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# The Role of Exercise in Mitigating Cancer Treatment Side Effects: A Comprehensive Review

Riaz Ahmed

## ABSTRACT

Cancer treatments, while life-saving, often cause debilitating side effects that impair patients' quality of life. This review synthesizes current evidence on the role of exercise in mitigating treatment-related toxicities, including fatigue, neuropathy, cognitive decline, and musculoskeletal complications. Findings demonstrate that structured exercise interventions incorporating aerobic, resistance, and mind-body modalities effectively reduce symptom severity, enhance physical function, and improve psychological well-being across diverse cancer types and treatment phases. Biological mechanisms include modulation of inflammation, immune function, and metabolic health. Despite robust evidence, implementation challenges persist, including limited referral pathways and inadequate institutional support. The narrative review highlights the need for standardized exercise oncology protocols integrated into clinical practice to optimize patient outcomes. Future research should focus on personalized prescriptions, long-term adherence strategies, and the potential synergistic effects of exercise with emerging therapies.

**Keywords:** Exercise oncology, Cancer treatment side effects, Fatigue management, Personalized exercise prescriptions, Implementation challenges

## Introduction

### Overview of Cancer Prevalence and Historical Context

Cancer remains a significant global health burden, with 19.3 million new cases diagnosed in 2020 and nearly 10 million deaths recorded.<sup>1</sup> Patients undergoing cancer treatments such as chemotherapy, radiation therapy, and hormone therapy often experience debilitating side effects, including fatigue, depression, anxiety, reduced quality of life (QoL), and sleep disturbances, which negatively impact multiple physiological systems. Historically, exercise was not widely recommended for cancer patients due to concerns about exacerbating treatment-related complications. However, emerging evidence highlights the critical role of structured exercise interventions in mitigating these adverse effects.<sup>4</sup>

Figure 1 illustrates “exercise effects has on the immune system and inflammation associated with a cancer diagnosis.”<sup>4</sup> A systematic review of preclinical and clinical studies indicates that exercise enhances the efficacy of chemotherapy and tamoxifen in rodent models, either additively, synergistically, or by sensitizing tumors to treatment.<sup>2</sup> Another study demonstrates that physical activity decreases the severity of treatment side effects, reduces fatigue, improves QoL, enhances mental health, and boosts aerobic fitness in cancer patients, while also lowering the risk of cancer recurrence and mortality.<sup>1</sup>

Preliminary clinical evidence suggests that exercise during neoadjuvant, primary, and adjuvant therapy may improve treatment outcomes, though further research is needed to confirm these findings.<sup>2</sup> Despite these benefits, cancer patients often lack awareness of exercise's role in their care. A cross-sectional study found that only 3.2–14.4% of patients reported a strong understanding of exercise recommendations, highlighting a gap in patient education.<sup>3</sup> Current guidelines emphasize incorporating aerobic and resistance training into cancer care, with most recommending 150 minutes per week of moderate-intensity activity plus resistance training twice weekly.<sup>5</sup>

However, challenges persist in determining the optimal type, intensity, and duration of exercise for individual patients, given variations in cancer type, treatment phase, and patient condition.<sup>1</sup> High-quality guidelines exist, but further research is needed to refine tailored exercise prescriptions and improve implementation in clinical practice.<sup>5</sup> Figure 2 shows that “although the most recent recommendations tried to provide indications regarding the physical activity dosage, most still resulted in generic.”<sup>5</sup> Exercise modulates inflammation, immune function, and metabolic health, contributing to improved patient outcomes.<sup>1</sup> However, barriers such as a lack of standardized protocols, limited patient awareness, and insufficient integration into oncology care hinder widespread adoption.<sup>3</sup> Future research should address these gaps to establish evidence-based exercise oncology programs as a standard component of cancer treatment.

## Research Objectives

- To analyze how treatments such as chemotherapy, radiation, and hormone therapy impact patients both physically and mentally.
- To investigate whether specific exercise can mitigate the side effects of cancer treatment.
- To summarize the clinical evidence, aerobic, resistance, and mind-body exercises are recommended for various cancer types and stages of treatment.
- To explore the underlying mechanisms by which exercise modulates inflammation, immune function, metabolic health, and QoL in cancer patients.
- To identify implementation challenges and research gaps in integrating exercise oncology into standard cancer care protocols.

## Scope of Review and Its Relevance to Survivorship Care

This review outlines both the physical and emotional issues caused by cancer treatment, including tiredness, problems with the heart, muscles, and nerves, and feelings of forgetfulness. It also examines how structured

exercise, such as aerobics, muscle training, and mind-body training, can help alleviate these issues. It discusses how exercise influences inflammation, immune responses, and metabolism, highlighting the challenges of incorporating exercise into medical practice.<sup>5</sup> The focus is on the care of cancer survivors, with a special emphasis on personalized exercise programs to ensure lasting good results. Supporting and encouraging exercise during cancer treatment could help patients survive and recover.<sup>1,5</sup>

**Methodology**

This review employs a **narrative literature review** methodology to assess the role of exercise in mitigating the side effects of cancer treatment. The review synthesizes current evidence from preclinical, clinical, and observational studies published between 2017 and 2025, focusing on the integration of exercise interventions into cancer care across different treatment phases. The methodology follows a rigorous process to ensure transparency, reliability, and comprehensiveness (Table 1).

**PRISMA Flow Chart**

The PRISMA flow diagram (Figure 3) is a standardized tool for documenting the process of identifying, screening, assessing, and including studies in a systematic review. Here is a breakdown of each stage in the diagram.<sup>6</sup>

Initial searches across selected databases (e.g., PubMed, Scopus, Web of Science) yielded 69 records relevant to the topic. Out of the 69 records, 14 were identified as duplicates and removed, resulting in 55 unique records for screening. The remaining records underwent title and abstract screening to determine their relevance to the study objectives. 17 records were excluded at this stage due to irrelevance, likely based on title/abstract content. Of the 55 records screened, 38 were deemed potentially relevant and moved forward for full-text review. Two articles were excluded after full-text review due to being non-peer-reviewed sources and not including an exercise component (key inclusion criterion).

