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## **Physical Exercise as an Element of Cancer Recurrence Prevention — A Review of Recent Research**

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### **ABSTRACT**

**Background.** Cancer recurrence represents a growing public health concern, increasingly affecting long-term survivorship and the functional well-being of individuals after oncological treatment. Emerging evidence demonstrates that structured physical activity is not only a behavioral health factor but also a modifiable component of educational and preventive programs. Exercise may influence recurrence risk through improvements in immune competence, reduction of chronic inflammation, optimization of metabolic regulation, and favorable modulation of molecular pathways associated with tumor progression.

**Aim.** This review aims to evaluate current scientific evidence on the role of physical exercise in preventing cancer recurrence, with particular emphasis on mechanisms relevant to health promotion, behavioral change and interdisciplinary survivorship support.

**Review methods.** Scientific literature addressing the relationship between physical exercise and cancer recurrence was identified through major biomedical databases. Studies were selected according to predefined criteria ensuring relevance and clarity, and those providing clinical, biological or psychosocial insights were included in the review.

**Keywords:** physical exercise, cancer recurrence, survivorship, health promotion, inflammation, oxidative stress, behavioral interventions, preventive oncology, health education

## **1. Introduction**

Cancer recurrence continues to pose a significant challenge for long-term survivors, affecting not only survival rates but also functional capacity and psychosocial well-being [1,2,3]. While modern oncological therapies have extended life expectancy, there remains a critical need for effective preventive strategies that are safe, accessible and sustainable. In this context, regular physical exercise emerges as a powerful non-pharmacological tool: mounting evidence suggests that it can modulate key biological processes — such as immune surveillance, inflammation, metabolic signaling, and oxidative stress — that are implicated in tumor relapse [4–7,16].

Beyond its physiological benefits, physical activity offers considerable psychosocial advantages. Many cancer survivors experience fatigue, anxiety, and reduced social participation; structured exercise programs have been shown to improve mood, strength and overall quality of life [6,25]. However, there is a lack of integrative reviews that consider not only clinical and biological evidence, but also educational and behavioral dimensions relevant to long-term survivorship care. This review addresses this gap by examining recent research on exercise and cancer recurrence from a multifaceted perspective, with implications for health promotion, patient education, and interdisciplinary survivorship support.

