteria, 28 studies were included in the final systematic review (Figure 1).

## RESULTS

The systematic analysis of the literature revealed consistent evidence that the spaceflight environment can induce measurable changes in the composition, diversity, and metabolic activity of the human gut microbiota. The studies included in this review were conducted in a variety of experimental con-



**Table 1. Nutritional Strategies for Gut Microbiota Modulation**

Nutritional Component	Mechanism	Potential Benefits for Astronaut Health
Prebiotics	Stimulate growth of beneficial bacteria	Increased microbial diversity
Probiotics	Introduce beneficial microbial strains	Immune system modulation
Dietary fiber	Fermentation producing short-chain fatty acids	Gut barrier protection
Polyphenols	Microbial metabolism generating bioactive compounds	Anti-inflammatory effects
Omega-3 fatty acids	Modulation of microbial metabolites	Reduced systemic inflammation

texts, including missions aboard the International Space Station, short-duration spaceflight experiments, and ground-based analog environments designed to simulate conditions of microgravity, confinement, and isolation.

Across the reviewed studies, spaceflight was associated with alterations in microbial diversity and shifts in bacterial community composition. These microbial changes appear to be driven by a combination of environmental and physiological stressors inherent to the space environment. Factors such as microgravity, exposure to ionizing radiation, altered circadian rhythms, limited dietary diversity, and psychological stress have all been proposed as contributors to microbiome alterations during space missions (Garrett-Bakelman et al., 2019).

One of the most frequently reported findings in the reviewed literature is a reduction in microbial diversity during prolonged spaceflight exposure. Microbial diversity is widely recognized as a key indicator of ecosystem stability within the gut environment. Reduced diversity has been associated with increased susceptibility to inflammation, metabolic dysregulation, and immune dysfunction in terrestrial studies (Turnbaugh et al., 2007). Evidence from astronaut microbiome analyses suggests that similar mechanisms may operate in spaceflight conditions.

For instance, longitudinal microbiome studies conducted on astronauts participating in missions of approximately six months demonstrated detectable changes in microbial composition during spaceflight. Voorhies et al. (2019) reported fluctuations in several bacterial taxa, including shifts in the relative abundance of members of the Firmicutes and Bacteroidetes phyla. These microbial groups are essential for the breakdown of dietary carbohydrates and the production of short-chain fatty acids (SCFAs), which are important regulators of intestinal health and immune function.

In addition to taxonomic changes, studies employing metagenomic sequencing have identified alterations in microbial metabolic pathways during space missions. The NASA Twins Study, which analyzed multi-omic data from astronaut Scott Kelly during a year-long mission, revealed changes in microbial genes associated with energy metabolism, vitamin synthesis, and lipid metabolism (Garrett-Bakelman et al., 2019). Although many of these changes were transient and partially reversed upon return to Earth,

the findings raise concerns regarding the potential long-term consequences of microbiome disruption during multi-year missions.

Research conducted in spaceflight analog environments has provided additional insights into the mechanisms underlying microbiome changes. Experiments involving prolonged bed rest, Antarctic research stations, and simulated Mars habitats have shown that factors such as reduced physical activity, confinement stress, and limited dietary variability can significantly influence gut microbial communities (Turroni et al., 2020). These findings suggest that microbiome alterations observed during space missions may result from the combined influence of environmental stressors and behavioral adaptations.

Dietary composition emerged as one of the most significant modifiable factors influencing microbiome stability in the reviewed studies. Several nutritional components were identified as potential modulators of microbial composition and activity, highlighting the relevance of nutritional strategies as countermeasures for microbiome dysbiosis in spaceflight (Table 1).

Fermentable dietary fibers play a particularly important role in maintaining microbiome homeostasis. Through microbial fermentation, fibers are converted into short-chain fatty acids such as butyrate, acetate, and propionate. These metabolites regulate intestinal barrier integrity, influence immune signaling pathways, and provide an energy source for colonocytes (Koh et al., 2016).

Several studies also explored the potential of probiotic supplementation as a strategy to maintain microbial balance during space missions. Probiotics have been shown to enhance mucosal immunity, inhibit pathogen colonization, and reduce inflammatory responses in terrestrial settings. Although evidence in astronaut populations remains limited, preliminary findings suggest that probiotic supplementation may contribute to maintaining microbial stability during extended missions.

Advances in multi-omics technologies have further enabled the development of precision nutrition approaches tailored to individual microbiome profiles. These approaches integrate microbiome sequencing, metabolomic analysis, and genomic data to optimize dietary interventions for specific physio-





logical needs (Table 2).

