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# Cardio-Oncology Rehabilitation: Strategies for Cardiovascular Risk Reduction and Recovery in Cancer Survivors

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## Abstract

**Background:** Improved cancer survival has increased the number of survivors at risk of cardiovascular disease due to therapy-related cardiotoxicity. Pharmacological treatment alone often fails to address cardiovascular and functional impairments. Cardio-oncology rehabilitation (CORE) combines structured exercise with comprehensive cardiovascular risk management.
**Aim:** To summarize current evidence on the role of CORE in cardiovascular risk reduction and functional recovery in cancer survivors exposed to cardiotoxic therapies.
Materials and methods: A narrative review of PubMed, Scopus, and Google Scholar was performed, including randomized trials, observational studies, systematic reviews, meta-analyses, guidelines, and consensus documents focusing on adult cancer survivors.
**Results:** Cancer survivors frequently exhibit elevated cardiovascular risk and reduced cardiorespiratory fitness. Exercise-based CORE programs consistently improve fitness, functional capacity, fatigue, and quality of life, with emerging benefits for cardiometabolic risk factors and vascular function. Evidence for reduced major cardiovascular events remains limited, although higher physical activity is associated with improved survival. Digital and hybrid CORE models appear feasible.
**Conclusions:** CORE represents an effective strategy to enhance cardiovascular health and functional recovery in cancer survivors, though large trials are needed to confirm long-term outcomes.

**Keywords:** cardio-oncology rehabilitation; cancer survivorship; cardiotoxicity; exercise training; cardiovascular risk; cardiac rehabilitation

**AI statement:** Artificial intelligence tools have not been used to produce or alter the scientific content of the paper. Publicly available AI-powered websites have been used to identify better wording for certain expressions and sentences to ensure a smooth reading experience, while having no impact on the interpretation of cited evidence.

## 1. Introduction

Cancer survival has improved significantly over recent decades owing to advances in screening, diagnostics, and multimodality therapy. As a result, the global population of cancer survivors is steadily increasing. Parallel to this success, however, has emerged a substantial burden of

treatment-related cardiovascular disease (CVD). Anthracyclines, human epidermal growth factor 2 (HER2)-targeted therapies, immune checkpoint inhibitors, vascular endothelial growth factor (VEGF) inhibitors, androgen deprivation, radiotherapy to the chest or mediastinum, and hematopoietic cell transplantation all contribute to a spectrum of cardiovascular toxicities, including left ventricular (LV) dysfunction and heart failure, ischemic heart disease, arrhythmias, hypertension, thromboembolism, pulmonary hypertension, and peripheral vascular disease [1–4]. For many cancer survivors, CVD is now a leading cause of long-term morbidity and mortality, rivaling or exceeding the risk of recurrent malignancy [2,5-7].

This confluence of cancer and cardiovascular disease has catalyzed the emergence of cardio-oncology as a dedicated subspecialty focused on preventing, detecting, and managing cardiovascular complications across the cancer continuum [4,8]. Within this field, there is growing recognition that pharmacological management alone is insufficient to mitigate the complex, multisystem impairments produced by cancer and its treatments. Cardiotoxic therapies can impair not only cardiac structure and function but also vascular health, autonomic regulation, skeletal muscle mass and quality, mitochondrial function, and overall cardiorespiratory fitness (CRF) [8-11]. These changes often coexist with traditional CVD risk factors, physical inactivity, sarcopenia, frailty, and psychosocial distress, producing a “whole-organism” cardiovascular-skeletal muscle toxicity phenotype.

Exercise-based cardiac rehabilitation is a cornerstone of secondary prevention in traditional cardiology. In patients with coronary artery disease and heart failure, multidisciplinary cardiac rehabilitation reduces all cause and cardiovascular mortality, improves CRF and quality of life, and lowers rehospitalization rates [12-14]. Given the overlapping mechanisms of cardiovascular injury and the robust evidence supporting exercise in people with cancer, there is growing interest in adapting cardiac rehabilitation principles to the oncology context. This has led to the concept of Cardio-Oncology Rehabilitation (CORE): comprehensive, multidisciplinary programs that integrate structured exercise training with CVD risk factor control, nutrition counseling, psychosocial support, and education tailored to patients with or at risk for cancer therapy-related cardiovascular toxicity [15-18].