## **2. Results**

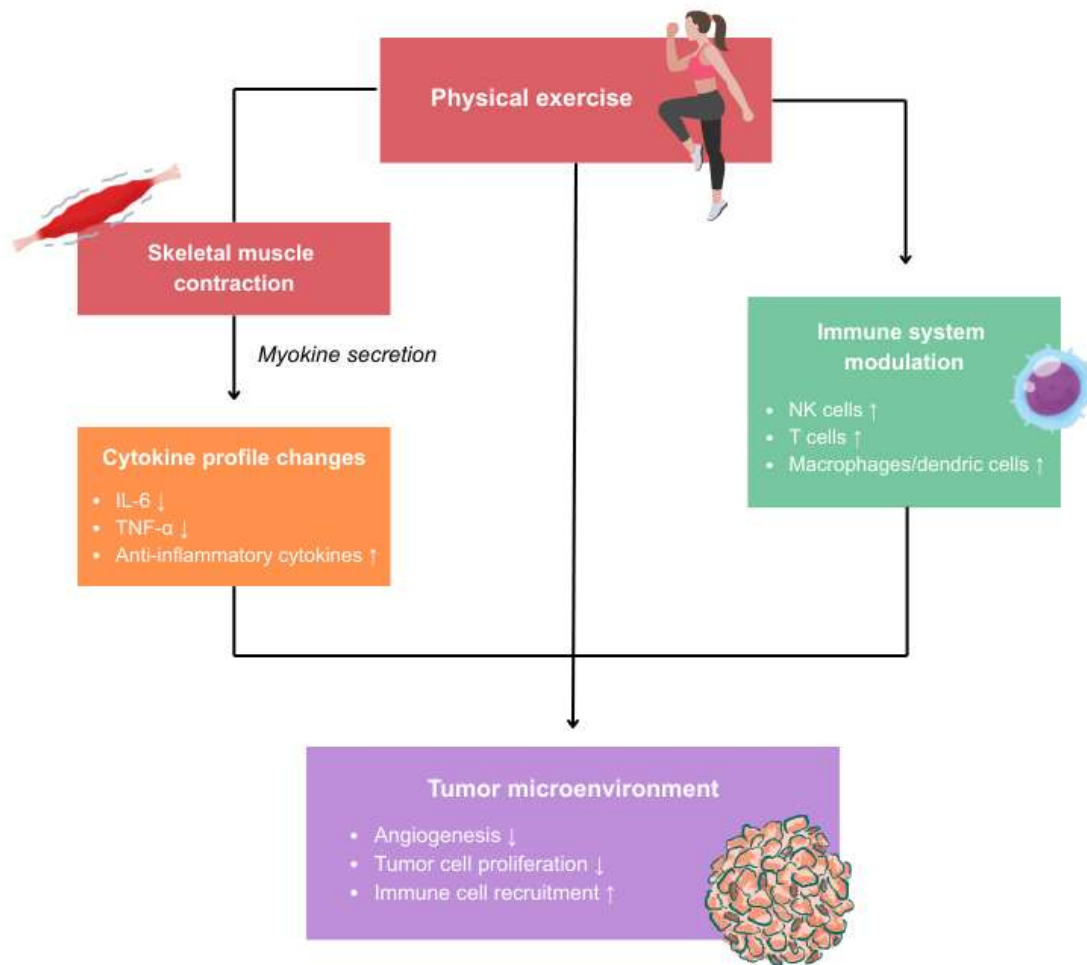
### **2.1. Immunological Mechanisms**

Physical exercise has been shown to exert significant effects on the immune system, which may contribute to the prevention of cancer recurrence. Regular activity enhances both innate and adaptive immunity, influencing natural killer (NK) cells, T lymphocytes, macrophages, and dendritic cells. Increased NK cell cytotoxicity and enhanced T cell proliferation have been observed in survivors engaging in structured exercise programs, suggesting improved immune surveillance against residual tumor cells [4,7–12,14,16,17,19].

Exercise also modulates cytokine and chemokine profiles, reducing pro-inflammatory mediators such as tumor necrosis factor-alpha (TNF- $\alpha$ ) and interleukin-6 (IL-6), while promoting anti-inflammatory signals [8,10,11]. In addition, contracting skeletal muscles release myokines, which are signaling proteins that can affect distant tissues, including tumors. Myokines play a role in modulating immune responses, reducing inflammation, and influencing the tumor microenvironment by regulating angiogenesis, cell proliferation, and immune cell recruitment [2,3,5,6,7,14,16,19].

The combination of enhanced immune cell function, reduced inflammation, and favorable modulation of signaling molecules provides a biological rationale for the protective role of exercise against cancer relapse.

**Figure 1.** Schematic representation of immunological mechanisms influenced by physical exercise in cancer survivors.



## 2.2. Molecular and Epigenetic Pathways

Physical exercise influences several molecular and epigenetic pathways that are relevant to cancer biology and long-term tumor control. These pathways regulate cell survival, DNA repair, oxidative stress responses, metabolic signaling, and gene expression patterns that shape the cellular environment in cancer survivors [6,14,25].

One key mechanism involves the modulation of PI3K/Akt/mTOR signaling, a central regulator of cell growth and metabolism [6,14,17,31]. Exercise-induced changes in metabolic

flux, nutrient availability, and intracellular energy balance can shift the activity of this pathway. Alterations in mTOR activity influence protein synthesis, autophagy, and cellular stress tolerance while contributing to long-term regulation of proliferation in various tissues [18,25]. Parallel adjustments in the AMPK pathway, triggered by increased energy demand, further regulate metabolic homeostasis by promoting catabolic processes and supporting mitochondrial maintenance [14,30].