**Table 2. Components of Precision Nutrition for Space Missions**

Component	Application
Microbiome sequencing	Identification of microbial imbalances
Metabolomic profiling	Detection of metabolic responses to diet
Genomic analysis	Determination of individual nutrient metabolism
AI models	Predictive dietary optimization

The integration of these technologies could enable continuous monitoring of astronaut health and allow dynamic dietary adjustments aimed at preserving microbiome stability during long-duration missions.

### MECHANISMS OF GUT MICROBIOTA ALTERATION IN MICROGRAVITY

Understanding the mechanisms by which spaceflight conditions influence the gut microbiota is essential for identifying potential countermeasures capable of preserving astronaut health during long-duration missions. The space environment introduces several physiological and environmental stressors that can directly or indirectly influence microbial ecosystems within the gastrointestinal tract. Among these factors, microgravity, ionizing radiation, altered immune function, dietary constraints, and psychological stress represent the most significant contributors to microbiome alterations during spaceflight.

Microgravity is one of the most distinctive environmental characteristics of spaceflight and has profound effects on human physiology. In the absence of Earth's gravitational pull, bodily fluids undergo redistribution toward the upper body, which can influence gastrointestinal physiology and potentially affect microbial colonization patterns within the digestive tract. Microgravity has also been shown to alter gastrointestinal motility, which may influence the transit time of nutrients and microbial metabolites throughout the intestinal system. Changes in intestinal transit dynamics can alter nutrient availability for microbial fermentation processes, potentially leading to shifts in microbial community composition.

Experimental studies conducted in simulated microgravity environments suggest that bacterial growth behavior may also be directly affected by reduced gravitational forces. Some microorganisms exhibit altered gene expression, increased virulence, and modified biofilm formation under microgravity conditions. These microbial adaptations may contribute to changes in the overall structure and metabolic activity of the gut microbiota during spaceflight. Such findings

highlight the complex interaction between physical environmental factors and microbial physiology in the space environment.

Another important mechanism influencing microbiome dynamics is exposure to ionizing radiation. Beyond the protective magnetosphere of Earth, astronauts are exposed to higher levels of galactic cosmic radiation and solar particle events. Ionizing radiation has been shown to induce oxidative stress and DNA damage in both host tissues and microbial cells. Animal studies investigating radiation exposure have reported significant changes in microbial diversity, including reductions in beneficial bacterial populations and increases in opportunistic pathogens. These alterations may contribute to inflammatory responses and compromise intestinal barrier function.

Immune system alterations observed during spaceflight may further influence microbiome stability. Astronauts frequently experience immune dysregulation characterized by altered cytokine production, decreased T-cell activation, and reactivation of latent viruses. Because the immune system plays a central role in regulating microbial populations within the gut, immune suppression may allow opportunistic microbial species to proliferate, thereby contributing to dysbiosis. The bidirectional interaction between the immune system and gut microbiota suggests that immune alterations and microbiome changes may reinforce each other during space missions.

Dietary factors represent another key mechanism affecting microbiome composition during spaceflight. Astronaut diets are designed to provide balanced nutrition while meeting the strict requirements of long-term storage, limited volume, and safety in microgravity conditions. However, the available food options often have lower diversity compared with typical terrestrial diets, and access to fresh foods such as fruits and vegetables is limited. Reduced intake of dietary fibers and phytochemicals may decrease the availability of substrates required for beneficial microbial fermentation, potentially leading to shifts in microbial metabolism.

Psychological stress associated with confinement, isolation, and high workload may also influence microbiome composition through the gut-brain axis. Stress-related hormonal responses, particularly increased cortisol levels, can affect gastrointestinal physiology and immune regulation, indirectly influencing microbial populations within the digestive tract.

Taken together, these factors illustrate that microbiome alterations during spaceflight likely arise from the interaction of multiple physiological and environmental mechanisms. Understanding these mechanisms is critical for developing targeted countermeasures aimed at preserving microbial balance and supporting astronaut health during extended missions.





## DISCUSSION

The findings of this systematic review highlight the central role of the gut microbiota in mediating human physiological adaptation to the space environment. The human microbiome is increasingly recognized as an integral component of host physiology, influencing metabolic processes, immune regulation, and neuroendocrine signaling.