Exercise oncology research demonstrates that structured physical activity can attenuate declines in CRF during treatment, improve peak oxygen uptake ($VO_{2peak}$) and functional capacity after treatment, reduce fatigue and depression, and potentially improve cancer-specific and overall

survival in several malignancies [19-23]. More recently, early-phase trials and observational studies in high-risk populations (e.g., anthracycline-treated breast cancer survivors) suggest that targeted exercise interventions may preserve or enhance cardiac function and vascular health and improve cardiometabolic risk profiles [16,18,24–26]. International expert groups have begun to articulate the scientific rationale, core components, and research priorities for cardio-oncology rehabilitation [15,27].

Despite this momentum, several questions remain unresolved. These include the optimal timing (prehabilitation, during therapy, early survivorship, late survivorship), intensity and modality of exercise, criteria for risk stratification and referral, integration with standard oncology and cardiology care, and cost-effectiveness. In parallel, digital health tools, such as mobile health (mHealth) interventions and remote monitoring, are being explored as scalable strategies to deliver exercise and lifestyle support to geographically dispersed or medically complex survivors [28].

The purpose of this review is to synthesize the current literature on cardio-oncology rehabilitation with a focus on strategies for cardiovascular risk reduction and recovery in cancer survivors. Specifically, the review aims to:

- Describe the burden and mechanisms of cardiovascular toxicity across the cancer continuum.
- Summarize evidence on the effects of exercise and comprehensive CORE models on CRF, cardiac function, cardiometabolic risk factors, symptoms, and clinical outcomes in cancer survivors.
- Discuss implementation strategies, including risk stratification, timing of intervention, behavioral support, and digital delivery models.
- Highlight key gaps, methodological limitations, and priorities for future research in cardio-oncology rehabilitation.

## 2. Research materials and methods:

### 2.1. Data collection and analysis

A comprehensive literature review was conducted by utilising Google Scholar, Scopus, and PubMed databases. The following keywords were used for the search: “cardio-oncology rehabilitation”, “cancer”, “cardiac rehabilitation”, “exercise training”, “cardiorespiratory fitness”, “cardiovascular toxicity”, “anthracyclines”, “HER2-targeted therapy”,

"cardiomyopathy", "radiotherapy", "cancer survivorship", "secondary prevention", "mobile health", and "digital health" in various combinations. The search strategy included studies of adult cancer patients and survivors exposed to potentially cardiotoxic therapies or with established CVD in the context of cancer. Randomized controlled trials, prospective and retrospective cohort studies, case–control studies, systematic reviews, meta-analyses, clinical practice guidelines, and expert consensus statements were considered. Priority was given to studies that evaluated structured exercise or comprehensive rehabilitation programs with cardiovascular outcomes such as $VO_{2peak}$, LV function, vascular parameters, CVD risk factors, or clinical events.

The author reviewed articles referring to direct physiological effects of cancer therapies on the cardiovascular and skeletal muscle systems, performance outcomes (e.g., CRF, functional capacity, physical performance tests), cardiovascular risk factor modification, quality of life, and models of cardio-oncology rehabilitation program organisation and delivery. The author took note of the journals of publication to identify reliable sources, and appropriate measures were taken to check the reliability of citations that provided the relevant information.

## 3. Results:

### 3.1. Burden and mechanisms of cardiovascular toxicity in cancer survivors

#### 3.1.1. Epidemiology of cardiovascular disease in cancer survivors

Epidemiological data from large population-based cohorts indicate that cancer survivors are at elevated risk of CVD compared with the general population, even after adjustment for traditional risk factors [2,5-7]. Among breast cancer survivors, for example, long-term follow-up studies have shown increased rates of heart failure, cardiomyopathy, ischemic heart disease, and stroke, particularly after exposure to anthracyclines, trastuzumab, left-sided chest radiotherapy, or early menopause induced by endocrine therapies [3,6,29,30]. Similar patterns are observed in lymphoma, childhood cancers treated with high-dose anthracyclines or mediastinal radiation, and testicular cancer survivors treated with cisplatin-based regimens [1–3,7].

The relative contribution of cancer, therapy, and background risk factors varies by age and cancer type. In younger survivors, the absolute risk of late cardiomyopathy or premature coronary disease may be several-fold higher than population norms, whereas in older survivors, the combination of age-related risk and treatment exposure leads to high absolute event rates [2,6,7]. As survival after cancer continues to improve, the cumulative incidence of CVD over decades of follow-up increases, underscoring the need for long-term surveillance and preventive strategies.