Ultimately, 36 studies were included in the final qualitative synthesis (e.g., thematic analysis, evidence mapping). This diagram reflects a transparent and systematic approach to selecting literature for inclusion. It enhances reproducibility and meets reporting standards expected in high-quality systematic reviews, such as those outlined in the PRISMA 2020 Statement.

**Comparative Table**

The key outcomes and comparative insights are presented in Table 2, which provides a comprehensive overview of the study's findings.

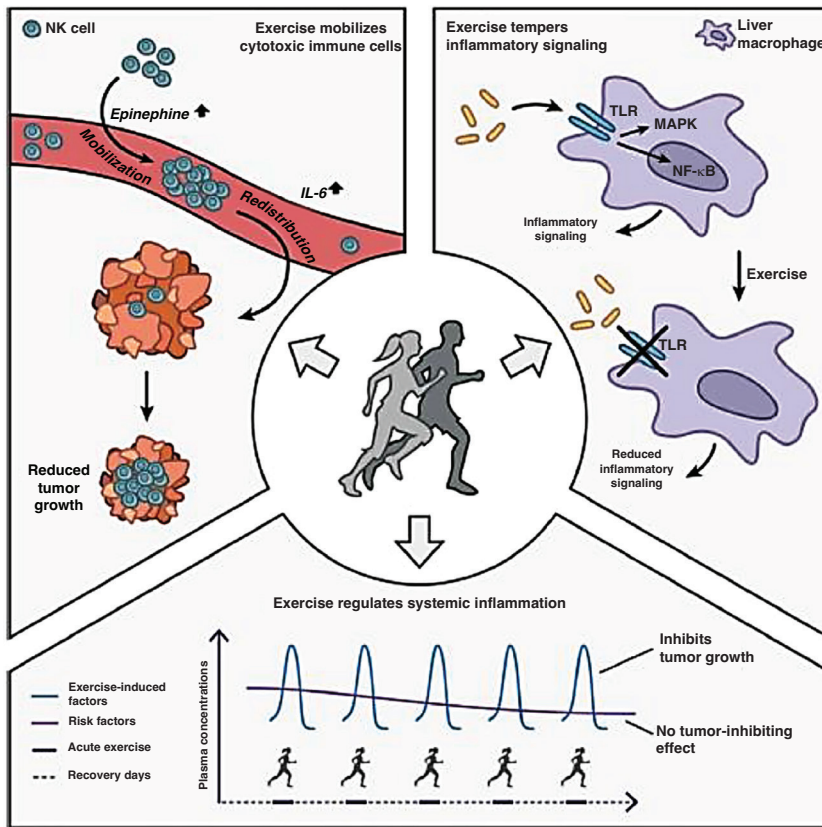


Fig 1 | Effects of exercise on the immune system<sup>6</sup>

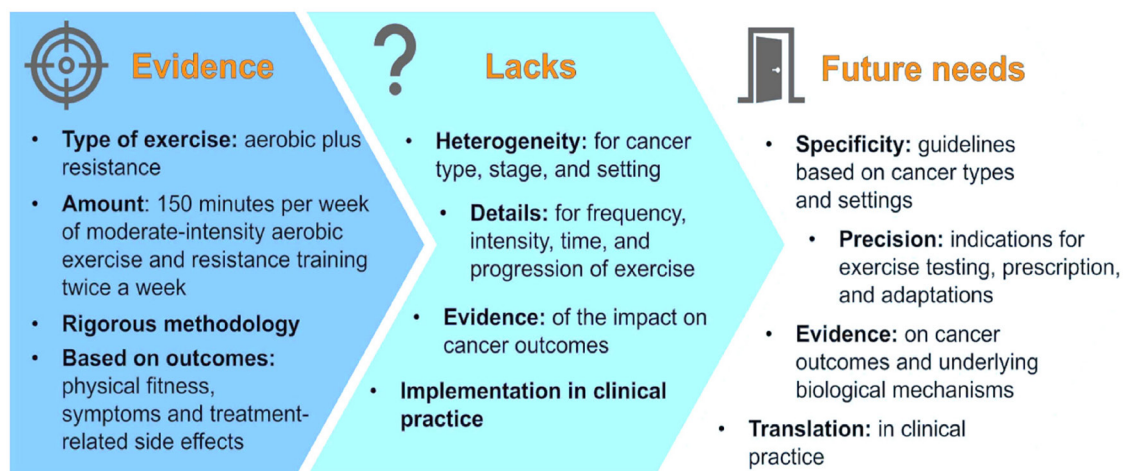


Fig 2 | Current evidence, gaps, and future needs for guidelines in exercise oncology<sup>5</sup>