Exercise is also associated with characteristic changes in oxidative stress-related molecular networks. Repeated elevations of transient reactive oxygen species (ROS) during physical exertion can activate adaptive responses involving Nrf2, a transcription factor linked with antioxidant defense [10,24,29]. Activation of these systems promotes enhanced detoxification capacity, mitochondrial turnover, and stability of the intracellular redox environment. These adaptations may modulate the susceptibility of cells to oxidative DNA damage and influence the long-term integrity of genomic maintenance systems [24,30].

At the epigenetic level, physical activity has been linked to modifications in DNA methylation, histone acetylation, and chromatin accessibility in tissues involved in systemic metabolism, immune regulation, and cellular stress responses [14,18,25]. Changes in promoter methylation can adjust the transcription of genes responsible for inflammation, apoptosis, metabolic control, and cellular senescence. Modifications in histone structure influence transcriptional plasticity and may contribute to sustained alterations in gene expression profiles after repeated exercise stimuli [14,18,20,25].

Exercise-associated epigenetic remodeling also includes regulation of non-coding RNAs, particularly microRNAs (miRNAs) involved in pathways associated with cell cycle control, apoptosis, mitochondrial function, and immune signaling [14,25]. By modifying miRNA expression, exercise can influence post-transcriptional regulation of numerous targets relevant to cell survival and tissue resilience.

Collectively, these molecular and epigenetic mechanisms provide a conceptual framework through which physical activity may contribute to long-term regulation of cellular environments in cancer survivors. They form the mechanistic basis that underlies later consideration of clinical and epidemiological evidence.

### **2.3. Clinical and Epidemiological Evidence**

Clinical and population-based data consistently indicate that regular physical activity is associated with reduced cancer recurrence and improved survival across multiple tumor types. A key meta-analysis by Morishita et al. demonstrated that engagement in structured exercise

was linked to lower all-cause mortality and decreased recurrence risk among cancer survivors, with pooled estimates suggested an association across diverse cohorts [13]. These findings align with epidemiological observations that sustained moderate-to-vigorous physical activity contributes to improved long-term outcomes following primary cancer treatment.

Prospective cohort studies included in recent systematic evaluations consistently compared cancer survivors engaging in higher versus lower weekly volumes of physical activity. Across these cohorts — most frequently involving breast and colorectal cancer survivors — higher levels of moderate-to-vigorous activity were associated with reduced recurrence rates and cancer-specific mortality, typically in a dose-responsive pattern. Although definitions of activity levels, timing of post-treatment assessment, and statistical adjustments varied between studies, the direction of association remained uniform, reinforcing the robustness of these epidemiological signals [13]. Evidence from prospective cohort research has also shown that higher levels of habitual physical activity are associated with a lower risk of recurrence and disease progression in non-muscle-invasive bladder cancer, supporting the generalizability of exercise-recurrence associations beyond the most frequently studied tumor types [26].

Complementary clinical data arise from meta-analyses focusing on physiological and biochemical outcomes in survivors. Zhou et al. synthesized evidence from controlled trials in breast cancer survivors, demonstrating that structured exercise interventions improved inflammatory markers and components of the IGF axis [17]. These biomarkers are relevant because dysregulated inflammation and IGF signaling are repeatedly cited as mechanistic pathways linking physical inactivity with cancer progression and potential recurrence. While these studies do not measure recurrence directly, their findings provide clinical support for exercise-induced modulation of pathways associated with disease outcomes [17]. These biomarker-level results align with broader narrative evidence summarized by Brown and Gilmore, who reported consistent observational associations between higher post-diagnosis physical activity and reduced recurrence risk across several cancer types, while emphasizing the need for long-term randomized trials to establish causality [21].

Cormie et al. [24] provide strong evidence supporting these observations, demonstrating in their systematic review of randomized controlled trials that structured exercise consistently improves cancer-related fatigue, physical function, strength, and quality of life across multiple tumor groups. Although recurrence outcomes were rarely measured directly, the authors highlight that these clinically meaningful adaptations influence inflammatory, metabolic, and physiological pathways that are also implicated in long-term disease control [24].