### 3.1.2. Mechanisms of treatment-related cardiovascular and skeletal muscle toxicity

Anthracyclines induce dose-dependent cardiomyopathy through several mechanisms, including oxidative stress, mitochondrial dysfunction, DNA damage via topoisomerase-IIβ inhibition, impaired calcium handling, and maladaptive remodeling [1,3,8]. HER2-targeted agents, such as trastuzumab, can disrupt cardiomyocyte survival signaling, particularly when combined with anthracyclines. Radiation therapy to the chest can damage coronary arteries, valves, pericardium, conduction system, and myocardium, leading to ischemia, valvular disease, pericardial constriction, and conduction abnormalities years to decades later [3,4].

Other systemic therapies, including tyrosine kinase inhibitors, angiogenesis inhibitors, immune checkpoint inhibitors, and hormonal therapies, may induce hypertension, thrombosis, myocarditis, arrhythmias, dyslipidemia, or metabolic syndrome [4,8]. These therapy-specific effects are superimposed on pre-existing or treatment-induced risk factors such as obesity, diabetes, dyslipidemia, and smoking.

Importantly, cancer and its treatments also affect skeletal muscle and vascular systems. Pro-inflammatory cytokines, physical inactivity, malnutrition, and direct drug effects contribute to sarcopenia, muscle fiber atrophy, capillary rarefaction, and mitochondrial dysfunction [9-11,19]. The result is a significant decline in CRF, often measurable as a reduction in $VO_{2peak}$, which is a powerful predictor of cardiovascular and all-cause mortality [10,11,31]. This broader "cardiovascular-skeletal muscle toxicity" framework supports interventions that target the whole cardiometabolic and musculoskeletal system, not only the left ventricle.

### 3.1.3. Cardiorespiratory fitness and prognosis

Reduced CRF is common both during and after cancer treatment. Meta-analytic data suggest that many patients experience a decline in $VO_{2peak}$ of 10-25% during adjuvant chemotherapy or chemoradiation, with incomplete recovery in survivorship [10,11,19]. In breast cancer, observed $VO_{2peak}$ values are typically 15-25% lower than age-matched controls, even years after therapy cessation [10,24]. Low CRF is independently associated with higher cardiovascular and all-cause mortality, hospitalizations, and reduced quality of life in non-cancer populations [12–14,31]. Emerging evidence suggests similar prognostic implications in cancer survivors: lower $VO_{2peak}$ has been linked to higher rates of cardiac events and mortality among patients undergoing hematopoietic cell transplant or intensive chemotherapy [10,31]. Thus, improving or preserving CRF is a critical target for cardio-oncology rehabilitation strategies.

### 3.2. Concept and core components of cardio-oncology rehabilitation

#### 3.2.1. Rationale for adapting cardiac rehabilitation to cancer

Traditional cardiac rehabilitation (CR) is a comprehensive, supervised program involving exercise training, education, lifestyle counseling, and risk factor management designed for patients with coronary artery disease, heart failure, or following cardiac surgery or intervention [12-14]. Numerous randomized trials and meta-analyses demonstrate that CR reduces all-cause mortality by approximately 20-30%, decreases recurrent myocardial infarction and hospitalizations, improves CRF and health-related quality of life, and promotes adherence to cardioprotective medications and lifestyle [12-14].

Given that many cancer survivors share similar or greater levels of cardiovascular risk and frequently develop therapy-related cardiomyopathy or ischemic heart disease, it is logical to leverage CR models in oncology. Cardio-oncology rehabilitation (CORE) extends CR principles to the cancer population, emphasizing prevention and management of treatment-related cardiovascular toxicity while also addressing cancer-specific issues such as fatigue, cachexia, lymphedema, and psychological distress [15-18].

#### 3.2.2. Definitions and models of cardio-oncology rehabilitation

Cardio-oncology rehabilitation can be broadly defined as a structured, multidisciplinary, exercise-centered program tailored to individuals with cancer who either have established CVD or are at increased risk due to cardiotoxic therapies or pre-existing risk factors. Conceptual frameworks proposed by international working groups describe CORE as encompassing several interrelated domains [15,17,27]:

- Patient assessment and risk stratification: Baseline evaluation of cardiovascular risk, including history, physical examination, biomarkers, imaging (e.g., echocardiography), and CRF testing where feasible.
- Structured exercise training: Individually prescribed aerobic and resistance training, typically following the FITT (Frequency, Intensity, Time, Type) principle, adapted to treatment stage, comorbidities, and symptom burden.
- Risk factor management: Optimization of blood pressure, lipids, glycemic control, weight, and smoking cessation, in coordination with cardiology and primary care.
- Education and counseling: Information on cardiovascular health, physical activity, nutrition, symptom recognition, medication adherence, and self-management skills.
- Psychosocial and behavioral support: Screening and intervention for anxiety, depression, and distress; motivational interviewing and behavioral strategies to enhance adherence.

