

# **The Association between Physical Activity and Cancer Prevention, Recovery, and Recurrence: A Narrative Review**

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## **Abstract**

Cancer is the first most common cause of mortality in the United Kingdom and, after cardiovascular diseases, the second most common cause of mortality globally, accounting for around one in six deaths worldwide. The gravity of this situation highlights the need to find effective ways for prevention and adequate recovery from cancer. Physical activity includes all energy-consuming bodily movements that are produced using skeletal muscles. According to current estimates, one in four, or 28%, adults do not engage in adequate physical activity. Physical inactivity is currently the fourth major risk factor for mortality worldwide. Around one-third of deaths from cancer are caused by inadequate physical activity and diet-related factors. Physical activity is associated with both cancer risk and survival for several cancer types; therefore, for controlling cancer, the role of physical activity may be crucial. In this study, a narrative review is presented about physical activity and its association with cancer prevention, recovery, and recurrence to help synthesize the information presented in previous studies and enhance that information to provide stronger evidence for the benefits of physical activity in the fight against cancer. To conduct that, databases including Google Scholar and PubMed were searched for relevant research literature with the help of key terms “cancer” and “physical activity” leading to an inclusion and review of a total of 58 studies published between 1998 and 2023. According to the findings of this study, participation in adequate physical activity according to the recommended guidelines is linked to a decreased risk of various cancer types such as breast cancer, endometrial cancer, kidney/renal cancer, colon cancer, rectal cancer, liver cancer, lung cancer, bladder cancer, head and neck cancer, gastric cardia, esophageal adenocarcinoma, myeloma, myeloid leukemia, lung cancer, bladder cancer, head and neck cancer, gastric cancer, esophageal adenocarcinoma, myeloma, myeloid leukemia, and non-Hodgkin lymphoma; furthermore, it aids cancer patients of all ages in recovery by reducing the cancer treatment side effects, improving physical fitness, mental health, and quality of life, and additionally, decreases the risk of cancer recurrence after remission. Physical activity impacts cellular processes and tumor growth by controlling body weight and metabolic variables, enhancing mitochondrial and immune function, controlling genomic instability, releasing myokines, and regulating several hormones and circulating biomarkers such as insulin and bile acid. Despite previous research on the benefits of physical activity for cancer patients, combining physical activity and therapy is not found to be frequent in real-world settings. Physical symptoms such as pain and fatigue, lack of motivation, lack of time, and lack of exercise information were reported as the major hindrances to physical activity. Therefore, personalized physical activity goals are recommended for all ages, such as active play for children with cancer. In conclusion, an increase in all types of physical activity in all domains of life in the general population and cancer patients according to the recommended guidelines or adapted according to the individual needs of patients can significantly contribute to reducing the burden of cancer and improving overall well-being. Furthermore, there is a need for future studies exploring different domains, various specific types of physical activity, and the association of physical activity with specific cancer sites, with currently limited studies.

**Keywords:** Neoplasms, Cancer, Physical Activity, Primary Prevention, Post-Exercise Recovery, Relapse Prevention, Physiological Phenomena

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## Introduction

Cancer can occur in any body region and is characterized by uncontrollable abnormal cell growth or proliferation that has the capacity to metastasize or spread to other bodily regions and that may cause death from cancer (1). Cancer is the first most common cause of mortality in the United Kingdom, and after cardiovascular diseases, the second most common cause of mortality globally, accounting for around one in six deaths worldwide (1, 2). In 1990, there were 8.1 million new cases of cancer and 5.8 million deaths from cancer (2, 3). This increased to 19.3 million new cases of cancer and 9.96 million cancer-related deaths worldwide in both genders and all ages in 2020, and as a result of the annual increase in both new cases and deaths, it is anticipated that by 2040, there will be 30.2 million and 16.3 million new cases and deaths, respectively (4). According to an estimate, there will be 1,958,310 new cases of cancer and 609,820 cancer-related deaths in the US in 2023 (5). Cancer is not just common in adults; worldwide, around 0.4 million children are diagnosed with cancer every year (1). In 2020, the cancer types with the highest incidence included breast cancer, lung cancer, colorectal cancer, prostate cancer, skin cancer, and stomach cancer; furthermore, the cancer types with the highest mortality included lung cancer, colon and rectum cancer, liver cancer, stomach cancer, and breast cancer (1). Overall, as well as in females, the highest incidence was of breast cancer, and that also caused the highest mortality in females, whereas in males, the highest incidence was of lung cancer, and that caused the overall highest mortality as well as the highest mortality in males; furthermore, leukemia, brain cancer, non-Hodgkin lymphoma, and kidney cancer were the cancers with the highest incidence and mortality in children and adolescents in 2020 (6). The gravity of this situation highlights the need to find effective ways for prevention and adequate recovery from cancer.