**Table 1 | Summary of methodological approaches used in the study**

Section	Description
Database Selection and Search Strategy	<ul style="list-style-type: none"> <li>Multiple databases were searched: PubMed, CINAHL, Scopus, Web of Science, and Google Scholar.</li> <li>Search terms included “exercise oncology,” “cancer treatment side effects,” and others.</li> <li>Boolean operators were used to combine search terms.</li> </ul>
Search Period	<ul style="list-style-type: none"> <li>Search conducted in January 2025; studies published until this date were included.</li> </ul>
Inclusion Criteria	<ul style="list-style-type: none"> <li>Adult cancer patients (18+ years)</li> <li>Structured exercise programs (aerobic, resistance, mind-body) during any stage of cancer treatment</li> <li>Clinical trials, cohort, observational studies</li> <li>Studies reporting exercise dose, type, and intensity</li> </ul>
Exclusion Criteria	<ul style="list-style-type: none"> <li>Animal studies</li> <li>Non-peer-reviewed studies</li> <li>Studies not in English</li> <li>Studies without an exercise component</li> </ul>
Data Extraction and Synthesis	<ul style="list-style-type: none"> <li>Data extracted using a standardized form: Study design, sample size</li> <li>Type of cancer and treatment phase</li> <li>Exercise interventions (dose, type, intensity)</li> <li>Outcomes (fatigue, psychological health, etc.)</li> <li>Key findings and conclusions</li> </ul>
Synthesis Method	<ul style="list-style-type: none"> <li>Narrative synthesis was used to summarize and integrate findings.</li> <li>Studies were grouped by cancer type, treatment phase, and type of exercise intervention.</li> </ul>
Quality Assessment	<ul style="list-style-type: none"> <li>Studies assessed using the AGREE II instrument for clinical practice guidelines</li> <li>Cochrane Risk of Bias Tool for randomized controlled trials</li> <li>Rating based on study design, sample size, outcome measures, and risk of bias</li> </ul>
Limitations	<ul style="list-style-type: none"> <li>Language bias (only English studies)</li> <li>No meta-analysis (limits quantitative comparison)</li> <li>Variability in study design, exercise prescription, and outcome measures</li> <li>Exclusion of studies published before 2017</li> </ul>
Future Directions	<ul style="list-style-type: none"> <li>Future reviews may broaden the time range of included studies and include meta-analysis for more robust quantitative comparisons.</li> </ul>

### Side Effects of Cancer Treatments Physiological and Psychological Side Effects of Cancer Treatments

Cancer treatments, including chemotherapy, radiation therapy, and hormone therapy, induce a broad spectrum of physiological and psychological side effects by damaging healthy tissues and organs.<sup>6</sup> The National Cancer Institute documents over 25 specific treatment-related complications, ranging from fatigue (reported in 58–90% of patients), neuropathy (30–40% of chemotherapy recipients), and cognitive dysfunction (35% of survivors) to lymphedema (affecting 20–40% of breast cancer patients after lymph node removal).<sup>6,8</sup> Chemotherapy’s mechanism of attacking rapidly dividing cells explains its frequent collateral damage to hair follicles (causing alopecia in 65% of patients), bone marrow (leading to neutropenia in 80% of cases), and gastrointestinal mucosa (resulting in nausea/vomiting in 70–80% of recipients).<sup>9</sup>

Although each patient’s experience may differ, it is helpful to understand the most common side effects and how to manage them (see Figure 4).<sup>9</sup> The CDC notes that neutropenia occurs when white blood cell counts drop below 1,500 cells/ $\mu$ L, increasing the risk of infection by about 21-fold during treatment.<sup>10</sup> Long-term effects persist in over 15 million US cancer survivors, with projections reaching 20 million by 2026.<sup>8</sup> Breast cancer survivors (>3.5 million in the United States) particularly face cardiotoxicity (28% incidence after anthracyclines), endocrine disruptions (100% in estrogen-receptor positive cases), and sexual dysfunction (50–75% prevalence).<sup>8</sup>

### Emerging Management Strategies and the Need for Personalized Rehabilitation

Zheng’s review emphasizes that 60% of rehabilitation candidates require special precautions for bone metastases, thrombocytopenia (<50,000 platelets/ $\mu$ L), or cachexia (present in 50–80% of advanced cases).<sup>7</sup> Emerging data from the CDC report indicate that cooling caps reduce chemotherapy-induced alopecia by 50% in anthracycline regimens, although efficacy varies by drug class.<sup>10</sup> Current management strategies prioritize multimodal approaches, combining pharmacological interventions with physical modalities.<sup>7</sup> However, 40% of patients report inadequate side effect control, highlighting gaps in supportive care.<sup>8</sup> The AGREE II instrument validated guidelines recommend 150 minutes/week of moderate exercise to combat treatment toxicities, though only 35% of survivors meet this threshold due to persistent fatigue.<sup>5,7</sup> These findings underscore the critical need for personalized rehabilitation protocols addressing the complex interplay of treatment-specific toxicities and patient-specific vulnerabilities.<sup>7,8</sup>

### Exercise as a Therapeutic Modality for Cancer Evidence Supporting Exercise in Cancer Care

Exercise has emerged as a crucial therapeutic modality in cancer care, with increasing evidence supporting its role in enhancing patient outcomes. The 2019 International Multidisciplinary Roundtable established that exercise training is generally safe for cancer survivors, recommending that every survivor should “avoid inactivity.”<sup>11</sup> Their consensus highlighted that

