DOI:10.31557/APJCC.2026.11.5.777

REVIEW

The Crosstalk Between Exercise, the Gut Microbiome, and Cancer: Mechanistic Insights and Therapeutic Perspectives

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Abstract

The bidirectional interaction between exercise, the gut microbiome, and cancer has become a key biological connection linking metabolism, immunity, and tumor biology. Growing evidence shows that physical activity not only lowers cancer risk but also affects treatment response, partly through microbiome-related mechanisms. This review combines experimental and clinical studies from 2010 to 2025 to explain how different types and intensities of exercise influence gut microbial composition, microbial metabolites, immune regulation, and cancer pathways. Regular moderate exercise consistently improves gut microbial diversity, boosts beneficial bacteria, and raises short-chain fatty acid (SCFA) production, which reduces systemic inflammation, strengthens intestinal barriers, and enhances immune monitoring. Conversely, gut dysbiosis promotes cancer development through chronic inflammation, genotoxic metabolite production, weakened mucosal defenses, and changes in tumor microenvironment signaling. New evidence suggests that exercise impacts bile acid metabolism, hydrogen sulfide levels, and reactive oxygen and nitrogen species, forming key links between muscle activity, gut immunity, and tumor control. Notably, while moderate and sustained physical activity provides protective effects via the microbiome, excessive or long-term high-intensity exercise might temporarily disrupt gut barrier function and increase inflammation. Although clinical applications are still limited, current research indicates that combining structured exercise programs with microbiome-targeted strategies could be a promising approach for cancer prevention and treatment, especially in colorectal cancer. Collectively, this review provides a mechanistic framework for understanding exercise–microbiome–cancer crosstalk and highlights future directions toward personalized, microbiome-informed exercise prescriptions to improve metabolic health, immune competence, and cancer outcomes.

Keywords: Exercise- Physical Activity- Gut Microbiome- Cancer- Colorectal Cancer- Dysbiosis- Short-Chain Fatty Acids

Asian Pac J Cancer Care, **11 (5)**, 777-788

Submission Date: 05/19/2026 Acceptance Date: 07/22/2026

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Introduction

The gut microbiome, a diverse community of trillions of microorganisms within the human gastrointestinal system, plays a vital role in supporting host health and maintaining balance. Its main function is aiding in nutrient digestion and absorption, while also producing essential vitamins and nutrients that the body cannot generate on its own. The microbiome significantly influences the development and maturation of the immune system. Beyond nutrient digestion and vitamin biosynthesis, the gut microbiome actively regulates immune surveillance and inflammatory tone through continuous bidirectional signaling with host immune cells [1].

Additionally, the close communication between gut microbiota and immune cells establishes a symbiotic relationship that significantly shapes systemic immune responses. An imbalance in this microbial community can lead to the development of various diseases [2]. Beneficial microbes help protect humans from harmful microbes in a simple way. It is now understood that many complex diseases, such as obesity, type 2 diabetes, rheumatoid arthritis, fatty liver disease, inflammatory bowel diseases, Alzheimer's, Parkinson's, schizophrenia, cancer, and others, are negatively affected by dysfunctional microbiota [3-13].

Current research on whether different exercise types can lower inflammatory markers is still highly debated. Some studies support that exercise positively impacts inflammation in obese people, including aerobic, resistance, and other types of training. These findings indicate that regular, moderate exercise can influence the immune system, reduce chronic inflammation, and improve metabolic issues linked to obesity [14].

Importantly, dysbiosis-driven chronic inflammation and microbial metabolite imbalance are increasingly recognized as central contributors to carcinogenesis. The gut microbiome is a diverse collection of microorganisms inhabiting the gastrointestinal tract, playing a crucial role in human health and physiological functions [15, 16].

In cancer treatment, the interaction between anticancer drugs and the gut microbiome has become a focus, as disturbances in microbiome composition and function can affect drug metabolism, effectiveness, and side effects [16]. Importantly, dysbiosis-driven chronic inflammation and microbial metabolite imbalance are increasingly recognized as central contributors to carcinogenesis [17, 18].