Physical activity includes all energy-consuming bodily movements that are produced using skeletal muscles (7). This may include skeletal muscle movements that may happen during transportation, occupational, domestic, or leisure time (7, 8). According to current estimates, one in four, or 28%, adults do not engage in adequate physical activity according to the current recommended physical activity guidelines of at least 150 minutes per week of moderate-intensity physical activity or 75 minutes per week of vigorous-intensity physical activity (7, 9). Women all over the world are found to be more physically inactive compared to men, and 1 in 3 or 32% of women do not have adequate physical activity, whereas the prevalence of inadequate physical activity in men is 1 in 4 or 23% (7, 10, 11). At 36.8%, the prevalence of inadequate physical activity is even higher in developed countries; furthermore, 35% of women in high-income countries in comparison with 24% of women in low-income countries are found to have inadequate physical activity, whereas 26% of men in high-income countries engage in inadequate physical activity in comparison with 12% of men in low-income countries (7, 11). This difference in developed countries is due to passive transportation modes, the use of technology, and a rise in sedentary behavior at home, at work, and even during leisure time (6). Inadequate physical activity is not just limited to adults; 81% of adolescents worldwide do not engage in adequate physical activity according to the current recommended WHO guidelines for adolescents of moderate to vigorous intensity physical activity of at least 60 minutes per day (7,

9). Similar to adults, there is a higher prevalence of inadequate physical activity in adolescent females, and 85% of adolescent females are inadequately physically active compared to 78% of adolescent males (7).

Physical inactivity is currently the fourth major risk factor for mortality worldwide (9). Around one-third of deaths from cancer are caused by inadequate physical activity and diet-related factors (1). Physical activity is associated with both cancer risk and survival for several cancer types; therefore, for controlling cancer, the role of physical activity may be crucial (12, 13). Although many studies have been done on physical activity and its relationship with cancer, there is a need to integrate this information, especially the recent findings, and explore its different perspectives. Therefore, in this study, a narrative review is presented about physical activity and its association with cancer prevention, recovery, and recurrence, exploring the different perspectives, to help synthesize information presented in previous studies and enhance that information to provide stronger evidence for the benefits of physical activity in the fight against cancer.

## **Methods**

A narrative literature review was conducted in November 2023, and to conduct that, databases including Google Scholar and PubMed were searched for relevant research literature with the help of key terms “cancer” and “physical activity” with a search strategy in accordance with the criteria of a narrative review that was broader and less systematic, leading to the inclusion and review of a total of 58 studies in this study, including books, data repositories, and other websites, and a wide range of research articles, including reviews, reports, meta-analyses, prospective cohort studies, controlled clinical trials, surveys, and qualitative studies published between 1998 and 2023. The inclusion criteria included all the research literature in the English language relevant to the key terms, whereas literature not relevant to the key terms and not in the English language was excluded. The data and findings from each included study were reviewed and evaluated to determine the relationship between physical activity and cancer. Furthermore, the study synthesized the relevant findings from all the reviewed literature.

## **Types of Physical Activity and Their Association with Cancer**

Physical activity is categorized into different types based on differences in physiologic effect or domain (12, 14). Aerobic physical activity and anaerobic physical activity is one way of categorizing physical activity based on difference in physiological effect; furthermore, aerobic physical activity includes physical activity such as walking, or soccer, that is sufficiently intense and performed for enough duration that it can preserve or enhance a person's cardiorespiratory fitness, or aerobic capacity, whereas anaerobic physical activity is high-intensity physical activity such as power lifting or sprinting that exceeds the cardiovascular system's capacity to supply oxygen to muscle cells for the typical oxygen-consuming metabolic pathways and can only be sustained for two to three minutes at a time (14). The domain-based types of physical activity are determined by the area of life or domain in which they take place and include

domestic or household physical activity that is done inside the home or during a household task, occupational physical activity that is performed during occupational work, transportation physical activity that is performed to move or transport from one location to another, and leisure-time physical activity that is performed by one's own choice during free time, such as recreation, sports, playing games, and exercise (8, 12, 14)

Irrespective of the domain in which it is undertaken, physical activity is beneficial to health (14). Regarding cancer, most research that has been done is about the leisure time physical activity domain for a number of cancer types such as liver cancer, colon cancer, lung cancer, kidney cancer, rectal cancer, bladder cancer, endometrial cancer, breast cancer, head and neck cancer, gastric cardia, esophageal adenocarcinoma, myeloma, and myeloid leukemia, and, to a lesser extent, research that has been done about the occupational physical activity domain for a few cancer types, including esophageal, gastric, kidney, and bladder cancers and these studies show a 10 to 20% lower cancer risk when compared to low activity levels; furthermore, much less information and very few studies are available for walking, active transportation, and domestic activity, although the limited information on these types of physical activities and a few cancer types including endometrial, breast, and colon cancers also demonstrates protective associations (12, 13). The different activity patterns of leisure time and occupational physical activity currently show the most benefit, but these different patterns of activity from these two domains indicate that a variety of activity types may reduce the risk of certain cancers, although more conclusive evidence is required for other physical activity domains (12). A number of studies have been done on aerobic physical activity to determine its association with the risk of cancer, but regarding cancer incidence, anaerobic muscle-strengthening activity like weightlifting, which can be incorporated into leisure time as well as other physical activity domains and is an essential part of the current recommendations for physical activity, is another type of physical activity that is understudied (13, 14, 15).