**Table 2 | Comprehensive comparison of findings across different parameters**

Study	Study Focus	Cancer Type	Exercise Modality	Outcomes Measured
Misiąg et al. (2022) <sup>1</sup>	Physical activity and cancer care review	General Cancer Types	Various modalities (aerobic, resistance)	Fatigue, QoL
Yang et al. (2021) <sup>2</sup>	Exercise effects on cancer treatment efficacy	General Cancer Types	Aerobic, resistance	Treatment efficacy, fatigue
Oğul & Ercan (2022) <sup>3</sup>	Knowledge of exercise in cancer patients	General Cancer Types	Aerobic, resistance	Patient knowledge, exercise engagement
Gillespie (2018) <sup>4</sup>	Summary of exercise and cancer interventions	General Cancer Types	Aerobic, resistance	Fatigue, physical function
Avancini et al. (2025) <sup>5</sup>	Physical activity guidelines in oncology	General Cancer Types	Aerobic, resistance	Guidelines adherence, treatment outcomes
National Cancer Institute (2025) <sup>6</sup>	Side effects of cancer treatment	Various cancer types	Various modalities	Side effects (fatigue, immune function)
Zheng et al. (2021) <sup>7</sup>	Safety and precautions in cancer rehabilitation	General cancer types	Aerobic, resistance	Physical function, safety
Gegechkori et al. (2017) <sup>8</sup>	Long-term effects of cancer treatments	Specific cancer types (e.g., breast cancer)	Various modalities	Long-term side effects
Cleveland Clinic (2023) <sup>9</sup>	Chemotherapy side effects management	Chemotherapy patients	Aerobic, resistance	Chemotherapy side effects
CDC (2025) <sup>10</sup>	Side effects of cancer treatment	General cancer types	Various modalities	Side effects (immune function, fatigue)
Campbell et al. (2019) <sup>11</sup>	Exercise guidelines for cancer survivors	General cancer types	Aerobic, resistance	Fatigue, physical function, QoL
Stout et al. (2020) <sup>12</sup>	Rehabilitation and exercise recommendations	Various cancer types	Aerobic, resistance	Physical function, QoL
Chen et al. (2025) <sup>13</sup>	Exercise to mitigate cancer metastasis risk	Various cancer types	Aerobic, resistance	Cancer metastasis, physical function
Tête & Wilson (2025) <sup>14</sup>	Physical activity and return to work postcancer	Various cancer types	Aerobic, resistance	Return-to-work self-efficacy (RTW-SE), anxiety, depression
DePolo (2022) <sup>15</sup>	Exercise guidelines for cancer patients	Breast cancer	Aerobic, resistance	Fatigue, physical function
NCI (2020) <sup>16</sup>	Physical activity and cancer prevention	General cancer types	Aerobic, resistance	Cancer prevention, fatigue
Cancer Research UK (2018) <sup>17</sup>	Benefits of exercise for cancer patients	Various cancer types	Aerobic, resistance	Physical function, immune function
American Cancer Society (2019) <sup>18</sup>	Exercise and survivorship care	Various cancer types	Aerobic, resistance	QoL, fatigue
Wendler (2022) <sup>19</sup>	Exercise during cancer treatment	General cancer types	Aerobic, resistance	Fatigue, psychological distress
Hirano (2020) <sup>20</sup>	IL-6 modulation by exercise in cancer	Various cancer types	Aerobic, resistance	IL-6 levels, inflammation
Caldirolì et al. (2025) <sup>21</sup>	Resilience in cancer patients	Various cancer types	Aerobic, resistance	Psychological resilience, QoL
Barre et al. (2018) <sup>22</sup>	Psychological interventions in cancer	Various cancer types	Cognitive therapy, psychoeducation	Stress, QoL
Huang et al. (2025) <sup>23</sup>	Cancer and Living Meaningfully (CALM) therapy for cancer patients	Various cancer types	Psychoeducation, therapy	Anxiety, depression, QoL
Chen et al. (2025) <sup>24</sup>	RTW-SE in renal cancer	Renal cancer	Aerobic, resistance	Anxiety, depression, and self-efficacy
Zyzniewska-Banaszak et al. (2021) <sup>25</sup>	Physiotherapy and physical activity	Various cancer types	Physiotherapy, aerobic	Psychological distress, physical function
Santa Mina et al. (2021) <sup>26</sup>	Prehabilitation in cancer care	Various cancer types	Aerobic, resistance	Recovery, physical function
Courneya et al. (2024) <sup>27</sup>	Exercise across the cancer continuum	Various cancer types	Aerobic, resistance	Physical function, recovery
An et al. (2024) <sup>28</sup>	Exercise in cancer survivorship	Various cancer types	Aerobic, resistance	Physical function, QoL
Chowdhury et al. (2020) <sup>29</sup>	Rehabilitation and palliative care	Palliative cancer care	Physiotherapy, exercise	Symptom management, QoL
Yang et al. (2024) <sup>30</sup>	Physical Activity and Cancer Control (PACC) framework in cancer control	Various cancer types	Aerobic, resistance	Cancer outcomes, QoL
Kennedy et al. (2021) <sup>31</sup>	Barriers to exercise in oncology	Various cancer types	Aerobic, resistance	Barriers to implementation
Herrero López et al. (2024) <sup>32</sup>	Exercise referral pathways in oncology	Various cancer types	Aerobic, resistance	Referral systems, exercise prescription
Kennedy et al. (2021) <sup>31</sup>	Implementation barriers to integrating exercise	Various cancer types	Aerobic, resistance	Barriers to implementation
Mizrahi et al. (2024) <sup>33</sup>	Expanding the role of exercise oncology	General cancer types	Aerobic, resistance	Patient outcomes, physical function
Brown & Ligibel (2019) <sup>34</sup>	Putting exercise into oncology practice	General cancer types	Aerobic, resistance	Treatment outcomes, QoL

specific doses of aerobic exercise (30–60 minutes of moderate-intensity 3 times weekly) and resistance training (2 sets of 8–12 repetitions) can significantly reduce fatigue, anxiety, depressive symptoms, physical functioning, and health-related QoL.<sup>11,15</sup>

For lymphedema management, supervised resistance training programs focusing on large muscle groups, 2–3 times weekly, are beneficial without exacerbating symptoms, challenging previous recommendations to avoid exercise.<sup>15</sup> Current guidelines emphasize personalized exercise prescriptions based on

cancer type, treatment, and individual health status. A 2020 systematic review of 69 oncology guidelines found that 32 provided specific rehabilitation recommendations, though only 21 met high-quality standards on the AGREE II tool (scoring  $\geq 45$ ).<sup>12</sup>

### Challenges in Implementation

Despite these recommendations, clinical utilization remains low, highlighting a gap between evidence and practice.<sup>12</sup> Emerging research demonstrates exercise's potential to reduce the risk of cancer metastasis,