Exercise has been shown to enhance immune checkpoint inhibitor efficacy in preclinical and clinical models, yet the microbiome-dependent mechanisms underlying this effect remain largely unexplored. A healthy microbiome promotes proper drug metabolism, boosts immune responses, and minimizes side effects, emphasizing its vital role in the success of cancer therapies [17].

Exercise has long been recognized for reducing cancer risk and boosting treatment effectiveness, with increasing evidence suggesting that physical activity can improve outcomes with immune checkpoint inhibitors (ICIs) in both preclinical and clinical settings. While increased T cell infiltration and immune activation are thought to contribute to this benefit, the exact mechanisms by which exercise enhances ICI responses remain unclear. Earlier research has demonstrated that exercise can alter the gut microbiome's composition in both mice and humans. A study published in Cell by Phelps et al. highlights the vital role of the gut microbiota in mediating exercise's immunological benefits in melanoma [19].

Although there has been significant research into how the gut microbiome influences immune regulation and the response to anticancer therapies, as well as growing evidence of exercise's benefits on metabolism, inflammation, and immune health, the detailed mechanistic relationship between exercise, the gut microbiome, and cancer remains underexplored. Most prior studies have examined the effects of exercise or microbiota on cancer separately [20, 21].

Despite growing interest in the independent roles of exercise and the gut microbiome in cancer biology, integrative mechanistic analyses examining their combined effects on tumor immunity and progression are scarce. Therefore, this review aims to synthesize current mechanistic and clinical evidence to elucidate how exercise-driven modulation of the gut microbiome influences cancer development, immune regulation, and therapeutic responsiveness.

Search strategy

This narrative review was conducted in accordance with established recommendations for transparent literature synthesis. Studies published between 2010 and 2025 investigating the relationships among exercise, physical activity, gut microbiome composition, and cancer were systematically searched in PubMed, Scopus, and Web of Science databases.

An initial database search was performed, followed by duplicate removal and screening of titles and abstracts. Full-text assessment was subsequently conducted, and studies meeting the predefined inclusion criteria were included in the final analysis. We included only original preclinical and clinical research articles published in English. Review articles, editorials, commentaries, and studies lacking direct relevance to exercise–microbiome interactions in cancer were excluded.

Results and Discussion

1. The gut microbiome and cancer

The gut microbiome plays a vital role in cancer development and treatment by interacting with the immune system and the tumor microenvironment. Evidence consistently links gut microbiota composition to cancer progression [22]. The human microbiome is a complex, multispecies community that interacts symbiotically with the host at various body sites. These host-microbiome interactions influence numerous physiological processes and are associated with various multifactorial diseases.

Over the past decade, microbiome communities have been linked to the development, progression, metastasis,

and treatment responses of multiple cancer types. Although causal relationships are still being investigated, gaining a deeper molecular understanding of these cancer-related interactions is regarded as highly important scientifically and clinically [23].

The microbiome, which encompasses the total number of microorganisms and their genetic material, often greatly influences human health. It differs from the microbiota, which refers specifically to the microbial communities in various body ecosystems [24, 25]. These microbiotas perform numerous complex biochemical and metabolic functions [26].

The native microbiota can also influence epithelial and systemic responses, including the development and activity of the immune system, affecting antitumor responses. Disruptions to the symbiosis between mammalian hosts and their microbial partners can lead to various diseases, notably affecting the development and progression of colorectal cancer (CRC). As the third most common cancer in the US, with an estimated 153,020 cases per 100,000 people in 2023, and the second leading cause of cancer-related death, with around 52,550 deaths per 100,000 people, CRC imposes substantial morbidity and healthcare challenges [27].

Growing evidence indicates that the gut bacterial microbiome significantly influences carcinogenesis. Recent studies suggest that dysbiosis disruption of the microbial balance along with immune system changes, the production of genotoxic substances, and alterations in metabolic pathways could all contribute to the initiation and progression of cancer [28].