- Coordination of care: Integration with oncology, radiation therapy, surgery, hematology, and primary care teams to ensure continuity and safety across the cancer trajectory.

Program models vary across institutions and health systems. Some embed CORE within existing CR centers, accepting referrals from oncology, similar to post-myocardial infarction patients [16-18]. Others create stand-alone oncology-focused programs that are co-led by cardiologists and oncologists. Home-based or hybrid models using telemedicine and mHealth technologies are emerging as alternatives to center-based programs, particularly for patients with limited access or immunosuppression [28].

#### 3.2.3. Exercise prescription in cardio-oncology rehabilitation

Exercise is the central component of CORE. Prescription typically follows general cancer and cardiac rehabilitation guidelines but is modified by cancer-specific factors such as treatment phase, infection risk, anemia, thrombocytopenia, neuropathy, bone metastases, and surgical reconstruction [19,20,32]. Aerobic training often involves moderate-intensity continuous exercise (e.g., walking, cycling) performed on most days of the week, accumulating at least 150 minutes per week of moderate intensity or 75 minutes per week of vigorous intensity, or an equivalent combination [20,32]. Intensity may be guided by heart rate reserve, perceived exertion scales, or percentage of baseline $VO_{2peak}$. High-intensity interval training (HIIT) has been explored in selected, medically stable patients, demonstrating substantial improvements in CRF with lower total time commitment [19,24-26]. Resistance training is aimed at preserving or restoring muscle mass and strength, which are critical for functional independence and metabolic health. Typical protocols include 2-3 sessions per week targeting major muscle groups, using 1-3 sets of 8-12 repetitions at moderate intensity (approximately 60-70% of one-repetition maximum), progressing over time [19,20,32]. Flexibility and balance exercises are incorporated to reduce fall risk and improve joint mobility. Exercise prescription in CORE requires careful screening and monitoring due to potential complications such as cardiomyopathy, arrhythmias, anemia, neutropenia, thrombocytopenia, and bone fragility. Collaboration between exercise professionals, cardiologists, and oncologists is essential to adjust intensity, temporarily withhold exercise when medically indicated, and promptly address symptoms such as chest pain, palpitations, dyspnea, or syncope.

### 3.3. Effects of exercise and cardio-oncology rehabilitation on cardiovascular risk and recovery

#### 3.3.1. Cardiorespiratory fitness and functional capacity

Randomized trials and meta-analyses in cancer populations consistently show that exercise training improves CRF. A meta-analysis of exercise interventions in patients with cancer

reported a mean increase in $VO_{2peak}$ of approximately 2-3 mL · $kg^{-1}$ · $min^{-1}$, representing a clinically meaningful improvement in aerobic capacity [19,21,31]. These benefits are observed across tumor types, including breast, colorectal, hematologic, and mixed solid tumors, and are evident both during and after treatment [19-21,31,33]. In anthracycline-treated breast cancer survivors, structured aerobic training has been shown to partially reverse long-standing deficits in CRF. Trials including long-term survivors (often a decade or more post-treatment) demonstrate that supervised moderate- to vigorous-intensity aerobic training three times per week for several months can significantly increase $VO_{2peak}$, although improvements may be smaller than those observed in age-matched, cancer-free controls under similar training conditions [24-26]. This suggests that prior cardiotoxic therapy may blunt physiological adaptation but does not abolish trainability. Functional capacity as measured by six-minute walk distance, submaximal exercise tests, and performance-based tasks (e.g., chair stands, stair climb) also improves with exercise training in cancer survivors [19–21,33]. Gains in functional capacity are particularly important for older and frail patients, in whom maintenance of independence and prevention of disability are key goals of survivorship care.

**3.3.2. Cardiac structure, function, and biomarkers**

Evidence on the direct effects of exercise and CORE on cardiac structure and function is emerging. Small randomized trials and prospective cohort studies in breast cancer and lymphoma have examined echocardiographic parameters such as LV ejection fraction (LVEF), global longitudinal strain (GLS), and diastolic function in patients undergoing or after anthracycline ± trastuzumab therapy [16,18,24–26].

Some studies report that exercise training during anthracycline therapy can attenuate or prevent declines in LVEF and GLS compared with usual care, although findings are not entirely consistent and sample sizes are modest [16,18,25,26]. In survivorship populations with stable or mildly reduced LVEF, exercise appears safe and may improve diastolic function, LV remodeling indices, and myocardial deformation, similar to observations in non-cancer heart failure cohorts [13,14,16].