### **Physical Activity's Role in the Prevention of Cancer**

According to the 2018 Physical Activity Guidelines Advisory Committee Report, the committee found strong evidence of the association of increased physical activity with a 10% to 20% decreased risk of breast cancer, bladder cancer, colon cancer, esophageal adenocarcinoma, endometrial cancer, gastric cancer, and renal cancer; furthermore, moderate evidence was found regarding the association of increased physical activity with a 25 percent reduction in lung cancer risk (14). Along with that, the committee found limited evidence about the association of increased physical activity with decreased risk of prostate cancer, ovarian cancer, pancreatic cancer, head and neck cancer, and hematologic cancer. These effects seem to hold for most cancer subtypes across all sexes and racial and ethnic groups, irrespective of body weight (14).

The metabolic equivalent of task, or MET, is a measure of the intensity of physical activity and is the ratio of a physical activity's metabolic rate to a standard resting metabolic rate of one that is obtained during quiet sitting (16). According to the Compendium of Physical Activities, which, in accordance with MET, codes physical activities, MET values range from 0.9 for

sleeping to 23 METs for running at 14.0 mph (17). The amount or energy cost of an activity can be calculated by multiplying its MET value by the duration of time allotted to it (MET-minutes or MET-hours) (15, 16). Sedentary behavior MET values range from 1.0 to 1.5 METs, light-intensity physical activity ranges from 1.6 to 2.9 METs, moderate-intensity physical activity ranges from 3 to 5.9 METs, and vigorous physical activity is 6 or above 6 METs (17).

In a study that analyzed prospective cohort data of 1.44 million American and European participants, increased moderate and vigorous leisure-time physical activity with a MET range of 3 to 6 or more METs was found to be associated with decreased risks of 13 types of cancers, including liver cancer, colon cancer, lung cancer, kidney cancer, rectal cancer, bladder cancer, endometrial cancer, breast cancer, head and neck cancer, gastric cardia, esophageal adenocarcinoma, myeloma, and myeloid leukemia (13). Furthermore, increased leisure-time physical activity was linked to a 7% overall decreased risk of cancer and a 20% or more decreased risk for 7 types of cancer, including lung cancer, liver cancer, kidney cancer, endometrial cancer, esophageal adenocarcinoma, gastric cardia, and myeloid leukemia (13).

Another study that analyzed prospective cohort data of 755,459 American, European, and Australian participants found a statistically significant lower risk of many cancer types associated with 7.5–15 MET hours/week participation in physical activity according to the recommended guidelines, including up to 10% decreased risk of breast cancer, up to 17% decreased risk of kidney cancer, up to 27% decreased risk of liver cancer, up to 18% decreased risk of endometrial cancer, up to 19% decreased risk of myeloma, up to 14% decreased risk of colon cancer in men, and up to 18% decreased risk of non-Hodgkin lymphoma in women (15). In addition, moderate-intensity activity was found to be associated with a significantly decreased risk of kidney and breast cancer, whereas vigorous-intensity activity was found to be associated with a significantly decreased risk of endometrial cancer (15). The reduced risk for cancer associated with physical activity is summarized in Table 1.

Table 1. Physical Activity Association with Cancer Risk Based on Studies by Moore et al. (13), Matthews et al. (15), and 2018 Physical Activity Guidelines Advisory Committee Report (14)

Cancer Type	Recommended Physical Activity Cancer Risk (15)	Increased Leisure-Time Physical Activity Cancer Risk (13)	Reduced Cancer Risk Evidence (14)
Breast Cancer	6-10% reduced risk	Reduced risk	Strong Evidence
Endometrial Cancer	10%-18% reduced risk	>20% reduced risk	Strong Evidence
Kidney/Renal Cancer	11%-17% reduced risk	>20% reduced risk	Strong Evidence
Colon Cancer	8%-14% reduced risk in men	Reduced risk	Strong Evidence
Rectal cancer		Reduced risk	

Liver Cancer	18%-27% lower risk	>20% reduced risk	
Lung Cancer		>20% reduced risk	25% reduced risk moderate evidence
Bladder Cancer		Reduced risk	Strong evidence
Head and Neck Cancer		Reduced risk	Limited Evidence
Gastric Cardia		>20% reduced risk	Strong Evidence
Esophageal Adenocarcinoma		>20% reduced risk	Strong Evidence
Myeloma	14%-19% reduced risk	Reduced Risk	Limited Evidence
Myeloid Leukemia		>20% reduced risk	Limited Evidence
Non-Hodgkin Lymphoma	11%-18% reduced risk in women		Limited Evidence
Hematologic Cancer			Limited Evidence
Prostate Cancer			Limited Evidence
Ovarian Cancer,			Limited Evidence
Pancreatic Cancer			Limited Evidence

Based on the evidence obtained regarding reducing the risk of breast and colon cancer, the World Health Organization especially recommends regular participation in moderate- to vigorous-intensity physical activity for a minimum of 30 to 60 minutes each day to prevent breast and colon cancer (9).

Since it can take years for normal cells to transform into invasive tumors, participation in physical activity for an extended period or over one's lifetime may be an etiologically relevant factor determining the development of cancer (12, 18). In this regard, long-term physical activity is linked to a lower risk of gastric cancer, bladder cancer, and esophageal cancer; recent physical activity is more strongly connected with a lower risk of renal cancer than activity that was done earlier in life; and early, later, and throughout adulthood, physical activity is linked to a lower risk of colon and breast cancers (12).