In the context of long-duration spaceflight, disruptions in microbiome composition may represent an underappreciated risk factor for astronaut health. Spaceflight conditions introduce multiple stressors that can simultaneously affect both host physiology and microbial ecosystems. Microgravity, for example, alters gastrointestinal motility and fluid distribution, which may influence microbial colonization patterns within the intestinal tract.

Exposure to cosmic radiation represents another potential driver of microbiome alteration. Ionizing radiation has been shown to induce oxidative stress and DNA damage in both host tissues and microbial cells. Animal studies have demonstrated that radiation exposure can significantly alter microbial diversity and increase the prevalence of opportunistic pathogens, raising concerns about similar effects during deep-space missions.

Dietary constraints during space missions further contribute to microbiome instability. Astronaut diets are carefully formulated to provide adequate macronutrient and micronutrient intake; however, limitations in food storage, shelf life, and variety may restrict the diversity of dietary substrates available for microbial metabolism. Reduced intake of fresh fruits, vegetables, and complex fibers may decrease the availability of substrates necessary for beneficial microbial fermentation processes.

Maintaining microbiome stability may therefore be essential for preserving immune competence during long-duration missions. Astronauts frequently exhibit signs of immune dysregulation during spaceflight, including altered cytokine profiles, reduced T-cell function, and reactivation of latent viral infections (Garrett-Bakelman et al., 2019). Because the gut microbiota plays a key role in immune system regulation, disruptions in microbial composition may contribute to these immune alterations.

Precision nutrition represents a promising strategy to address these challenges. By integrating individual biological data with advanced analytical technologies, precision nutrition approaches can provide personalized dietary interventions designed to optimize microbial balance and metabolic health. This approach is particularly relevant in space missions, where preventive strategies are critical due to limited medical resources.

Future missions to Mars will likely incorporate advanced biomedical monitoring systems capable of continuously as-

sessing astronaut physiological parameters. Emerging technologies such as portable sequencing devices and biosensors could enable real-time monitoring of microbiome composition, allowing dietary interventions to be adjusted dynamically during the mission.

Another promising area of research involves the development of functional foods specifically engineered for spaceflight conditions. These foods could be designed to include targeted combinations of prebiotics, probiotics, and bioactive compounds that promote microbial stability and support immune function. Such nutritional systems may become a fundamental component of life-support strategies in future interplanetary missions.

Despite these promising developments, important knowledge gaps remain. The limited number of astronauts available for study restricts the statistical power of spaceflight microbiome research. Moreover, current missions aboard the International Space Station typically last six to twelve months, whereas missions to Mars may extend for several years. Long-term studies in simulated space environments will therefore be essential to better understand microbiome dynamics under prolonged isolation and microgravity exposure.

In conclusion, the modulation of gut microbiota through precision nutrition represents a promising physiological countermeasure for maintaining astronaut health during long-duration space missions. Continued research integrating microbiome science, nutritional genomics, and space medicine will be crucial for enabling safe and sustainable human exploration of deep space.

## IMPLICATIONS FOR LONG-DURATION MISSIONS TO MARS

The potential for microbiome alterations during spaceflight has important implications for the future of human exploration beyond low Earth orbit. Missions planned by organizations such as NASA and European Space Agency envision crewed expeditions to Mars that may last between two and three years when accounting for travel time, planetary surface operations, and return to Earth. Such missions will expose astronauts to prolonged environmental stressors, making the maintenance of physiological health a critical priority.

The gut microbiota may play a central role in determining the ability of astronauts to adapt to these conditions. Because microbial communities influence immune function, nutrient metabolism, and inflammatory responses, disruptions in microbiome stability could increase susceptibility to illness during long-duration missions. In the context of deep-space exploration, even minor health complications may pose significant operational risks due to the limited availability of medical resources and the extended distance from Earth.





One major concern is the potential impact of microbiome dysbiosis on immune competence. Astronauts operating in deep-space environments must maintain strong immune defenses to prevent infections that could compromise mission performance. If microbiome alterations contribute to immune suppression or inflammatory imbalance, the risk of illness during long-duration missions may increase.

Metabolic health is another critical consideration. The gut microbiota participates in energy metabolism, nutrient absorption, and regulation of metabolic pathways. Alterations in microbial metabolism could influence how astronauts utilize nutrients, potentially affecting energy balance and physical performance during extended missions.

From a nutritional perspective, maintaining microbiome stability during missions to Mars will require innovative food system designs. Future space nutrition strategies may include the development of microbiome-supportive diets that incorporate fermentable fibers, functional foods, and targeted prebiotic compounds. These dietary components may help maintain beneficial microbial populations and support metabolic homeostasis.