Serial measurements of cardiac biomarkers, such as troponin and N-terminal pro-B-type natriuretic peptide (NT-proBNP), have been used to monitor cardiotoxicity. Some exercise trials suggest that active participants may show lower or blunted rises in biomarkers during chemotherapy compared with sedentary controls, although data are limited and heterogeneous [16,25]. Overall, while exercise appears unlikely to exacerbate cardiotoxicity when appropriately prescribed, more robust evidence is needed to determine its capacity to prevent or reverse structural cardiac injury.

### 3.3.3. Cardiometabolic risk factors and vascular health

Cardio-oncology rehabilitation targets traditional cardiometabolic risk factors that are highly prevalent in cancer survivors. Observational and interventional studies indicate that exercise and comprehensive lifestyle interventions can improve blood pressure, lipid profiles, insulin sensitivity, body composition, and inflammatory markers [21-23,27,34].

In breast and colorectal cancer survivors, combined aerobic and resistance training programs have been associated with reductions in fat mass, waist circumference, and fasting insulin, and improvements in high-density lipoprotein cholesterol and triglycerides [21-23,34]. Limited data suggest that patients participating in oncology-focused rehabilitation engage in higher levels of habitual physical activity and adhere better to cardiovascular medications and dietary recommendations than non-participants [16-18].

Vascular function, assessed by endothelial function tests (e.g., flow-mediated dilation) and arterial stiffness measures, may also benefit from exercise. Early studies indicate that supervised aerobic training improves endothelial function and reduces arterial stiffness in cancer survivors, potentially counteracting radiation- and chemotherapy-induced vascular damage [10,16,19]. However, long-term data linking these intermediate changes to clinical cardiovascular event reduction are currently sparse.

### 3.3.4. Symptom burden, quality of life, and psychosocial outcomes

Cancer therapy-related fatigue, dyspnea, reduced exercise tolerance, depressive symptoms, and anxiety are prevalent and significantly impair quality of life. Exercise interventions demonstrate consistent benefits in reducing fatigue and improving overall quality of life and physical functioning [19-23,33]. In the context of cardio-oncology, improvements in CRF and functional capacity are often accompanied by enhanced vitality, reduced distress, and greater participation in daily and social activities [24-26].

Multidisciplinary CORE programs that integrate exercise with psychosocial support and education may further amplify these benefits. Some studies report reductions in depressive symptoms and anxiety scores, improved self-efficacy for physical activity, and better perceived health among participants in structured rehabilitation compared with usual care [16–18,21–23]. Given the bidirectional relationship between psychological stress and cardiovascular risk, these benefits are particularly relevant to long-term cardiovascular outcomes.

### 3.3.5. Clinical cardiovascular outcomes and survival

Direct evidence that cardio-oncology rehabilitation reduces “hard” cardiovascular endpoints (e.g., myocardial infarction, heart failure hospitalization, cardiovascular mortality) is limited

but evolving. Observational studies suggest that cancer survivors who engage in higher levels of physical activity after diagnosis experience lower rates of cardiovascular events and mortality [22,29,30]. For example, post-diagnosis physical activity has been associated with improved overall and cancer-specific survival in breast and colorectal cancer populations, even after adjustment for traditional prognostic factors [22,29,30].

While these data are encouraging, they derive largely from self-reported physical activity rather than structured CORE programs and are subject to residual confounding. There is a pressing need for adequately powered randomized controlled trials that evaluate the impact of CORE on clinically relevant cardiovascular outcomes and long-term survival.

### 3.4. Implementation strategies and emerging models

#### 3.4.1. Risk stratification and referral pathways

Effective implementation of CORE requires systematic identification of patients who would benefit most from rehabilitation. Proposed risk stratification frameworks integrate baseline cardiovascular risk factors, type and dose of cancer therapy, prior CVD, and early signs of cardiotoxicity to categorize patients into low, intermediate, and high risk [4,15,27,33]. High-risk groups may include those receiving high-dose anthracyclines, anthracycline–trastuzumab combinations, chest radiotherapy involving the heart, prior radiation or anthracycline exposure, pre-existing heart failure or severe risk factor burden, and those with early declines in LVEF or GLS.

Referral pathways can be embedded into oncology workflows, similar to standard referrals to physiotherapy or nutrition. Automatic referral triggers based on treatment regimens or early cardiotoxicity markers may improve uptake. Collaboration between oncology, cardiology, and rehabilitation services is critical to define eligibility criteria, timing (e.g., pre-treatment "prehabilitation" versus post-treatment), and monitoring requirements for safe participation.