Excessive sitting time is a behavioral risk factor for some cancers distinct from insufficient amounts of moderate-vigorous physical activity and could be a significant additional target for intervention in the effort to increase daily physical activity (19, 20, 21). The 2018 Physical Activity Guidelines Advisory Committee found strong evidence of an association between increased sedentary behavior and a 20–35% statistically significant increased risk of lung, colon, and endometrial cancers (14). After adjusting for moderate-to-vigorous physical activity, prolonged sitting is linked to a 21 to 27% greater risk of lung cancer, a 30 to 36% greater risk of endometrial cancer, and a 30% increased risk of colorectal cancer, with an increased risk of rectal cancer than colon cancer (20, 22, 23, 24).

## **Increased Melanoma Risk Associated with Physical Activity**

Increased physical activity is found to be associated with a 27% greater risk of melanoma compared to low physical activity (12). Melanoma is a type of skin cancer mostly caused by sun exposure, and as physically active people usually spend more time outdoors, this association may be due to increased sun exposure, but further research is needed to validate this hypothesis (12, 25).

## **Physical Activity Role in Promotion of Recovery and Prevention of Recurrence of Cancer**

Cancer patients face unique health challenges because of their cancer diagnosis and the impact that treatment has had on their physical and mental well-being (26). Cancer therapies such as chemotherapy and radiotherapy have a variety of side effects that have a detrimental influence on many facets of cancer patients' lives and lower their quality of life (27). Cancer treatment has a detrimental effect on several systems, including the immune system, the digestive system, the nervous system, the cardiovascular system, the respiratory system, and the endocrine system, and may cause metabolic changes, skin changes, pain, lymphedema, and systemic symptoms like fatigue that can last for years after treatment (26). Patients with cancer may suffer from anxiety, depression, reduced quality of life (QoL) fatigue, and sleep issues, and as chemotherapy negatively impacts and reduces mitochondrial function and lung function, it may reduce their interest in physical activity (27). Physical activity is essential and advantageous for cancer patients because it reduces the cancer treatment side effects, positively impacts mental health, reduces fatigue, increases aerobic fitness, and improves the quality of life; furthermore, it decreases the risk of cancer-related death and recurrence (27).

In one study on 798 ovarian cancer patients, increased physical activity was found to be associated with decreased depression and improved quality of life (QoL) (28). In another study on prostate cancer patients with bone metastases, exercise intervention for three months, including aerobic and anaerobic resistance and flexibility exercises three days per week, led to improved lower body muscle strength and improved self-reported physical functioning (29). According to a study on colorectal cancer patients, participation in exercise led to significant improvements in QoL, fatigue, aerobic fitness, sleep, and upper-body strength, and significantly reduced depression, body fat, and fatigue (30). In another study, physical activity in patients with colorectal cancer was found to have a positive and significant association with self-efficacy (31). In a study on lung cancer patients, preoperative exercise training improved cardiorespiratory fitness in patients before pulmonary resection (32). Furthermore, in children with cancer, exercise interventions positively impacted the immune system, improved body composition, decreased fatigue, increased strength, improved activity levels, improved physical functioning, improved sleep, and increased quality of life (33).

There is an increased probability of the development and recurrence of different types of cancer in the presence of metabolic syndrome (34, 35). The combination of resistance and aerobic exercises decreases cancer patients' risk of metabolic syndrome (27). According to a controlled trial including 100 breast cancer patients, an improvement in all metabolic syndrome variables and insulin resistance biomarkers, including reduction of BMI, blood pressure, and triglycerides, blood glucose, estradiol, leptin, adiponectin, insulin, and IGF-1 levels, was seen in the exercise group after the exercise intervention, and this improvement remained at the 3-month follow-up (35). Furthermore, following exercise intervention, metabolic syndrome was present in 15% of patients, compared to 78% of patients at baseline, whereas in the control group without exercise intervention, the number of patients with metabolic syndrome increased from 76% at baseline to 80% (35). In another study, breast cancer patients who achieved the minimum physical activity recommended levels both before and after the cancer diagnosis had a greater than 50% decreased recurrence risk compared to patients not achieving the minimum levels both pre- and post-diagnosis; furthermore, in a 2-year follow-up, decreased recurrence risk was also seen in the patients who met the minimum physical activity recommended levels only after the diagnosis (36). These findings are summarized in Table 2.

Research on prostate, breast, and colorectal cancer has shown that in comparison with pre-diagnosis physical activity, post-diagnosis physical activity is more strongly associated with better mortality outcomes and lesser mortality; furthermore, pre- and post-diagnosis physical activity is found to be more strongly associated with reduced all-cause mortality than cancer-specific mortality, since cardiovascular disease is another major cause of death for cancer patients (12). Thus, regular physical activity has advantages that go beyond only helping with cancer treatment, as these benefits include improved physical fitness, improved cardiovascular health, a lower risk of comorbidities, better day-to-day functioning, and improved well-being (27).