Additional clinical insights come from the network meta-analysis by Liu et al. [12], which evaluated exercise modalities in cancer patients with sarcopenia. Improvements in muscle mass and physical function are clinically important, as sarcopenia is associated with poorer tolerance of cancer treatment, reduced survival, and systemic inflammation—factors that indirectly shape recurrence risk. Exercise modalities such as resistance training and multicomponent programs showed the strongest benefits, reinforcing the relevance of structured physical activity within survivorship care [12].

A clinically relevant perspective on sustaining physical activity in cancer survivors is offered by Grimmer et al. [11], who provide a conceptual framework for supporting long-term engagement. Their work highlights behavioral determinants—including motivation, environmental support, and tailored program design—that shape adherence across different phases of survivorship. These insights are important because sustained participation in physical activity, rather than short-term intervention effects alone, is the pattern associated with reduced recurrence risk in epidemiologic studies [11,13].

Taken together, clinical and epidemiological evidence from the included sources supports a consistent association between higher levels of physical activity and improved clinical outcomes, including reduced recurrence in cohorts summarized in meta-analyses. However, the literature also emphasizes methodological heterogeneity, potential confounding, and the need for high-quality prospective intervention trials to establish causal relationships and refine exercise prescriptions [13,15,17,23,31].

## **2.4. Exercise Types, Dose and Frequency**

Research examining structured exercise programs in cancer populations describes several commonly implemented training modalities, including aerobic exercise, resistance training, and high-intensity interval training (HIIT). These modalities differ in physiological demands but are frequently applied in clinical and rehabilitation settings, forming the basis for practical exercise recommendations in survivorship contexts [24–27,29,31].

Aerobic exercise represents one of the most frequently utilized modalities in cancer-related training programs. Interventions described in the literature commonly include brisk walking, cycling, treadmill protocols, or other rhythmic, large-muscle activities performed at moderate intensity. Aerobic exercise is consistently associated with improvements in cardiovascular fitness, metabolic regulation, inflammatory balance, and overall physical functioning, thereby supporting physiological pathways relevant to long-term survivorship [24,25,29,31].

Resistance training is another core modality incorporated in cancer rehabilitation. Programs generally involve progressive exercises targeting major muscle groups using machines, free weights, resistance bands, or body-weight movements. Resistance training contributes to maintenance or improvement of muscle mass, strength, and functional capacity—outcomes of particular relevance for cancer survivors who often experience treatment-related muscle loss or sarcopenia. Such adaptations may indirectly influence factors associated with recurrence biology, including metabolic health and systemic inflammation [24,25,31].

HIIT has emerged as a complementary or alternative training modality, characterized by brief bouts of vigorous activity interspersed with recovery intervals. Studies including cancer survivors report that HIIT elicits significant cardiometabolic adaptations despite relatively short total training time. Its application in rehabilitative settings reflects growing interest in time-efficient exercise approaches that may support participation and consistency among cancer survivors [2,15,25-27].

Exercise interventions described in the literature vary considerably in their structure, delivery format, and degree of supervision. Remote and technology-supported delivery models have become increasingly evaluated; a recent meta-analysis indicates that telehealth exercise-based rehabilitation can effectively increase physical activity and improve fitness among cancer survivors, offering a viable alternative or complement to supervised, centre-based programs [22]. While exact optimal dosage remains an area of ongoing investigation, interventions frequently involve multiple weekly sessions, moderate-to-vigorous intensity, and progressive increases in training load, aligning with patterns commonly adopted in clinical exercise oncology [15,17,31]. Evidence from a recent systematic review also indicates that individualized exercise programs—tailored to patient characteristics, treatment history, and functional capacity—tend to yield more consistent improvements across different outcomes, highlighting the relevance of personalized approaches in exercise prescription for cancer survivors [28]. Reported adaptations across diverse programs suggest that consistency of engagement and gradual progression may be more influential than the exclusive selection of a single training modality [24–27,29,31].

Together, aerobic, resistance, and interval-based training models provide a practical framework for exercise prescription in cancer survivorship. Although dose-response relationships require continued examination, available evidence supports multi-modal programs incorporating elements of endurance and strength training while emphasizing regular participation, safety, and individualized progression.