Recent studies have revealed a significant connection between the human microbiome's composition and the development of various cancers, although this research is still in its early stages. Improvements in high-throughput sequencing techniques have uncovered relationships that were previously difficult to identify because many microbes cannot be cultured in the lab (fewer than 30% of species are culturable).

Evidence from human and animal studies indicates that dysbiosis may be linked to chronic inflammation and the activation of pathways that promote cancer. In esophageal cancer, notable changes in bacterial populations have been documented: normally, Streptococcus species dominate, but in conditions such as esophagitis, Barrett's esophagus, or esophageal adenocarcinoma, there's an increase in anaerobic gram-negative bacteria, such as Veillonella and Fusobacterium [29, 30].

Additionally, Toll-like receptors (TLRs) are expressed at higher levels across various stages of gastric and esophageal cancers, suggesting a reciprocal interaction between microbes and the innate immune system in cancer progression. In colorectal cancer, Fusobacterium nucleatum, along with species like Porphyromonas, Peptostreptococcus, Prevotella, Parvimonas, Leptotrichia, and Campylobacter, are often found in tumor tissues [31-37].

These microbes have been linked to processes such as inflammation, disruption of the mucosal barrier, and epigenetic alterations. Metagenomic studies reveal that the fecal microbial profile of colorectal cancer patients differs notably in diversity and abundance from that of healthy individuals, sometimes matching the accuracy of fecal occult blood tests (FOBT) for cancer screening [36].

Supporting animal studies show germ-free mice with genetic predispositions to cancer (like p53 or APC gene deletions) develop fewer tumors, but recolonising their microbiome increases intestinal adenocarcinoma risk [38-41]. These findings imply that intestinal bacteria, especially species like F. nucleatum and B. fragilis, may contribute to cancer development through inflammation and immune system disruption [42].

2. Microbiome and Histopathological Correlates in Cancer

Accumulating immunohistochemical and histopathological evidence demonstrates that gut microbiome dysbiosis is closely associated with precancerous lesions and early malignant transformation. Immunohistochemical studies have confirmed that Toll-like receptor (TLR) expression is significantly upregulated across gastrointestinal carcinogenesis. In gastric cancer, TLR2 and TLR4 are overexpressed in tumor epithelium and correlate with NF-κB activation and H. pylori infection [43-45]. In colorectal cancer, TLR4 expression increases progressively from dysplastic crypts to invasive adenocarcinoma, while TLR2, TLR4, and TLR5 are elevated in colonic adenomas and associated with dysbiosis [46, 47].

Histopathologically, dysbiosis is directly linked to tissue-level premalignant alterations. In Barrett's esophagus, a shift from Streptococcus-dominant microbiota toward gram-negative anaerobes, including Veillonella and Fusobacterium, is accompanied by intestinal metaplasia, crypt architectural distortion, and dysplastic transformation of the esophageal epithelium [29, 30, 48]. In colorectal adenomas, enrichment of Fusobacterium nucleatum and Bacteroides fragilis correlates with epithelial DNA damage, nuclear atypia, and progression from low-grade dysplasia to invasive carcinoma [37, 49, 39, 41]. Metagenomic and tissue-based analyses have shown that enrichment of taxa such as Fusobacterium nucleatum and Bacteroides fragilis correlates with epithelial DNA damage, activation of oncogenic signaling pathways, and progression from low-grade dysplasia to invasive carcinoma [31-33].

Within the tumor microenvironment, IHC profiling reveals that Fusobacterium nucleatum-enriched tumors exhibit reduced $CD8^+$ T cell infiltration and increased PD-L1 expression [50]. Microbial metabolites, particularly short-chain fatty acids, promote M2 macrophage polarization and regulatory T cell accumulation, visualized via CD163 and FoxP3 immunostaining [51, 52]. These stromal and immune alterations provide a direct histopathological link between microbial composition and tumor behavior [53, 54].