Table 2. Physical Activity Association with Cancer Recovery and Recurrence

<b>Author(s)</b>	<b>Study Design and Participants</b>	<b>Findings</b>
Beesley et al. (28)	798 ovarian cancer patient participants of a prospective Quality of Life Study ancillary to Australian Ovarian Cancer Study	Increased physical activity was found to be associated with decreased depression and improved quality of life (QoL)
Galvão et al. (29)	Randomized controlled trial of 57 prostate cancer patients with bone metastases in Australia	Exercise intervention for three months, including aerobic and anaerobic resistance and flexibility exercises three days per week, led to improved lower



		body muscle strength and improved self-reported physical functioning
Singh et al. (30)	A meta-analysis of 19 randomized, controlled, exercise trials of colorectal cancer patients, participant mean age: 64.6 years (SD = 6.9)	Participation in exercise leads to significant improvements in QoL, fatigue, aerobic fitness, sleep, and upper-body strength, and significantly reduced depression, body fat, and fatigue
Li et al. (31)	A cross-sectional study of 282 colorectal cancer patients in China	Physical activity has a positive and significant association with self-efficacy
Jones et al. (32)	Experimental single-group study of 25 lung cancer patients in USA with aerobic endurance exercise intervention until surgical resection	Preoperative exercise training improved cardiorespiratory fitness in patients before pulmonary resection
Baumann et al. (33)	A systematic review of children with cancer	Exercise interventions positively impacted the immune system, improved body composition, decreased fatigue, increased strength, improved activity levels, improved physical functioning, improved sleep, and increased quality of life
Dieli-Conwrigh et al. (35)	A controlled trial in United States including 100 breast cancer patients, randomly assigned to usual care (n = 50) or exercise (n = 50) groups	An improvement in all metabolic syndrome variables and insulin resistance biomarkers, including reduction of BMI, blood pressure, triglycerides, blood glucose, estradiol, leptin, adiponectin, insulin, and IGF-1 levels, was seen in the exercise group after the exercise intervention for four months, and this improvement remained at the 3-month follow-up. Furthermore, following

		exercise intervention, metabolic syndrome was present in 15% of patients, compared to 78% of patients at baseline, whereas in the usual care group without exercise intervention, the number of patients with metabolic syndrome increased from 76% at baseline to 80%
Cannioto et al. (36)	A prospective Diet, Exercise, Lifestyle and Cancer Prognosis questionnaire study ancillary to a clinical trial of 1340 breast cancer patients in the United States, with pre-diagnosis, during treatment, and 1- and 2-year post-enrollment data collection.	Patients who achieved the minimum physical activity recommended levels both before and after the cancer diagnosis had a greater than 50% decreased recurrence risk compared to patients not achieving the minimum levels both pre- and post-diagnosis; furthermore, in a 2-year follow-up, decreased recurrence risk was also seen in the patients who met the minimum physical activity recommended levels only after the diagnosis

### **The Physiological Impact of Physical Activity on Cancer**

Physical activity impacts cellular processes and tumor growth through its effects on immune system function, inflammation, oxidative stress, insulin/glucose metabolism, sex hormones, myokines, and genomic instability (12). Physical activity may also reduce the risk of cancer caused by obesity, as obesity is positively correlated with the risk of developing at least 13 types of cancer (37, 38). In postmenopausal women, weight loss due to physical activity led to reduced estradiol and C-reactive protein levels, leading to a reduced risk of endometrial and breast cancer (12, 39). Physical activity reduces proinflammatory biomarkers and metabolic syndrome variables, including reduction of BMI, blood pressure, blood glucose, triglycerides, estradiol, leptin, and adiponectin, leading to a reduction in the risk of cancer incidence and recurrence caused by metabolic syndrome; furthermore, it leads to reduced circulating insulin, HOMA-IR, and IGF-1 levels, decreasing the risk of hyperinsulinemia or insulin resistance (35).

Hyperinsulinemia increases the risk of cancer recurrence and mortality, especially in breast cancer, by promoting residual cancer cell growth and survival (35, 40). Hyperinsulinemia also reduces sex hormone-binding globulins (SHBG), which results in increased bioavailability of sex hormones, which can drive cell proliferation (12). There is a probability that physical activity reduces insulin concentrations by increasing and enhancing the function of glucose transporter proteins such as GLUT4, and a 20% to 25% decrease in insulin concentration can increase 5-year breast cancer survival by 5% to 6% (40). Physical activity also reduces bile acid concentration (41) Bile acid causes DNA damage, promotes frequent apoptosis, and is considered carcinogenic at high concentrations (42). Tumor growth in many types of cancer can be slowed down by physical activity, and repetitive exercise decreases cell proliferation, activates tumor suppressor genes like p53, and promotes apoptosis in tumor tissue (12). Exercise may lead to improved blood flow, which may result in increased oxygenation and perfusion of tumors, which may enhance the delivery of cytotoxic chemotherapy, improve the efficacy of radiation therapy, and increase the penetration of cytotoxic immune cells into tumors (43). According to some research, myokines generated by contracting skeletal muscle may promote the mobilization of natural killer cells and the subsequent infiltration of immune cells into tumors (43). Additionally, a study shows potential evidence for an acute exercise-induced myokine response involving SPARC, OSM, IL-6, and IL-15, as well as tumor growth inhibition in serum, in patients with advanced prostate cancer following a bout of high-intensity interval exercise (44). It is hypothesized that physical activity decreases the risk of recurrence and improves survival through an identical process; a better blood supply to the tumor may prevent the release of tumor cells from the primary tumor; and improved cytotoxic immune function may decrease the survival of cancer cells and the formation of distant metastatic lesions (43). Maintaining metabolic functions and regulating cell apoptosis depend on healthy mitochondria (45). Inflammatory diseases and inflammatory mediators, including tumor necrosis factor-alpha (TNF $\alpha$ ) and interleukin-1 beta (IL-1 $\beta$ ), lead to mitochondrial dysfunction (46). Chronic inflammation can hinder tissue regeneration and cause harm to the afflicted organ because, due to mitochondrial dysfunction, it may become difficult for mitochondria to maintain and control the cells (45). Physical activity such as an active lifestyle, aerobic endurance exercise, and anaerobic resistance exercise have been demonstrated to enhance mitochondrial function and may lessen the incidence or severity of cancer (45). The physiological impact of physical activity on cancer is summarized in Table 3.