## **2.5. Psychosocial and Educational Implications**

Psychosocial factors play a significant role in shaping cancer survivors' engagement in physical activity. Beyond the physiological and molecular adaptations associated with exercise, multiple studies highlight improvements in emotional well-being, perceived energy, and overall quality of life, which can reinforce continued participation in health-promoting behaviors. Broader mechanistic perspectives also point to the systemic regulatory effects of physical activity — including enhanced inter-organ communication and modulation of stress-related pathways — which may indirectly support psychosocial functioning and overall resilience in survivorship [6,16,24].

Sustained physical activity is additionally associated with enhanced social integration, as participation in structured or community-based exercise programs provides opportunities for interpersonal interaction and shared goal pursuit. These psychosocial benefits contribute to a positive feedback loop in which improved mood, confidence, and social connectedness support motivation to remain physically active. Available evidence indicates that adherence is strongly influenced by behavioral determinants such as self-efficacy, perceived competence, and access to supportive environments [11,25].

Educational strategies play a key role in supporting long-term engagement in physical activity among cancer survivors. Technology-assisted approaches, including telehealth and remote supervision, extend the reach of educational and rehabilitative services and have been shown in meta-analytic data to raise activity levels and physical capacity among survivors who might otherwise face geographic, logistical, or medical barriers to in-person programmes [22]. Providing clear, evidence-informed guidance on exercise modalities, safe intensity ranges, and principles of progression helps survivors navigate uncertainties surrounding post-treatment physical activity. Structured educational interventions can address concerns related to safety, symptom management, or appropriate workload, thereby enhancing confidence and supporting the transition from supervised rehabilitation to independent activity [25,28]. Incorporating behavioral tools such as goal setting, progress tracking, and personalized feedback further reinforces engagement and self-management capacity.

For health educators and physiotherapists, these findings underscore the importance of individualized program design. Effective educational practice includes assessment of baseline functional status, identification of potential barriers, and adaptation of exercise plans to align with personal needs, preferences, comorbidities, and daily routines. Emphasis on autonomy, flexibility, and gradual progression is particularly important, as these elements have been linked to long-term adherence in survivorship contexts [11,25].

Educational and community-based models — ranging from supervised clinical programs to home-based or hybrid formats — can facilitate sustainable engagement when paired with supportive communication and tailored instruction. These approaches integrate practical guidance with psychosocial support and offer flexible pathways for survivors to incorporate regular physical activity into their daily routines.

### **3. Discussion**

The findings presented in this review highlight the multidimensional ways in which physical activity may contribute to reduced cancer recurrence risk and improved survivorship outcomes. When considered collectively, mechanistic, clinical and psychosocial evidence reveals a coherent pattern [23]: exercise exerts broad, systemic influences that affect biological processes, functional capacity and behavioral patterns relevant to long-term disease control.

Mechanistic research provides detailed insight into the biological pathways through which physical activity may modulate factors associated with cancer progression. Exercise-induced adaptations in immune surveillance, including enhanced natural killer cell activity, improved T-cell function and reductions in myeloid-derived suppressor cells, describe pathways that may influence the ability of the host to recognize and eliminate malignant cells [1,4,6–9,14,16,20,27]. Similarly, exercise-related reductions in chronic inflammation and improvements in oxidative stress regulation contribute to a more physiologically balanced environment, which may be less permissive to tumor-promoting conditions [10,17,24,29,30]. Metabolic adaptations — including modulation of insulin pathways and components of the IGF axis — further support mechanistic links between regular activity and reductions in processes associated with proliferation, angiogenesis and impaired apoptosis [17,21,31]. Epigenetic alterations in methylation, histone structure and microRNA expression suggest an additional layer of regulation through which repeated exercise stimuli may influence long-term cellular behavior [14,18,25]. Together, these biological observations provide a plausible conceptual framework for the potential protective role of exercise against cancer recurrence.