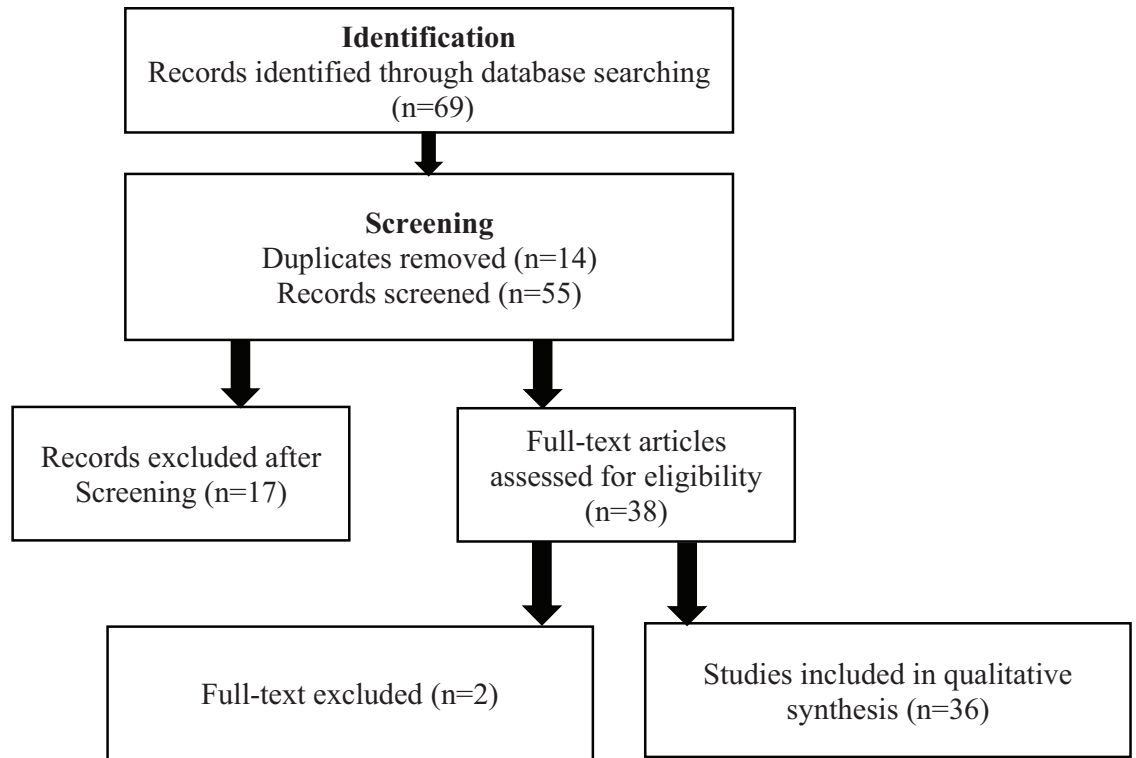


Fig 3 | PRISMA flow diagram

Chemotherapy side effects

 <b>Fatigue.</b>	 <b>Hair loss.</b>	 <b>Skin changes.</b>
 <b>Nausea, vomiting, bowel habit changes.</b>	 <b>Loss of appetite, difficulty eating.</b>	 <b>A weakened immune system.</b>
 <b>Bladder, kidney problems.</b>	 <b>Bruising and bleeding.</b>	 <b>Peripheral neuropathy.</b>
 <b>Sex and fertility issues.</b>	 <b>Trouble remembering and concentrating.</b>	

Fig 4 | Chemotherapy side effects<sup>9</sup>

although the mechanisms remain under investigation. For example, Figure 5 highlights key regulatory pathways and cellular interactions at each stage, providing an integrated overview of the metastasis process relevant to understanding potential exercise intervention points.<sup>13</sup> With 50.6 million global cancer survivors in 2020, many working-age exercise interventions are increasingly recognized for their role in facilitating return to work by mitigating treatment-related fatigue, pain, and psychological distress.<sup>14</sup>

The integration of exercise into standard cancer care is supported by its multifaceted benefits, including enhanced treatment efficacy, reduced risk of recurrence, and improved survival outcomes.<sup>13,15</sup> However, challenges persist in implementing supervised, tailored programs, particularly for high-risk populations. Future directions call for expanded clinical trials, precision exercise therapy, and multidisciplinary collaboration to optimize exercise oncology protocols.<sup>13</sup>

#### Physiological Benefits of Exercise During Cancer Treatment Physiological Mechanisms of Exercise During Cancer Treatment

Exercise during cancer treatment provides significant physiological benefits through multiple biological mechanisms. Regular physical activity lowers estrogen and insulin levels, which are associated with reduced risk of hormone-driven cancers like breast and colon cancer.<sup>16</sup> “Being active can also be helpful for many people with cancer, during and after their treatment (see Figure 6).”<sup>17</sup>



Fig 5 | An effective approach to mitigate the risk of cancer metastasis<sup>13</sup>