Table 3. The Physiological Impact of Physical Activity on Cancer

Impact of Physical Activity	Effects on Cancer
Reduces Obesity and Metabolic Syndrome Variables	Reduces obesity and metabolic syndrome variables including reduced BMI, blood pressure, triglycerides, blood glucose, leptin and adiponectin levels, preventing cancer and decreasing the risk of cancer recurrence and mortality (35, 37)

Reduces Estradiol and C-Reactive Protein Levels	Weight loss due to physical activity reduces estradiol and C-reactive protein levels, reducing the risk of endometrial and breast cancer in postmenopausal women (12, 39)
Reduces Insulin Concentrations	Reduces insulin concentrations by increasing GLUT4 function, which leads to reduced circulating insulin, HOMA-IR, and IGF-1 levels, decreasing the risk of hyperinsulinemia and reduced sex hormone-binding globulins (SHBG), decreasing the risk of increased sex hormone-driven cell proliferation and cancer recurrence and mortality, especially in breast cancer (12,35, 40)
Reduces Bile Acid Concentration	Reduces bile acid concentration that causes DNA damage, promotes frequent apoptosis, and is considered carcinogenic at high concentrations (41, 42)
Slows Tumor growth	Slows tumor growth by decreases cell proliferation, activation of tumor suppressor genes like p53, and promotion of apoptosis in tumor tissue (12)
Improves Blood Flow and oxygenation	Improves blood flow, increases oxygenation, and perfusion of tumors, that enhances delivery of cytotoxic chemotherapy, improves efficacy of radiation therapy, and increases penetration of cytotoxic immune cells into tumors, and may prevent release of tumor cells from primary tumor (43)
Induces Myokine Response	Generates myokines and induces myokine response, mobilizing natural killer cells and infiltrating immune cells into tumors involving SPARC, OSM, IL-6, and IL-15 along with tumor growth inhibition in serum leading to improved cytotoxic immune function and decreased survival of cancer cells and formation of distant metastatic lesions (43, 44)
Enhances Mitochondrial Function	Enhances mitochondrial function and prevents mitochondrial dysfunction that is caused by inflammatory mediators such as TNF $\alpha$ and

	IL-1 $\beta$ , resulting in the maintenance of metabolic functions, regulation of cell apoptosis and tissue regeneration, and lessening incidence or severity of cancer (45, 46)
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**Recommended Guidelines for Physical Activity in Healthy Populations and Cancer Patients**

One of the most important things that anyone can do to prevent, treat, and control cancer is to engage in physical activity; therefore, health practitioners worldwide are recommended to encourage the general public and cancer patients to be as physically active as possible in accordance with their age, ability level, and cancer status (12).

WHO recommends a minimum of 60 minutes of moderate- to vigorous-intensity aerobic physical activity daily and vigorous-intensity activities, including muscle and bone strengthening activities, a minimum of 3 times per week for children and adolescents, and a minimum of 150 minutes of moderate-intensity aerobic physical activity or 75 minutes of vigorous-intensity aerobic physical activity per week with a minimum of 2 days of muscle-strengthening activities for adults (9). WHO recommendations on physical activity for children, adolescents, and adults are summarized in Table 4.

Table 4. WHO Physical Activity Recommendations for Children, Adolescents, and Adults (9)

Recommendations for Children and Adolescents	Recommendations for Adults
Minimum 60 minutes of moderate- to vigorous intensity mostly aerobic physical activity daily	Minimum 150 minutes of moderate-intensity aerobic physical activity or 75 minutes of vigorous-intensity aerobic physical activity or an equivalent combination of moderate- and vigorous-intensity activity per week
Vigorous-intensity activities including muscle and bone strengthening activities minimum 3 times per week	Muscle-strengthening activities minimum 2 days per week