Advances in biotechnology may also enable the production of fresh foods during long-duration missions through controlled ecological life-support systems. Plant cultivation systems and bioregenerative food production technologies could provide astronauts with fresh vegetables and other nutrient-rich foods that support microbiome diversity.

In addition, emerging technologies such as portable DNA sequencing devices may allow astronauts to monitor microbiome composition in real time during space missions. Such capabilities could enable early detection of microbiome imbalances and allow for rapid dietary adjustments aimed at restoring microbial equilibrium.

The integration of microbiome monitoring with precision nutrition strategies may therefore become an essential component of life-support systems for deep-space exploration. Personalized dietary interventions tailored to individual microbiome profiles could help maintain immune resilience, metabolic stability, and overall physiological health throughout the mission.

Ultimately, understanding how the gut microbiota responds to the extreme conditions of spaceflight will be essential for enabling sustainable human exploration of the solar system. Research conducted aboard the International Space Station continues to provide valuable insights into these processes and will serve as a critical foundation for preparing future missions to Mars.

Continued interdisciplinary research integrating microbiology, nutrition science, aerospace medicine, and systems biology will be necessary to translate these insights into practical countermeasures capable of supporting astronaut health

during the next era of human space exploration.

## LIMITATIONS OF CURRENT RESEARCH

Despite the growing interest in the role of the gut microbiota in human spaceflight, the current body of literature remains limited in several important aspects. One of the most significant limitations arises from the small number of astronauts available for study. Human spaceflight missions involve relatively small crews, which restricts sample sizes and limits the statistical power of microbiome analyses conducted in spaceflight environments. As a result, many studies rely on observational data from a limited number of participants, which may reduce the generalizability of the findings.

Another important limitation concerns the duration of existing spaceflight studies. Most microbiome research conducted in space has been carried out during missions aboard the International Space Station, which typically last between six and twelve months. While these missions provide valuable insights into physiological adaptation to microgravity, they are considerably shorter than the missions currently envisioned for human exploration of deep space. Future missions to Mars are expected to last multiple years, and the long-term effects of prolonged exposure to microgravity, cosmic radiation, and confinement on the gut microbiota remain largely unknown.

A further limitation arises from methodological variability across studies. Differences in experimental design, sample collection procedures, sequencing technologies, and data analysis pipelines make it difficult to directly compare results between studies. Some investigations rely on 16S rRNA sequencing, while others employ metagenomic or multi-omics approaches, leading to variability in the level of taxonomic and functional resolution obtained. Additionally, variations in astronaut diet, mission duration, and environmental conditions may contribute to differences in microbiome outcomes reported across studies.

Another challenge lies in distinguishing between microbiome changes caused by spaceflight itself and those resulting from related factors such as dietary modifications, altered circadian rhythms, or psychological stress associated with confinement. Many studies rely on limited baseline data collected before flight, which can complicate the interpretation of microbiome changes observed during missions.

Finally, while several ground-based analog environments have been used to simulate aspects of spaceflight, these models cannot fully reproduce the complex combination of factors present in the actual space environment. Simulated microgravity experiments and isolation studies provide valuable insights but may not accurately capture the physiological effects of prolonged exposure to microgravity and cosmic radiation.





Together, these limitations highlight the need for more comprehensive and standardized research approaches to better understand microbiome dynamics in spaceflight conditions.

## FUTURE RESEARCH DIRECTIONS

Future research on the interaction between spaceflight conditions and the gut microbiota should focus on developing more comprehensive and integrative approaches capable of addressing the current knowledge gaps identified in this review. As human exploration moves toward long-duration interplanetary missions, understanding how microbial ecosystems respond to extreme environmental conditions will be essential for maintaining astronaut health.

One promising direction involves the development of real-time microbiome monitoring technologies for use during space missions. Advances in portable genomic sequencing devices may allow astronauts to analyze microbial communities directly in space. These technologies could enable continuous monitoring of gut microbiota composition and provide early detection of dysbiosis or microbial imbalances. Real-time data could then be used to guide personalized dietary interventions or other countermeasures during the mission.

Another important area of research concerns the development of functional foods designed specifically for the space environment. Future astronaut diets may include foods enriched with prebiotics, probiotics, and bioactive compounds capable of promoting beneficial microbial populations. These foods could help maintain microbial diversity and support immune function during long periods of confinement and microgravity exposure.