Collectively, these immunohistochemical and histopathological findings bridge microbiome-driven molecular mechanisms with observable tissue-level pathology, demonstrating that microbial modulation

affects not only systemic immunity but also epithelial architecture, stromal composition, and immune infiltration within premalignant and malignant tissues.

3. Exercise as a modulator of the gut microbiome

The relationship between microbial diversity and metabolic health is closely linked to physical activity. Regular exercise promotes microbial diversity, creating a favorable environment for beneficial microbes that boost SCFA production. It also enhances overall well-being, including physical, mental, and gut health, through complex biological interactions. Regular physical activity helps manage and lower the risk of metabolic syndrome while also improving mental health, reducing anxiety, and alleviating depression [55, 56].

Exercise triggers an acute increase in interleukin-6 (IL-6), which helps decrease inflammation [49], Prolonged strenuous exercise can temporarily raise inflammation levels due to muscle damage. These effects also influence gut health, with regular exercise linked to reduced gut dysbiosis-related diseases [57-59].

Although the exact mechanisms are still under study, recent research shows that high-intensity, long-duration exercise may cause gut permeability and dysbiosis, whereas moderate exercise supports microbiome health [60]. Different types of exercise, such as endurance, resistance, or sports, have varying impacts on the microbiome [61].

Studies indicate that athletes often develop unique microbiome profiles after exercise, enriched with beneficial microbes and SCFAs [62]. In older adults, greater muscle strength correlates with specific microbiome compositions, suggesting that a healthy microbiome aids in preserving strength and function with age [63]. Conversely, a weakened gut barrier can lead to joint inflammation, impairing movement and physical performance [64].

Interventions combining various exercise routines, such as aerobic and resistance training, tend to have a greater effect on bacterial diversity than resistance training alone. Studies suggest that low-intensity exercise might offer only a modest benefit to gut microbiota diversity, whereas high-intensity workouts could have a more notable impact. Nevertheless, research also indicates that intense, prolonged exercise might elevate inflammation levels [60, 65].

Exercise impacts gut health through several interconnected mechanisms. During activity, mitochondria in skeletal muscles produce reactive oxygen and nitrogen species (RONS). RONS can activate immune responses in colon lining cells via serotonin pathways [66]. The immune response's effectiveness is closely tied to gut microbiota development [67].

Moderate aerobic exercise increases immunoglobulin A levels in the gastrointestinal tract, helping the gut microbiota prevent pathogen colonization [68]. Regular moderate exercise, especially resistance training, reduces circulating lipopolysaccharides (LPS) and toll-like receptor expression [69], leading to less inflammation and better gut barrier function [70].

Studies show exercise plays a key role in regulating bile acid pools, promoting gut microbiota health [71]. Bile salt metabolism is vital for microbiota function, with secondary bile acids activating receptors like FXR and G-protein-coupled bile acid receptor, which are crucial in energy metabolism. The microbiota can modulate metabolic capacity and muscle growth by inhibiting FXR [72].

Additionally, hydrogen sulfide, produced from cysteine breakdown by gut microbiota, regulates intestinal immune and epithelial cells [73]. Hydrogen sulfide may be a target for boosting muscle growth and function; supplementation with sodium hydrosulfide enhances myogenic gene expression and muscle regeneration in mice [74].

The effects of different exercise modalities and intensities on gut microbiome composition, microbial metabolites, and cancer-relevant biological pathways are summarized in Table 1.

4. Microbiome-Mediated Effects of Exercise Intensity and Duration on Cancer Risk

The impact of exercise on cancer risk depends strongly on intensity and duration, with the gut microbiome serving as a central mediator. Regular moderate-intensity exercise consistently enhances microbial diversity, increases SCFA production, and suppresses chronic inflammation key mechanisms underlying cancer prevention, particularly

Table 1. Exercise-Induced Modulation of the Gut Microbiome and Associated Mechanisms Relevant to Cancer.