Following a diagnosis, clinicians should immediately counsel their patients to get more physically active because doing so would have significant advantages (27). For cancer patients, exercise is typically regarded as safe, and it is recommended that patients avoid inactivity and try to be physically active as much as they can (26). The World Cancer Research Fund (WCRF), the American Institute for Cancer Research (AICR), and the American College of Sports Medicine (ACSM) all advocate for limiting sedentary behaviors, participation in physical activity in all domains such as household, leisure-time, transport, and occupational, engaging in at least 150

minutes of moderate-intensity aerobic exercise or 75 minutes of vigorous aerobic exercise a week, and engaging in strength training exercises minimum twice a week, as aerobic physical activity utilizes oxygen and enhances cardiovascular function and oxygen uptake, whereas anaerobic resistance training with weights does not utilize oxygen but promotes muscle strength and mass (14, 47, 48). According to the available research, an efficient exercise regimen that mostly improves health-related outcomes brought on by a cancer diagnosis and treatment includes a minimum of 30 minutes of moderate-intensity aerobic training at least three times weekly and resistance training at least twice weekly for at least 8–12 weeks; furthermore, compared to fully unsupervised or home-based programs, supervised exercise programs seem to be more successful (26).

### **Challenges for Initiating Physical Activity in Cancer Patients and Individualized Recommendations**

Despite extensive research on the benefits of physical activity for cancer patients, combining physical activity and therapy is not frequent in real-world settings (27). Leisure-time physical inactivity was reported by 35.5% of adult cancer patients in the US in 2020, including 33.2% of male patients and 37.7% of female patients (49). In one study, adequate physical exercise was reported by just 7% of cancer patients, and 93% of patients reported inadequate physical exercise (50). Participation in physical activity by child and adolescent cancer patients and survivors, such as children diagnosed with leukemia, is comparatively less than that of other children and adolescents, leading to adverse impacts on physiological, physical, psychological, and social health (51). The challenge for cancer patients is initiating regular physical activity, which is influenced by their coping strategies, as constructive optimistic fighting coping strategies help initiate and maintain physical activity, while destructive pessimistic anxious strategies reduce the patient's quality of life and motivation to engage in physical activity (27).

In a study on 1003 cancer patients, lack of time because of being busy, lack of motivation, and fatigue were reported as hindrances to physical activity participation (52). In another study on breast cancer patients, 72.7% of patients reported individual-level physical activity barriers, including physical injuries such as a broken ankle, physical symptoms such as pain and fatigue, lack of motivation, and lack of time; furthermore, 15.2% of patients reported social-level physical activity barriers such as family obligations and social commitments, and 28.8% of patients reported organizational/environmental-level physical activity barriers such as job demand and stress (53). In a study on prostate cancer patients, the major physical activity and specifically exercise barriers in patients aged less than 65 years were lack of time and poor health, whereas the major barriers in prostate cancer survivors aged more than 65 years were lack of exercise facilities and lack of exercise information; in addition, immediately after surgery, poor health and pain at the surgery site were the most common exercise barriers, whereas 6 months after surgery, the major barriers were lack of time and poor health (54).

Cancer patients find it particularly challenging to exercise in public because of medication side effects, including hair loss, as well as the fear of infection and overheating (55). Lack of experience, lack of an exercise partner, and fear of injury are some of the other hindrances to

exercise and physical activity (27). A lack of knowledge about how to exercise and what type of physical activity is best for them is mentioned by a large number of patients as the reason why they do not engage in physical activity (54). Patients' concern that a particular form of physical activity can be harmful to them because of their illness is another reason why they do not start physical activity (27). A study on cancer in children and adolescents shows that physical activity is often considered by patients and health care professionals as an intense exercise regimen performed in a gym or other specialized setting; therefore, initiating physical activity seems unachievable due to this limited knowledge about physical activity and the physical restrictions that many cancer patients face (51). These major challenges and barriers to initiating physical activity in cancer patients including physical symptoms such as pain and fatigue, lack of motivation, lack of time, and lack of exercise information, are summarized in Table 5.

Table 5. Challenges for Initiating Physical Activity in Cancer Patients

<b>Author(s)</b>	<b>Study Design &amp; Participants</b>	<b>Physical Activity Barriers</b>
Eng et al. (52)	Retrospective cross-sectional survey of 1003 adult cancer patients in Canada	Lack of time because of being busy, lack of motivation, fatigue
Cho & Park (53)	Secondary analysis of a lifestyle intervention randomized controlled trial of 173 female breast cancer patients in the USA	Physical injuries such as a broken ankle, physical symptoms such as pain and fatigue, lack of motivation, lack of time, family obligations, social commitments, job demand, stress
Min et al. (54)	Cross-sectional survey of 111 prostate cancer patients in Korea	<p>Patients aged &lt; 65 years: lack of time and poor health,</p> <p>Patients aged &gt; 65 years: lack of exercise facilities, lack of exercise information such as how to exercise and the type of physical activity best for them</p> <p>Post-surgery: poor health, pain at the surgery site</p>
Nielsen et al. (55)	Cross-sectional survey of 30 Breast cancer patients in USA	Exercising in public: hair loss and other medication side effects, fear of infection, overheating
Shabaniyan et al. (51)	Qualitative semi-structured interviews of healthcare	Physical restrictions. limited knowledge about physical