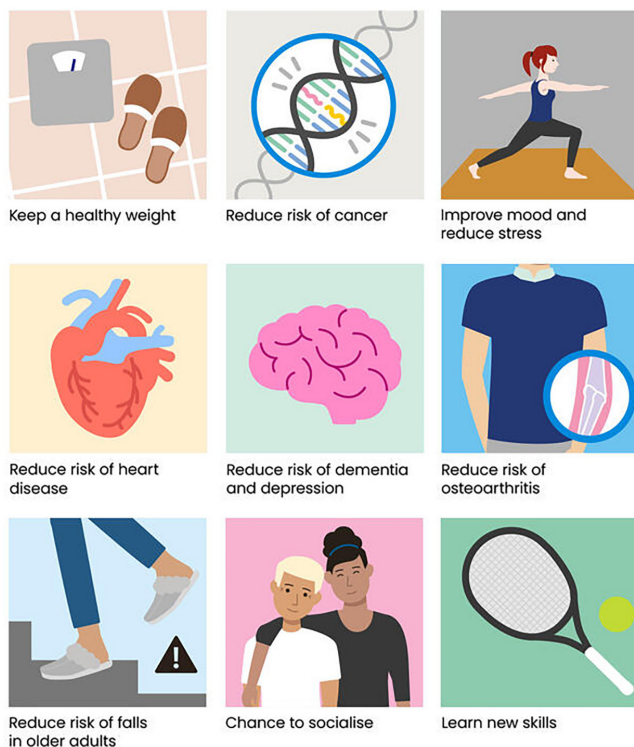


Fig 6 | Physical activity for people with cancer<sup>17</sup>

The National Cancer Institute reports that exercise reduces inflammation and enhances immune function, potentially helping the body identify and eliminate precancerous cells.<sup>16</sup> For colon cancer specifically, physical activity accelerates gut transit time by 30–40%, decreasing exposure to potential carcinogens in the digestive tract.<sup>16</sup> The American Cancer Society recommends 150–300 minutes of moderate exercise per week, including resistance training twice a week, to mitigate treatment side effects and improve outcomes.<sup>18</sup>

**Impact on Inflammation, Fatigue, and Recovery**

Emerging evidence demonstrates that exercise modulates key inflammatory pathways, particularly the IL-6-STAT3 axis, which is hyperactivated in chronic inflammation and cancer progression.<sup>20</sup> By suppressing this pathway, physical activity may disrupt the “IL-6 amplifier” feedback loop that promotes tumor microenvironment growth.<sup>20</sup> Clinical trials analyzed by ASCO (*n* = 100+) confirm that structured exercise during chemotherapy/radiation has been shown to reduce fatigue severity by 40–50%, while decreasing anxiety and depression scores by 30% compared to sedentary patients.<sup>19</sup> Notably, supervised programs incorporating aerobic (30–60 minutes/session) and

resistance training (2 sets of 8–12 repetitions) improve physical function and postsurgical recovery rates.<sup>18,19</sup>

Despite these benefits, only 35–45% of patients meet minimum activity guidelines during treatment.<sup>18</sup> Obesity-related mechanisms account for 20% of exercise’s protective effect, with additional cancer-specific benefits including enhanced NK cell activity and reduced oxidative stress.<sup>16,17</sup> MD Anderson’s research emphasizes that even light activity prevents treatment-related functional decline, challenging the outdated notion that patients should “rest” during therapy.<sup>19</sup> Future research should explore dose-response relationships and optimize personalized exercise prescriptions across cancer types and treatment phases.<sup>16,19</sup>

**Psychological and QoL Improvements for Cancer Treatments**

**Psychological Resilience and QoL in Cancer Care**

Psychological and QoL improvements represent essential components of comprehensive cancer care, with growing evidence supporting the effectiveness of integrated interventions. Recent studies demonstrate that psychological resilience serves as a critical mediator of QoL outcomes. A 2025 study of 110 hematology patients revealed that resilience scores significantly predicted better QoL ( $p < 0.001$ ) while partially buffering the negative impacts of depression and age.<sup>21</sup> The research showed that “resilience accounted for approximately 32% of the variance in QoL scores, highlighting its protective role in patient adjustment”.<sup>21</sup>

Combined medical and psychological interventions have shown powerful results, with a 2018 study reporting substantial stress reduction (Cohen’s  $d = 0.82$ ) and improvements across multiple QoL domains following implementation of psychoeducation, guided imagery, and cognitive therapy.<sup>22</sup> These interventions yielded statistically significant improvements in physical functioning ( $p = 0.003$ ), role functioning ( $p = 0.012$ ), and emotional well-being ( $p = 0.008$ ), while simultaneously reducing common symptoms, including fatigue ( $p = 0.001$ ) and pain ( $p = 0.038$ ).<sup>22</sup>

**Effectiveness of Physical Activity and Psychosocial Interventions**

The Managing CALM therapeutic approach has emerged as particularly effective, with a 2025 meta-analysis of 15 randomized controlled trials ( $n = 1,635$  patients) demonstrating large effect sizes for QoL improvement (SMD = 1.97) and spiritual well-being enhancement (WMD = 1.93).<sup>23</sup> The analysis revealed that CALM therapy reduced anxiety symptoms by 41% (SMD = -1.94) and depression by 34% (SMD = -1.28) compared to standard care.<sup>23</sup> Longitudinal research on RTW-SE in renal cancer patients ( $n = 282$ ) established important temporal relationships, showing that baseline RTW-SE scores predicted 17.7% of the variance in anxiety reduction ( $\beta = -0.177$ ) and 7.7% of the variance in depression reduction ( $\beta = -0.077$ ) at the 6-month follow-up.<sup>24</sup>

Physical activity interventions have demonstrated comparable benefits, with structured exercise programs reducing the incidence of depression by 28–35% and improving sleep quality in approximately 60% of participants.<sup>25</sup> However, implementation challenges remain significant, with only an estimated 35–45% of cancer patients currently receiving these evidence-based psychological supports.<sup>21,25</sup> The collective findings underscore the need for standardized, accessible psychosocial interventions throughout the cancer care continuum to optimize patient outcomes and quality of survival.