Exercise Modality / Intensity	Microbiome Changes	Key Microbial Metabolites	Immunological & Molecular Effects	Cancer-Relevant Outcomes
Moderate aerobic exercise	↑ Microbial diversity↑ SCFA-producing taxa (e.g., Faecalibacterium, Roseburia)	SCFAs (butyrate, acetate, propionate)	↑ Gut barrier integrity↓, Pro-inflammatory cytokines (TNF-α, IL-6)↑ , Treg differentiation	↓ Colorectal cancer risk↓: Chronic inflammation, improved immune surveillance
Resistance training	↑ Beneficial commensals↓: LPS-producing bacteria	SCFAs	↓ Circulating LPS↓ TLR4 signaling↑ Intestinal IgA production	Reduced inflammation-driven carcinogenesis
Combined aerobic + resistance	Strongest increase in diversity, enhanced microbial stability	SCFAs, secondary bile acids	Improved metabolic flexibility, enhanced mucosal immunity	Optimal microbiome profile for cancer prevention
High-intensity / prolonged exercise	Transient dysbiosis↓ Barrier-supporting taxa	↓ SCFAs↑ Inflammatory metabolites	↑ Intestinal permeability↑ Systemic inflammation	Potential short-term increase in cancer-promoting signals if chronic

in colorectal cancer [75, 20].

In contrast, prolonged or excessive high-intensity exercise may transiently disrupt gut barrier integrity, induce dysbiosis, and elevate inflammatory signaling due to increased intestinal permeability and oxidative stress. While these effects are often reversible, chronic exposure may attenuate the protective benefits of physical activity [76, 60].

Overall, evidence suggests that sustained moderate or combined aerobic–resistance exercise provides the most favorable microbiome profile for cancer risk reduction.

5. Crosstalk between Exercise–microbiome interactions in cancer

The gut microbiome is crucial for human health, affecting processes like metabolism, immune response, and even the development and progression of cancer [77]. This diverse community of microorganisms maintains a symbiotic relationship with its host, but when its balance is disturbed, known as dysbiosis, it can cause inflammatory and carcinogenic conditions [78-84].

Studies indicate that in cancers such as colorectal and esophageal types, the microbiome's composition changes, with certain species linked to tumor growth, persistent inflammation, and compromised mucosal barriers [85-88, 48, 89, 31].

For instance, bacteria like Fusobacterium nucleatum, along with Porphyromonas, Peptostreptococcus, Prevotella, Parvimonas, Leptotrichia, and Campylobacter, are found in tumor tissues [90-92]. Their roles in promoting inflammation and epigenetic modifications have been increasingly recognized [31, 30, 33-36]. Research involving humans and animals indicates that dysbiosis can trigger cancer-promoting pathways and affect the host's immune response [93].

Experiments with germ-free mice genetically prone to cancer such as those lacking p53 or APC genes demonstrate that without a microbiome, the occurrence of intestinal adenocarcinomas decreases. However, restoring the microbiome raises the likelihood of tumor formation. This data underscores the critical role of the gut microbiome in cancer prevention and therapy, implying that modifying microbial composition could help lower cancer risk and enhance treatment outcomes [93-97].

Exercise is recognized as a natural way to regulate the gut microbiome [60]. Regular physical activity boosts microbial diversity and encourages the growth of beneficial bacteria, which promote the production of short-chain fatty acids (SCFA) [98].

SCFAs exert anti-carcinogenic effects by reinforcing epithelial barrier integrity, suppressing pro-inflammatory cytokine production, and epigenetically regulating immune cell differentiation within the tumor microenvironment. These SCFAs are crucial for lowering inflammation, strengthening the intestinal mucosal barrier, and enhancing immune function [53, 54, 99].