#### 3.4.2. Program timing: prehabilitation, concurrent, and survivorship

Three temporal windows for CORE have been proposed:

- Prehabilitation: Initiation of exercise and risk factor optimization between cancer diagnosis and the start of therapy. This phase aims to improve CRF and physiological reserve, potentially enabling patients to better tolerate intensive treatments and reducing peri-treatment complications. Early studies suggest that prehabilitation can mitigate declines in CRF and improve postoperative and chemotherapy-related outcomes [19,20].
- Concurrent rehabilitation: Exercise and risk factor management during active chemotherapy, radiotherapy, or targeted therapy. Trials demonstrate that supervised exercise is generally safe in appropriately selected patients and can attenuate treatment-

related CRF decline, fatigue, and functional impairment [19–21]. However, logistical challenges (e.g., nausea, immunosuppression, scheduling) may limit adherence.

- Survivorship rehabilitation: Post-treatment programs focusing on recovery of CRF, reversal of cardiometabolic abnormalities, and long-term CVD prevention. Survivorship is currently the most common entry point for programs resembling traditional CR, especially in patients with newly diagnosed cardiomyopathy or ischemic heart disease after cancer therapy [16-18].

The optimal timing may vary by cancer type, treatment intensity, and baseline risk. A continuum of care model that begins with prehabilitation and extends through treatment into survivorship may offer the greatest potential for sustained cardiovascular benefit, but evidence is still emerging.

### 3.4.3. Integration with digital health and home-based models

mHealth and telehealth technologies provide promising avenues for scalable delivery of CORE. Smartphone apps, wearable activity trackers, remote heart rate and rhythm monitoring, and tele-coaching platforms can support exercise prescription, adherence monitoring, and behavior change outside of hospital-based centers [28].

Systematic reviews of mHealth interventions in cancer survivors suggest that digital tools can modestly increase physical activity levels and improve CRF compared with usual care, with standardized mean differences in favor of mHealth-supported exercise [28]. These interventions often incorporate motivational messages, self-monitoring features, goal setting, and feedback loops with healthcare providers.

In the cardio-oncology context, remote monitoring of vital signs, symptoms, and sometimes basic cardiac function (e.g., single-lead electrocardiography) can enhance safety, particularly in high-risk patients who might otherwise face barriers to center-based programs. Hybrid models that combine periodic in-person assessments with home-based digital support may offer a pragmatic balance between supervision and accessibility. However, digital literacy, access disparities, and data integration with clinical systems remain challenges.

### 3.4.4. Behavioral and health system considerations

Successful CORE implementation requires attention to behavioral and system-level factors. Patients may face multiple barriers: fatigue, transportation difficulties, financial toxicities, competing caregiving roles, fear of exercise safety, and limited awareness of cardiovascular risk. Health professionals may lack familiarity with exercise oncology, have safety concerns,

or face structural constraints such as insufficient resources, space, and reimbursement mechanisms [17,18,27].

Behavior change techniques such as motivational interviewing, individualized goal setting, self-monitoring, social support, and tailored feedback are key to enhancing uptake and adherence. Person-centered, flexible programs that respect individual preferences, cultural contexts, and fluctuating symptom burdens are more likely to succeed. At the system level, integrating CORE into standard cancer care pathways, securing sustainable funding models, and establishing quality metrics will be crucial for widespread adoption.

## 4. Discussion

Cardio-oncology rehabilitation represents an evolving paradigm that bridges oncology and cardiovascular medicine to address the growing burden of treatment-related CVD in cancer survivors. The evidence synthesized in this review suggests that structured exercise and comprehensive rehabilitation strategies can meaningfully improve CRF, functional capacity, cardiometabolic risk factors, and quality of life in this population. Although direct data on clinical cardiovascular events and mortality remain limited, the convergence of mechanistic, physiological, and epidemiological evidence strongly supports the inclusion of exercise-based rehabilitation within cardio-oncology care models.