**Rehabilitation Across the Cancer Continuum**

**Frameworks for Exercise Intervention Across the Cancer Continuum**

The evolving field of exercise oncology has developed comprehensive frameworks to guide interventions across the cancer continuum. The multiphasic prehabilitation approach extends beyond surgical settings to address modifiable risk factors throughout all treatment phases, recognizing the variability in cancer treatment experiences.<sup>26</sup> Figure 7 shows that “Prehabilitation familiarises patients with postoperative exercises for faster recovery, while rehabilitation builds on

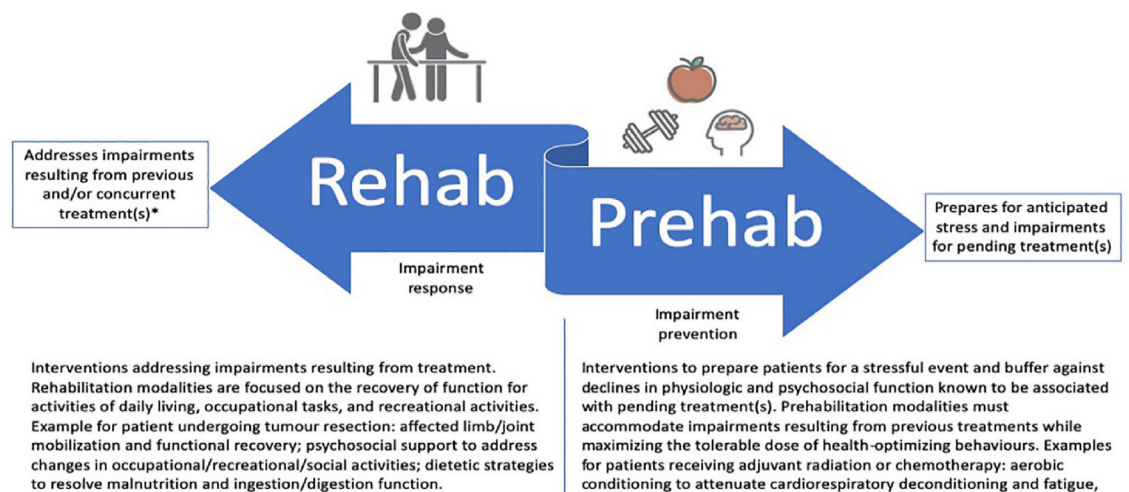


Fig 7 | Rehabilitation and prehabilitation relationship<sup>26</sup>

pretreatment behaviour strategies for long-term health maintenance.<sup>26</sup> Courneya et al. proposed the Exercise Across the Postdiagnosis Cancer Continuum Framework, which identifies six distinct treatment-related periods for exercise intervention: before treatments, during treatments, between treatments, immediately after successful treatments, during long-term survivorship, and end-of-life care.<sup>27</sup>

This framework introduces novel terminology, categorizing exercise as both a disease treatment (e.g., priming therapy, neoadjuvant therapy, salvage therapy) and supportive care intervention (e.g., prehabilitation, intrahabilitation, palliation).<sup>27</sup> Research demonstrates that appropriately timed exercise interventions can reduce complication risks by 30–40%, improve physical functioning, and enhance QoL across treatment phases.<sup>28</sup>

**Challenges in Exercise Oncology**

The PACC framework, updated in 2024, organizes research into eight cancer control categories, with current guidelines established for six categories, excluding detection and palliation.<sup>30</sup> Significant synergies exist between cancer rehabilitation and palliative care, as both disciplines adopt holistic approaches to manage chronic symptoms and improve patient outcomes throughout the disease trajectory.<sup>29</sup> While evidence supports the integration of exercise across all phases of survivorship, from presurgical preparation to extended survival, critical knowledge gaps remain regarding the optimal exercise type, dose, and timing

for specific cancer populations.<sup>28,30</sup> Only 35–45% of current studies examine exercise across multiple treatment periods within combination therapies.<sup>27</sup> Future research priorities include developing tailored exercise prescriptions for understudied cancer types and populations while implementing effective behavior change strategies to promote adherence.<sup>30</sup> The integration of implementation science will be crucial for translating evidence into real-world clinical practice and survivorship programs.<sup>27,30</sup>

**Barriers and Implementation Challenges for Cancer Treatments**

**Systemic Barriers to Exercise Integration in Cancer Care**

Despite overwhelming evidence supporting exercise as a beneficial therapy in oncology, significant implementation barriers hinder its integration into standard cancer care. A systematic scoping review identified 243 distinct barriers across health care system levels, with 40% (n = 93) occurring at the organizational level.<sup>31</sup> The most prevalent challenges include a lack of structural support systems and insufficient staff/resources for exercise program delivery.<sup>31</sup> Notably, while organizational barriers predominate, key decision-makers from health care administrations remain conspicuously absent from implementation research. The Spanish Society of Medical Oncology highlights additional systemic obstacles, including the absence of standardized referral pathways and inadequate multidisciplinary coordination between oncologists, rehabilitation specialists, and exercise professionals.<sup>32</sup>