In addition to improving physical and mental well-being, exercise directly benefits gut health and can reduce diseases associated with dysbiosis [57, 58]. While intense and prolonged workouts might temporarily elevate inflammation and increase intestinal permeability, moderate and consistent exercise supports microbial stability and overall gut health [60, 62].

The ways exercise influences the microbiome are complex and diverse. Physical activity leads to the production of reactive oxygen and nitrogen species in muscle mitochondria, which then activate immune responses in intestinal cells through serotonin pathways [61, 62, 67].

Both moderate aerobic exercise and resistance training boost immunoglobulin A levels in the gastrointestinal tract, helping prevent pathogen colonization by the microbiome [68]. Additionally, regular exercise lowers lipopolysaccharide (LPS) levels and Toll-like receptor expression, reducing inflammation and supporting the integrity of the intestinal mucosal barrier [69, 70].

These effects are linked to mechanisms involved in cancer prevention, as decreased inflammation and stronger mucosal barriers can lower the risk of gut dysbiosis-related cancers, such as colorectal cancer. Exercise influences bile acid metabolism, impacting metabolic capacity and muscle development by regulating secondary acid production and activating receptors like FXR and G protein-coupled receptors [71, 72].

Additionally, hydrogen sulfide produced by the microbiome, through cysteine breakdown, affects immune and intestinal epithelial cells, and exercise can boost this pathway [73, 74]. These mechanisms indicate that exercise may have anti-inflammatory and cancer-protective benefits by changing microbial metabolic activity. Additional evidence from human studies indicates that regular exercise creates a distinctive microbial profile in athletes, characterized by higher levels of beneficial bacteria and SCFAs [62].

In older adults, muscle strength correlates with a particular microbial makeup, implying that a healthy microbiome might help preserve physical and muscular function [63]. On the other hand, a compromised gut barrier can result in joint inflammation and decreased motor skills, potentially triggering inflammatory pathways linked to cancer [64].

Intervention studies show that combining aerobic and resistance training most effectively boosts microbial diversity, whereas resistance training alone has a smaller impact. Low-intensity exercise offers only modest microbiome benefits, but intense and prolonged exercise might raise inflammation levels [100, 101]. Therefore, both the intensity and type of exercise are crucial for influencing the microbiome and its potential anticancer benefits [102].

The interaction between exercise, the gut microbiome, and cancer is complex and bidirectional. Exercise helps lower the risk of gut-related cancers, like colorectal cancer, by boosting microbial diversity, generating beneficial metabolites, and reducing inflammation. Conversely, a healthy microbiome can enhance the body's response to exercise and amplify its positive impacts on immunity, metabolism, and overall health. These insights imply that combining microbiome management with regular physical activity could serve as a preventive and supportive

Table 2. Mechanistic Links between the Exercise–gut Microbiome Axis and Cancer Development and Therapeutic Responsiveness

Mechanistic Pathway	Microbiome Component	Exercise Effect	Downstream Impact on Tumor Biology
Inflammation regulation	SCFA-producing bacteria	↑ SCFA synthesis	Suppression of NF-κB signaling reduced chronic inflammation
Gut barrier integrity	Mucin-degrading & IgA-inducing microbes	↑ IgA secretion↓ Gut permeability	Reduced microbial translocation and carcinogenic inflammation
Immune modulation	Commensal-driven T cell regulation	↑ $CD8^+$ T cell infiltration↑ , Treg balance	Enhanced anti-tumor immunity, improved immune checkpoint inhibitor efficacy
Bile acid metabolism	Secondary bile acid–producing bacteria	Rebalanced bile acid pools	FXR and GPCR signaling modulation reduced tumor-promoting metabolic stress
Oxidative signaling	Microbiome–muscle interaction via RONS	Controlled RONS signaling	Activation of immune surveillance without DNA damage
Hydrogen sulfide signaling	Cysteine-metabolizing bacteria	↑ H_2S bioavailability	Improved epithelial homeostasis and anti-inflammatory signaling
Tumor microenvironment	Microbial metabolites (SCFAs, formate)	Favorable metabolic reprogramming	Reduced tumor growth and improved therapeutic responsiveness

approach in cancer prevention and treatment [102].