### 4.1. Implications of cardiorespiratory fitness as a therapeutic target

CRF is a central focus of CORE, both as an outcome and as a therapeutic target. Treatment-related declines in $VO_{2peak}$ reflect not only cardiac dysfunction but also vascular, pulmonary, and skeletal muscle impairments. Given that even modest increases in CRF are associated with substantial reductions in cardiovascular and all-cause mortality in non-cancer populations, the observed training-induced improvements in cancer survivors are likely clinically meaningful [10–14,31]. The evidence that long-term cancer survivors retain trainability, despite prior exposure to cardiotoxic therapies, is particularly important. It challenges the notion that late effects are entirely fixed and supports the concept of “cardiovascular and functional recovery” as a realistic goal. However, the attenuated magnitude of CRF gains observed in some anthracycline-treated cohorts suggests that tailored, possibly more intensive or longer-duration interventions may be required for those with substantial treatment-related injury [24–26].

### 4.2. Direct effects on cardiac and vascular outcomes

Data on the effects of CORE and exercise on cardiac structure and function are less definitive than for CRF. Although preliminary trials suggest that exercise may attenuate declines in LVEF and GLS during chemotherapy and possibly improve diastolic parameters in survivorship, sample sizes are small, follow-up is short, and endpoints are often surrogate rather than clinical [16,18,24-26]. Heterogeneity in imaging protocols, definitions of cardiotoxicity, and exercise modalities further complicates comparisons.

Extrapolating from cardiac rehabilitation in non-cancer populations, it is plausible that improvements in endothelial function, autonomic balance, and myocardial efficiency contribute to reduced event rates. However, the unique mechanisms of cancer therapy–related injury such as radiation-induced microvascular disease and anthracycline-related mitochondrial damage raise questions about whether conventional CR benefits fully translate to oncology. Dedicated, adequately powered trials with standardized imaging and biomarker protocols are needed to clarify the extent to which exercise can prevent or reverse these specific injuries.

### 4.3. Comprehensive risk factor management and the “polypill” effect of exercise

A major strength of CORE is its capacity to act as a “polypill” that addresses multiple cardiovascular risk pathways simultaneously. Exercise favorably influences blood pressure, lipid profiles, insulin sensitivity, body composition, inflammation, and endothelial function while also improving mood, sleep, and stress resilience [12–14,19,21–23,34]. Combining exercise with dietary counseling, smoking cessation support, and pharmacological risk factor control has the potential to substantially reduce global cardiovascular risk in cancer survivors.

Additionally, physical activity has been linked to improved cancer outcomes, including reduced recurrence and improved survival in breast and colorectal cancer survivors [22,29,30]. While causality cannot be definitively established from observational data, this dual potential-benefitting both cardiovascular and oncological endpoints-strengthens the rationale for integrating exercise into survivorship care.

### 4.4. Program design, timing, and patient-centered care

The optimal design and timing of CORE remain areas of active investigation. Prehabilitation may be particularly valuable in high-risk regimens such as anthracycline-based chemotherapy, hematopoietic cell transplantation, or major cancer surgery, where baseline CRF strongly predicts complications and recovery [19,20]. Exercise during treatment can attenuate functional decline but requires flexible and individualized scheduling to accommodate cycles of toxicity

and symptom fluctuations [19–21]. Survivorship-focused programs are more feasible to implement within existing CR structures but may miss opportunities to prevent early cardiotoxicity.

From a patient-centered perspective, CORE must accommodate heterogeneity in age, comorbidities, cancer types, treatment stages, and personal preferences. Younger survivors may prioritize return to work and high-level activity; older survivors may focus on maintaining independence and avoiding frailty. Some patients may favor group-based, supervised center programs, while others prefer home-based or digital formats. Programs that offer choice, cultural sensitivity, and shared decision-making are likely to achieve higher engagement.

### 4.5. Implementation challenges and health system integration

Despite compelling rationale, the implementation of CORE faces substantial barriers. Awareness among oncologists and cardiologists varies, and referrals are not yet routine. Many healthcare systems lack dedicated funding or reimbursement mechanisms for oncology-focused rehabilitation, and capacity within existing CR programs may be insufficient to accommodate growing numbers of survivors [15–18,27].

Training and education of rehabilitation professionals in cancer-specific issues (e.g., lymphedema, bone metastases, hematologic toxicities) are essential. Standardizing referral criteria, assessment protocols, and outcome measures will facilitate quality assurance and benchmarking across programs. Health policy initiatives that recognize CORE as an essential component of comprehensive cancer care could help secure sustainable resources.

### 4.6. Role of digital and hybrid models

Digital and hybrid models show promise in expanding access to CORE, particularly in rural or resource-limited settings and for patients facing travel or time constraints. mHealth-supported exercise programs have demonstrated feasibility and modest efficacy in improving CRF and physical activity in cancer survivors [28]. For cardio-oncology, integration of remote monitoring (e.g., heart rate, rhythm, blood pressure) can enhance safety and allow more frequent, low-burden follow-up than traditional center-based models.