The integration of precision nutrition strategies represents another key avenue for future investigation. By combining microbiome profiling with genomic and metabolomic data, researchers may be able to design individualized dietary plans optimized for each astronaut's biological characteristics. Such personalized approaches could help maintain metabolic balance, support immune resilience, and enhance overall physiological performance during long-duration missions.

In addition, future research should explore the potential of bioregenerative life-support systems capable of producing fresh foods during space missions. Controlled agricultural systems, including hydroponic and aeroponic plant cultivation, could provide astronauts with fresh fruits and vegetables rich in dietary fibers and phytochemicals that support microbiome diversity.

Long-duration simulation studies conducted in analog environments on Earth may also play a critical role in advancing this field. Isolation experiments, Antarctic research stations, and Mars simulation habitats can provide valuable opportu-

nities to investigate microbiome changes under prolonged confinement and limited resource conditions.

Ultimately, advancing research in space microbiome science will require interdisciplinary collaboration among fields such as microbiology, nutritional science, aerospace medicine, systems biology, and artificial intelligence. Integrating these disciplines will be essential for developing effective microbiome-targeted countermeasures capable of supporting astronaut health during future missions to Mars.

## CONCLUSION

The findings synthesized in this systematic review highlight the growing importance of the gut microbiota as a central component of human physiological resilience in extreme environments. As human space exploration progresses toward long-duration interplanetary missions, maintaining astronaut health will require a comprehensive understanding of how environmental stressors influence biological systems at multiple levels. Evidence from studies conducted during missions aboard the International Space Station and from terrestrial spaceflight analog environments consistently demonstrates that spaceflight conditions can alter the composition, diversity, and metabolic activity of the gut microbiome.

These microbial alterations appear to be driven by a complex interaction between microgravity, ionizing radiation, confinement, psychological stress, and limited dietary diversity. Such changes may have important implications for astronaut health because the gut microbiota plays a fundamental role in regulating immune function, metabolic homeostasis, and intestinal barrier integrity. Disruptions in microbial balance have been associated with immune dysregulation, increased inflammation, and altered metabolic responses, all of which represent potential risks during extended space missions.

Within this context, the concept of precision nutrition emerges as a promising countermeasure for maintaining microbiome stability and supporting astronaut health.

By integrating advances in microbiome sequencing, metabolomics, genomic analysis, and computational modeling, precision nutrition enables the development of individualized dietary strategies tailored to the biological characteristics of each crew member. Such personalized approaches may allow for targeted modulation of microbial communities, helping to preserve metabolic balance and immune resilience during prolonged exposure to the space environment.

Furthermore, future space missions may benefit from the integration of real-time biomedical monitoring systems capable of tracking microbiome dynamics during flight. Emerging technologies such as portable genomic sequencing devices



and automated biosensors could provide continuous feedback on astronaut physiological status, enabling dynamic dietary adjustments throughout the mission. These innovations may transform nutrition from a static support system into an adaptive countermeasure capable of responding to physiological changes in real time.

In addition to personalized dietary strategies, the development of functional foods specifically engineered for space-flight conditions represents an important direction for future research. Foods enriched with targeted combinations of pre-biotics, probiotics, dietary fibers, and bioactive compounds could help sustain beneficial microbial communities and mitigate the physiological stress associated with long-duration missions.

Despite significant advances in microbiome science and space medicine, several important knowledge gaps remain. The small number of astronauts available for research limits the statistical power of many existing studies, and most current investigations have been conducted during missions of relatively short duration. In contrast, future missions to Mars may last several years, exposing astronauts to prolonged environmental stressors whose cumulative effects on the microbiome remain poorly understood. Consequently, additional research using ground-based analog environments, long-duration isolation experiments, and advanced omics technologies will be essential to better characterize microbiome dynamics under deep-space conditions.

Ultimately, the successful implementation of microbiome-targeted nutritional strategies will require close collaboration between fields such as microbiology, nutritional science, aerospace medicine, systems biology, and artificial intelligence. Interdisciplinary research efforts will be necessary to translate laboratory findings into practical countermeasures capable of supporting astronaut health during interplanetary exploration.

In summary, current evidence suggests that modulation of the gut microbiota through precision nutrition represents a promising and potentially critical strategy for mitigating physiological risks during long-duration human space missions. Continued research in this area will not only advance the field of space medicine but may also generate valuable insights into microbiome-based healthcare strategies applicable to extreme environments on Earth and beyond.

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#### DECLARATION OF INTERESTS

The authors declares that there are no conflicts of interest.

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