Key mechanistic pathways linking exercise-induced microbiome modulation to tumor immunity, metabolism, and therapeutic responsiveness are outlined in Table 2.

6. Exercise–Microbiome Interactions in Cancer Immunotherapy

Growing evidence indicates that the gut microbiome critically influences responsiveness to cancer immunotherapies, particularly immune checkpoint inhibitors (ICIs) [103]. Microbial composition regulates antitumor immunity through modulation of T cell activation, cytokine signaling, and antigen presentation, while dysbiosis has been associated with poor therapeutic outcomes and increased toxicity [104].

Exercise has emerged as a promising adjuvant strategy capable of enhancing immunotherapy efficacy through microbiome-dependent mechanisms [105]. Preclinical studies demonstrate that physical activity increases $CD8^+$ T cell infiltration and interferon-γ signaling, partly mediated by exercise-induced microbial metabolites such as formate and short-chain fatty acids (SCFAs) [106, 103]. These metabolites promote immune activation and improve the tumor microenvironment.

Although clinical data remain limited, observational studies suggest that physically active patients may experience improved immunotherapy responses and reduced adverse events [105, 106]. Collectively, these findings support exercise as an immune-sensitizing intervention, with the gut microbiome serving as a key mediator of the relationship between physical activity and immunotherapy efficacy.

7. Clinical Implications of Exercise–Microbiome Interactions in Cancer Therapy

Emerging clinical and translational evidence suggests that structured exercise may enhance the efficacy of cancer treatment by modulating the immune system and remodeling the microbiome. While preclinical studies have consistently demonstrated that exercise improves antitumor immunity and augments immune checkpoint inhibitor (ICI) responsiveness, accumulating clinical data further support its translational relevance. Observational studies in patients with solid tumors receiving ICIs indicate that higher levels of physical activity are associated with improved progression-free survival and treatment tolerance, underscoring the potential role of exercise as an adjunct to immunotherapy [107, 108].

Despite these encouraging findings, robust randomized clinical trials directly linking exercise interventions to oncologic outcomes remain limited. Current recommendations are therefore largely extrapolated from consensus guidelines and survivorship studies. International expert panels endorse moderate-intensity aerobic and resistance exercise as safe and feasible across cancer types, provided that programs are individualized according to disease stage and treatment phase [76]. However, microbiome-guided exercise prescriptions remain speculative, highlighting the need for clinically actionable frameworks tailored to oncologic practice.

Importantly, potential risks associated with inappropriate exercise intensity, including transient immunosuppression, excessive fatigue, or adverse events in frail patients undergoing intensive therapy, warrant careful consideration. Recent reviews emphasize the necessity of stratifying exercise interventions based on performance status, treatment modality, and immune competence to maximize benefit while minimizing harm [109] (Table 3).

8. Microbiome-Guided Exercise and Clinical Implications

Emerging insights into the exercise gut microbiome–cancer axis highlight the need for personalized, microbiome-informed exercise prescriptions.

Rather than uniform recommendations, tailored exercise programs based on individual microbial and immunological profiles may optimize cancer prevention and therapeutic outcomes. Integrating structured exercise with dietary or microbiome-targeted interventions may enhance treatment efficacy and reduce toxicity, particularly in colorectal cancer.