	providers of child and adolescent cancer patients and survivors.	activity, physical activity considered as an intense exercise regimen performed in a gym or other specialized setting; therefore, initiating physical activity seems unachievable
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Cancer patients' response to a specific physical activity stimulus may vary depending on a variety of factors, including demographics like age, physiological effects from cancer treatments like anemia, and side effects from cancer treatments like fatigue that may lead to low exercise tolerance (26). Recommendations for physical activity should be specifically personalized for each individual with the overall goal of a gradual increase of physical activity to meet the Physical Activity Guidelines and should be lowered for patients with age, health and disease status, treatment status, comorbidities, or limitations in mobility that prevent them from completely following the guidelines (48). When weight and lean body mass loss are side effects of treatment, it is important to make sure that exercise training does not result in an excessive energy deficit that can exacerbate fatigue and weight loss, and dietary modifications to support adequate energy availability and replenishment during and after exercise should also be advised (26). When the side effects are weight gain and/or obesity, safety considerations related to cardiovascular disease risk should be ensured (56, 57). Goals to increase the duration or intensify physical activity are likely to be more successful than outcome-based objectives like weight loss or strength gain; furthermore, by addressing barriers to and locating resources and supports for behavior change that may aid in facilitating adherence to physical activity recommendations, clinicians can help patients develop and achieve SMART or Specific, Measurable, Action-based, Realistic, and Timely goals (58). The clinician can reduce the resistance of some patients to increasing physical activity by explaining the different kinds of physical activities that are available, such as hiking, walking, swimming, and exercise machines, and the methods to include physical activity in socially acceptable ways with friends and family; additionally, by encouraging progress over time and advising low-impact physical activities such as aquatic exercise, the clinician may be able to overcome the patient's reluctance to exercise due to discomfort or lack of experience (58). In addition, evidence-based prescriptions for the type, frequency, intensity, and duration of physical activity can be prescribed (26).

In a qualitative study, healthcare professionals recommended five strategies to encourage physical activity among children and adolescents diagnosed with cancer, including firstly, broadly defining physical activity to include any bodily movement that expends energy, such as walking, stretching, or any other low-intensity physical activity, taking online dance lessons, using household items instead of gym equipment, or doing physical activity at home; furthermore, unstructured, developmentally appropriate, enjoyable physical activity, such as active play, is especially recommended for pediatric cancer patients; secondly, tailoring physical activity recommendations based on individual interests and preferences, including activities such as patients' hobbies like ballet or skateboarding, participating in a sports team, or having a walk with friends to be physically active in an enjoyable way; thirdly, involving families in discussions about physical activity to debunk concerns related to the risk of injury or infection



and improve follow-through and maintenance of lifestyle change, especially in younger children and adolescents; fourthly, connecting patients to more inclusive and community-based physical activity programs, such as after-school and school-based physical education programs; and fifthly, enhancing patient motivation, as lack of motivation, influenced by social, psychological, and physical factors, is a significant barrier, and the "sick child mindset" and physical health restrictions associated with cancer treatment contribute to patients' reluctance to engage in physical activity, therefore, to address these challenges, healthcare professionals are encouraged to undergo behavioral training and evidence-based interventions, aiming to enhance patients' motivation and willingness to participate in physical activity (51).

### **Implications and Future Directions**

It can be observed from this study that physical activity plays a very important role in the prevention of cancer as well as in its recovery and prevention of recurrence. These findings may help in increasing the awareness of clinicians as well as the general healthy population and cancer patients and their families. This can lead to an increase in all types of physical activity in all domains of life in the general population, as well as the development and provision of more facilities for physical activity to the general population as a preventative public health measure for cancer. Furthermore, this can also lead to the development of measures and protocols and the provision of facilities for physical activities specifically for cancer patients, promoting cancer recovery and preventing recurrence. The clinicians may suggest physical activity according to the recommended guidelines, or these guidelines may be adapted according to the individual needs of patients and may include leisure-time exercise or physical activity in all domains to increase the ease with which patients can incorporate an adequate amount of physical activity in their daily lives. Furthermore, after remission, this may help in preventing the risk of cancer recurrence by modifying and reducing the risk factors. Although much information about the beneficial association of physical activity with cancer is present, there is still a gap in research on different domains and various specific types of physical activity; therefore, future studies exploring these aspects are recommended. Furthermore, there is a need for prospective cohort studies exploring the association of physical activity with specific cancer sites, with currently limited studies

### **Conclusions**

Physical activity plays a pivotal role in the prevention, recovery, and reduction of the risk of recurrence of cancer. It impacts cellular processes and tumor growth by controlling body weight and metabolic variables, enhancing mitochondrial and immune function, controlling genomic instability, releasing myokines, and regulating a number of hormones and circulating biomarkers such as insulin and bile acid. Participation in adequate physical activity according to the recommended guidelines is linked to a decreased risk of various cancer types; furthermore, it aids cancer patients in recovery by reducing the cancer treatment side effects, improving physical fitness, mental health, and quality of life, and additionally, decreasing the risk of cancer recurrence after remission. An increase in all types of physical activity in all domains of life in

the general population and cancer patients according to the recommended guidelines or adapted according to the individual needs of patients can significantly contribute to reducing the burden of cancer and improving overall well-being.

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