Clinical and epidemiological evidence aligns strongly with these mechanistic insights. Evidence from randomized controlled trials further supports this interpretation, showing that exercise interventions consistently improve functional capacity, fatigue, metabolic regulation, and quality of life—factors closely linked to biological processes relevant for long-term disease control [24]. Prospective cohort studies and meta-analyses consistently show that survivors who maintain moderate-to-vigorous levels of physical activity after treatment have lower recurrence rates and improved survival compared with those who remain inactive [13]. Although

heterogeneity exists in the quantification of physical activity and the timing of assessments across studies, the direction of association remains consistent. Complementary clinical data from controlled trials indicate that structured exercise interventions improve inflammatory markers, IGF-related measures, muscle mass and physical function—factors repeatedly linked to survivorship outcomes and treatment tolerance [12,17,19,25,31]. These findings reinforce the relevance of exercise-induced physiological adaptations in shaping pathways associated with long-term health after cancer.

Nonetheless, the available evidence base is shaped by several limitations. Exercise interventions vary widely in type, intensity, supervision and duration, complicating attempts to determine an optimal prescription for recurrence prevention. Most controlled trials are of relatively short duration and focus on intermediate physiological outcomes, while direct evidence regarding recurrence requires long-term follow-up that is difficult to implement in randomized settings. Observational studies, while informative, rely primarily on self-reported activity and remain subject to residual confounding linked to comorbidities, socioeconomic variables or lifestyle differences. Moreover, much of the long-term evidence concerns breast cancer survivors, limiting generalizability to other tumor types. These limitations highlight the need for future research employing standardized assessments of physical activity, harmonized definitions of recurrence outcomes and extended follow-up periods.

Psychosocial and educational dimensions further enrich the understanding of how exercise functions within survivorship care. Many survivors experience disruptions in emotional well-being, social participation and daily routines, and evidence suggests that physical activity can improve mood, perceived vitality and confidence—factors associated with greater willingness to maintain active lifestyles [11,24,25]. Behavioral determinants such as self-efficacy, perceived competence and access to supportive environments strongly influence long-term adherence, underscoring the importance of integrating educational guidance and behavioral support into exercise programming [11,25]. Clear instruction regarding safety, progression and self-monitoring can reduce uncertainty and support the transition from supervised rehabilitation to independent activity, while flexible program formats — including supervised, community-based and home-based models — allow exercise plans to be adapted to individual circumstances [25,28].

Taken together, the evidence reviewed supports a comprehensive understanding of physical exercise as a multidimensional contributor to survivorship outcomes [23]. Rather than acting through a single mechanism, exercise appears to influence several interconnected pathways spanning molecular biology, systemic physiology and behavioral engagement.

Integrating these domains into survivorship care may help translate research findings into sustainable, long-term health behaviors among cancer survivors. Continued interdisciplinary collaboration among clinicians, physiotherapists, educators and behavioral specialists will be essential for refining exercise recommendations and optimizing their effectiveness in recurrence-prevention strategies.

#### **4. Conclusions**

Physical exercise emerges from current scientific evidence as a safe, accessible and multifaceted strategy that may contribute to reduced cancer recurrence risk and improved long-term outcomes in survivors. Mechanistic studies illustrate how exercise modulates immune, inflammatory, metabolic and epigenetic pathways relevant to tumor control, while clinical and epidemiological data consistently associate higher levels of post-diagnosis physical activity with improved survival and reduced recurrence. Although uncertainties remain regarding optimal exercise modalities, intensities and long-term prescriptions, the convergence of findings across biological and clinical domains highlights the importance of incorporating structured physical activity into survivorship care.

The successful implementation of exercise-based strategies requires coordinated educational and psychosocial support. Clear guidance, individualized progression and behavioral tools can enhance confidence, improve adherence and enable survivors to maintain regular activity beyond supervised settings. Integrating exercise with patient education and psychosocial resources may therefore offer the most effective pathway for translating scientific insights into sustainable preventive practices.

Future research should prioritize long-term prospective studies with standardized physical activity assessment and recurrence outcomes, alongside efforts to identify personalized exercise prescriptions tailored to clinical history, functional capacity and behavioral readiness. Advancing this evidence base will be essential for optimizing the use of physical activity within comprehensive survivorship programs.

#### **Disclosure**

##### **Author Contributions**

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Software: not applicable;

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