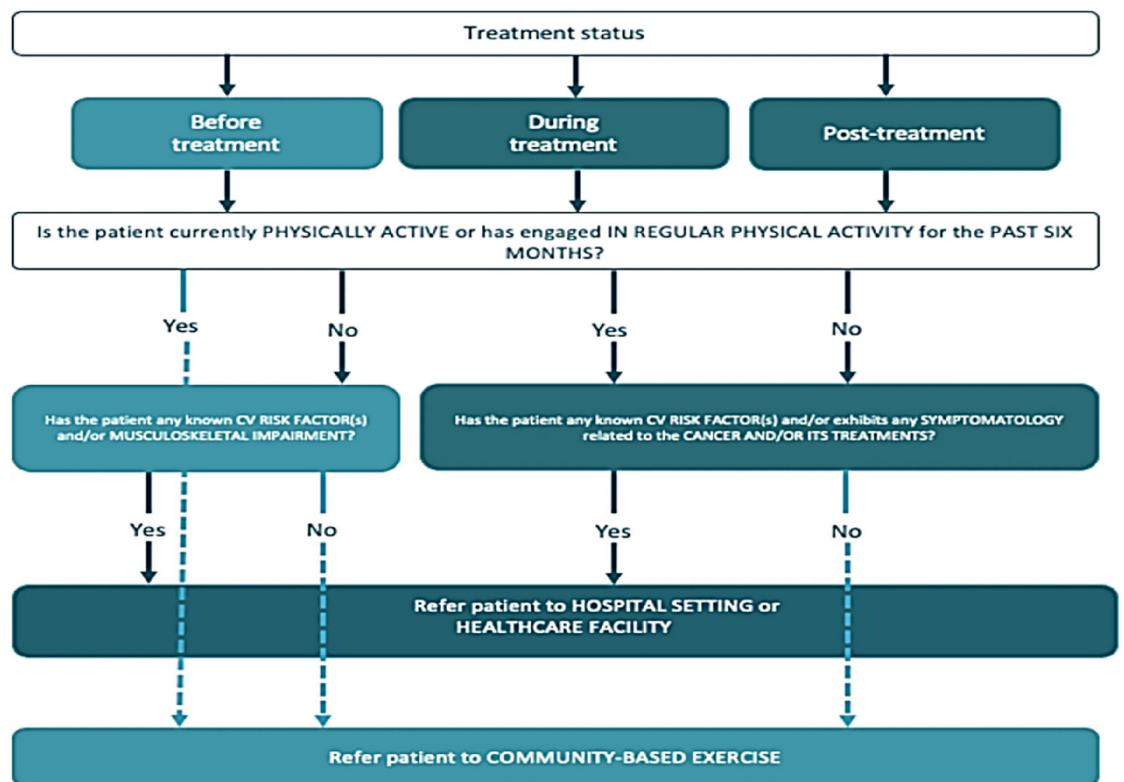


Fig 8 | Referral algorithm for exercise prescription decision in cancer patients<sup>32</sup>

Current health care infrastructures often lack dedicated exercise facilities and trained personnel to safely prescribe and supervise physical activity for cancer patients throughout various treatment phases. Referral processes remain inconsistent, with no widely adopted algorithms to guide exercise prescription based on individual patient needs, cancer type, and treatment status. The study shows that “a referral algorithm for oncologists to decide when, where, and who to refer cancer patients for an adequate exercise prescription” (see Figure 8).<sup>32</sup>

#### Financial and Policy Challenges in Exercise Oncology

Furthermore, reimbursement limitations and institutional prioritization of traditional therapies over integrative approaches create financial disincentives for implementing exercise oncology programs.<sup>31</sup> These systemic barriers persist despite clinical evidence demonstrating exercise’s efficacy in reducing treatment side effects by 30–40% and improving QoL metrics. The ecological framework analysis reveals an urgent need for policy-level interventions to address structural gaps, including workforce training initiatives, funding mechanisms, and electronic health record integration for exercise prescription tracking.<sup>31</sup> Multidisciplinary consensus statements recommend developing tiered assistance models with clear referral protocols to overcome current fragmentation in exercise oncology services.<sup>32</sup> Future implementation strategies must engage organizational stakeholders to create sustainable delivery systems that bridge the gap between research evidence and clinical practice.

#### Future Directions in Exercise Oncology for Cancer Treatments

The field of exercise oncology continues to expand, with emerging research demonstrating its multifaceted role across the cancer care continuum. Recent studies highlight 63% adherence rates to exercise programs during treatment and 68% posttreatment among breast cancer survivors, with adherence influenced by factors including baseline fitness, fatigue levels, and social support.<sup>33</sup> Innovative delivery models show promise, with the EXCEL study ( $n = 804$  participants) reporting high satisfaction rates for online supervised group exercise programs, which demonstrate improvements in both physical function and patient-reported outcomes.<sup>33</sup>

The Exercise as Cancer Treatment framework proposes nine distinct clinical scenarios for investigating exercise’s therapeutic potential, categorizing by tumor status (micrometastases, primary tumor, metastatic disease) and treatment phase (naïve, active, previously treated).<sup>34</sup> Current research predominantly focuses on primary tumors in preclinical models and micrometastases in human observational studies, while clinical trials remain limited across all scenarios.<sup>34</sup> Implementation strategies emphasize the need for standardized integration into oncology practice, with evidence supporting the benefits of exercise for physiological outcomes, QoL, and potentially cancer prognosis.<sup>35</sup>

Ongoing Phase III trials are investigating the impact of physical activity on clinical disease endpoints, while biomarker studies explore the mechanisms linking exercise to improved outcomes.<sup>35</sup>

Novel interventions, such as the Ballet after Breast Cancer program, demonstrate the importance of psychosocial factors, with participants reporting themes of connection, acceptance, and progress.<sup>33</sup> Future directions can include exploring exercise for primary brain tumor survivors and developing telehealth delivery models supervised by exercise physiologists.<sup>33</sup> As research advances, the development of tailored exercise prescriptions based on cancer type, treatment phase, and individual characteristics will be crucial for optimizing patient outcomes.<sup>34,35</sup> The growing evidence base supports exercise as a low-cost, high-impact intervention that should become a standard component of comprehensive cancer care worldwide.

#### Conclusion

The evidence presented in this comprehensive review demonstrates that exercise serves as a powerful, multitargeted intervention to mitigate the wide-ranging side effects of cancer treatment. Across chemotherapy, radiation therapy, and other treatment modalities, structured exercise programs consistently show benefits in reducing fatigue, improving physical function, enhancing QoL, and addressing psychological distress. The biological mechanisms through which exercise exerts these protective effects include modulation of inflammatory pathways, improvement of metabolic health, and enhancement of immune function. Remarkably, exercise can support individuals throughout every stage of cancer care, including before treatment, during survivorship, and even during palliative care.

Although cancer treatment, patient characteristics, and cancer type may influence the optimal exercise approach, recent studies suggest integrating aerobic and strength training. Even with proper programs in place, significant challenges remain, including the lack of standardized patient referral methods, a shortage of materials, and disjointed integration into daily work. However, the increasing number of studies suggests that cancer treatment should prioritize exercise as an important aspect. There is a need for further research on creating personalized exercise plans, increasing access to professional programs, and investigating how exercise can enhance treatment and long-term outcomes. This approach may be beneficial for providing high rewards with minimal risk to patients and caregivers throughout their cancer journey.

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