However, translation into clinical practice remains limited by heterogeneity in exercise protocols and microbiome assessment methods. Future trials combining

Table 3. Overview of the Current Published Physical Activity Recommendations for Patients with Cancer

Cancer Type	Exercise Type	Intensity & Duration	Treatment Phase	Clinical Rationale	References
Breast cancer	Aerobic ± resistance	Moderate intensity aerobic exercise ~150 min/week; resistance training at moderate intensity	During and after treatment	Improves cardiorespiratory fitness, reduces cancer-related fatigue, and is associated with improved quality of life and survival outcomes	[76, 110]
Prostate cancer	Aerobic + resistance	Moderate-to-vigorous aerobic exercise; resistance training at moderate intensity	During androgen deprivation therapy and post-treatment	Preserves muscle mass, mitigates metabolic dysfunction, and improves physical function during hormonal therapy	[110, 111]
Colorectal cancer	Aerobic (walking, jogging) ± resistance	Moderate intensity, 150–300 min/week	During and after systemic therapy	Associated with reduced inflammation, improved metabolic health, and improved disease-specific and overall survival	[110, 112]
Hematological cancers (non-HSCT)	Aerobic + resistance	Moderate intensity aerobic exercise; low-to-moderate intensity resistance training	During and after treatment	Improves physical function, reduces fatigue, and supports immune recovery	[110, 113]
Hematological cancers (HSCT)	Low-intensity aerobic ± resistance	Light-intensity, individualized duration	During transplantation and early recovery	Maintains functional capacity and reduces deconditioning during intensive treatment	[110]
Digestive cancers	Aerobic + resistance	Individualized; moderate intensity when tolerated	Perioperative and post-treatment	Supports postoperative recovery and functional capacity	[114]
Advanced cancer with bone metastases	Aerobic + resistance (adapted)	Individualized, low-to-moderate intensity	During and after treatment	Maintains mobility and physical function while minimizing skeletal-related risks	[76]
Mixed solid tumors	Aerobic ± resistance	Moderate intensity aerobic exercise ≥150 min/week	During active treatment	Improves overall physical function and reduces treatment-related symptoms	[115]

controlled exercise interventions with multi-omics microbiome profiling will be essential to establish evidence-based guidelines and identify responder subgroups [116, 117].

9. Limitations and future study

Despite encouraging findings, several limitations remain in the current body of research. Most studies are preclinical or cross-sectional, with few longitudinal or randomized controlled trials specifically examining how exercise affects the microbiome in cancer contexts. The differences in exercise type, intensity, and duration across studies make it difficult to compare results and develop standardized protocols.

Additionally, inconsistent microbiome assessment methods, such as various sequencing platforms and analysis pipelines, hinder reproducibility. Human studies often have small sample sizes and lack demographic diversity, limiting how broadly the findings can be applied. Furthermore, few studies have explored whether exercise-induced microbiome changes can translate into actual therapeutic or preventive benefits.

Future research should emphasize mechanistic and longitudinal studies to better understand the causal links between exercise-driven changes in the microbiome and their role in cancer prevention or treatment. Combining metagenomics, metabolomics, and immunoprofiling through integrated multi-omics approaches will be crucial to identify the specific molecular pathways involved in this interaction.

Additionally, clinical trials that include controlled exercise programs and microbiome tracking in cancer patients are necessary to develop evidence-based guidelines. Recognizing individual differences such as genetics, diet, and lifestyle will support the creation of personalized strategies that leverage exercise and microbiome modulation as complementary options for cancer prevention and treatment.

In conclusion, this review emphasizes exercise as a biologically meaningful modulator of the gut microbiome with significant implications for cancer prevention and therapy. Evidence from both preclinical and clinical research supports exercise as a key factor in improving gut microbial diversity, composition, and metabolic functions. Regular moderate exercise promotes healthy microbial balance, increases short-chain fatty acid production, improves mucosal barrier integrity, and reduces systemic inflammation, all of which can lower cancer risk, especially for colorectal cancer. On the other hand, dysbiosis can encourage tumor growth by causing chronic inflammation, weakening immune defenses, and disrupting tumor microenvironment signaling. Overall, the data suggest that improving microbial balance through physical activity may boost metabolism, immune responses, and treatment effectiveness in cancer patients.

Ethics approval

This manuscript does not encompass any research involving animals or people.

Funding

This research did not receive any specific grant.

Conflict and interest

The authors assert no conflict of interest in this work.

Acknowledgments

Not Applicable.

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