However, digital solutions must be designed to avoid exacerbating disparities. Older adults, individuals with lower socioeconomic status, or those with limited digital literacy may be less able to benefit unless interventions are tailored and supplemented by human support. Data privacy, interoperability with electronic health records, and sustainable reimbursement for remote care also require attention.

### 4.7. Methodological considerations in the current evidence base

The current evidence base for CORE is characterized by heterogeneity in study designs, populations, and outcomes. Many trials are small and single-center, with short follow-up and surrogate endpoints. Control conditions range from usual care to attention controls, making it difficult to isolate the specific contribution of exercise versus other program components. Adherence reporting and long-term maintenance of behavior change are often insufficiently described.

Moreover, high-risk populations—such as those with pre-existing heart failure, severe coronary disease, or advanced metastatic cancer—are frequently excluded from exercise trials, limiting generalizability to those who might benefit most from rehabilitation. Standardized definitions of cardiotoxicity, uniform imaging and biomarker protocols, and harmonized outcome measures are needed to enable meta-analyses and evidence synthesis.

**Limitations of the study include**

This review is narrative rather than systematic and therefore may be subject to selection bias. Although a comprehensive search strategy was used, some relevant studies may have been missed, particularly unpublished or non-English-language reports. The heterogeneity of study designs, patient populations, treatment regimens, and outcome measures limited the ability to directly compare effect sizes or construct pooled estimates. Much of the evidence comes from small randomized trials or observational cohorts, which are subject to confounding and may not be representative of broader clinical populations. Additionally, the rapidly evolving nature of both oncology and cardio-oncology means that newer therapies and interventions may not yet be adequately represented in the literature.

Future research should focus on large, multicenter randomized controlled trials evaluating comprehensive CORE programs with long-term follow-up and clinically relevant cardiovascular endpoints, including heart failure hospitalization, myocardial infarction, arrhythmias, and cardiovascular and all-cause mortality. Studies are needed to determine the optimal timing, intensity, and components of CORE for different cancer types and risk profiles, including comparisons of prehabilitation, concurrent, and survivorship-focused approaches. Research should address high-risk and understudied populations, such as older adults with multimorbidity, patients with advanced disease, and those from socioeconomically disadvantaged or minority groups. Implementation science approaches are required to identify

effective strategies for integrating CORE into routine oncology practice, including health system redesign, reimbursement models, and training of multidisciplinary teams. Finally, rigorous evaluation of digital and hybrid models, with attention to equity, usability, and cost-effectiveness, will be essential to scale cardio-oncology rehabilitation to meet the growing needs of cancer survivors worldwide.

## 5. Conclusions

Cardio-oncology rehabilitation is an emerging, yet highly promising, strategy to address the growing burden of cardiovascular disease in cancer survivors. Rooted in the proven framework of traditional cardiac rehabilitation and informed by expanding exercise oncology research, CORE integrates structured exercise training with comprehensive cardiovascular risk factor management, education, and psychosocial support tailored to individuals exposed to cardiotoxic cancer therapies.

Evidence to date indicates that exercise and CORE programs can significantly improve cardiorespiratory fitness, functional capacity, cardiometabolic profiles, and quality of life in cancer survivors, including those treated with anthracyclines and other cardiotoxic regimens. Preliminary data suggest potential benefits for cardiac and vascular function, although robust evidence on major cardiovascular events and survival is still lacking. Implementation of CORE requires coordinated efforts across oncology, cardiology, and rehabilitation services, as well as supportive health policies and reimbursement mechanisms.

As survival after cancer continues to improve, strategies that not only prevent recurrence but also promote cardiovascular health and functional independence are increasingly vital. Cardio-oncology rehabilitation offers a comprehensive model to achieve these goals. Continued investment in high-quality research, clinical infrastructure, and multidisciplinary collaboration will be essential to realize the full potential of CORE in reducing cardiovascular risk and fostering recovery in cancer survivors.

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**Author contributions**

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Ewa Szplit - investigation, formal analysis, project administration

Patryk Hebda - formal analysis, resources

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**Informed consent statement**

Not applicable.

**Data availability statement**

Not applicable.

**Conflict of interest**

The authors declare no conflict of interest in relation to this study.

**Declaration of Generative AI and AI-Assisted Technologies**

During the preparation of this work, the authors used ChatGPT (OpenAI) to improve grammar and language clarity. After using this tool, the authors reviewed and edited the content as needed and takes full responsibility for the content of the publication

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