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Exercise, Cancer-Related Fatigue and Physical Function in Individuals with Cancer: From General Recommendations to Individualised Prescription – A Narrative Review

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Abstract

Background. Cancer-related fatigue (CRF) and impaired physical function are common consequences of cancer and its treatment. Exercise may improve both outcomes, although their responses do not always occur in parallel.

Aim. To examine the effects of exercise on CRF and physical function and identify factors relevant to individualised exercise prescription.

Material and methods. A narrative review of 29 freely accessible full-text publications indexed in PubMed from January 2016 to August 2026 was conducted, including guidelines, systematic reviews, meta-analyses, randomised controlled trials and selected observational and mechanistic studies.

Results. Exercise was associated with reductions in CRF and improvements in physical fitness and functional performance, but no universally optimal modality, dose, timing strategy or supervision model was identified. CRF and physical function were related but distinct

outcomes. Response appeared to vary with baseline status, treatment context, supervision and individualisation, while adherence and accessibility influenced real-world effectiveness.

Conclusions. Exercise prescription in oncology should be individualised, outcome-oriented and adapted to baseline status, treatment context, tolerance and clinical needs. Further research should identify the most effective and sustainable prescriptions for specific patients and outcomes.

Key words: cancer-related fatigue, physical function, muscle strength, cardiorespiratory fitness, exercise prescription, exercise oncology, individualised exercise prescription.

1. Introduction

Cancer-related fatigue (CRF) is a persistent and multidimensional symptom characterised by physical, emotional and/or cognitive exhaustion. Patients experience CRF at various stages across the cancer continuum and it may persist for years after treatment completion. It differs from normal post-exertional fatigue in healthy individuals, as it is not necessarily relieved by rest or sleep. Moderate-to-severe CRF is estimated to affect approximately 38% of patients with cancer. It is reported before treatment initiation, appears to be highest during active therapy and remains considerable after treatment completion. Consequently, CRF should not be viewed merely as an acute treatment-related symptom. The high prevalence, persistence and multidimensional nature of CRF present a significant clinical challenge, impacting patients across all stages of the diagnostic and therapeutic continuum [1,2,3].

Physical function (PF) refers to the ability to perform daily activities that require physical effort. Cancer and its treatment may impair PF through several interrelated factors, including muscle loss, systemic deconditioning and reduced cardiorespiratory fitness. PF should not be considered synonymous with physical activity, physical fitness or muscle strength. PF can be assessed using complementary methods based on different modalities ranging from clinician- and patient-reported outcomes to performance-based tests and digital measures. The heterogeneity in the definition and measurement of PF can complicate comparisons across exercise oncology studies and should be considered when interpreting their findings [4,5,6].

Although cancer-related fatigue (CRF) and physical function (PF) are distinct constructs, available evidence suggests a close association between them. Higher levels of CRF have been associated with poorer performance in objective measures of physical function, such as walking capacity, mobility and lower-body functional performance [2]. Interestingly, higher CRF is associated with poorer real-world mobility performance, yet not necessarily with mobility capacity metrics [7]. This highlights the complex, multidimensional relationship between CRF and PF across different functional domains and assessment methodologies. This distinction is important when evaluating whether exercise-induced changes in fatigue and physical function occur in parallel.

Exercise is increasingly recognised as an evidence-supported component of cancer care. Evidence supports a reduction in fatigue severity following aerobic, resistance, or combined exercise programmes performed both during and after cancer treatment. These exercise modalities have also been associated with improvements in various domains of physical fitness and function. However, no specific exercise modality or dose has yet been identified as a universally optimal prescription for all patients, as therapeutic response likely depends on an interplay of exercise parameters, patient-specific characteristics, cancer diagnosis and treatment. Consequently, understanding how individualised exercise prescriptions influence CRF and PF carries substantial clinical value [3,8].

This narrative review aims to examine the effects of exercise on cancer-related fatigue and physical function in individuals diagnosed with cancer and to explore the relationship between these outcomes. The review also aims to discuss how exercise modality, dose, treatment phase and individual patient characteristics may guide exercise prescription.

2. Research materials and methods

This narrative review synthesised recent evidence on the effects of exercise in people with cancer across the cancer continuum, with a focus on CRF, PF, relationship between CRF and PF, and factors influencing individualised exercise prescription. This article was based on a literature search performed in the PubMed database. Publications from January 2016 to August 2026 were considered.

The search strategy included the following terms used alone and in combination: “cancer,” “cancer survivor,” “exercise,” “physical activity,” “physical function,” “physical performance,” “fatigue,” “cancer-related fatigue,” “functional capacity,” “physical fitness,” “resistance training,” “aerobic exercise,” “dose-response,” “exercise prescription,”

“supervision,” “adherence,” “sarcopenia,” “older adults,” “treatment phase,” “mediation,” and “long-term follow-up”.

Eligible sources included English-language clinical guidelines, systematic reviews, meta-analyses, RCTs and selected observational or mechanistic studies involving adults diagnosed with cancer during active treatment and/or post-treatment survivorship that evaluated exercise or structured physical activity and reported outcomes related to CRF and/or physical function, physical performance or physical fitness. Publications were excluded if they were not written in English, were published outside the selected time frame, were available only as conference abstracts, editorials, or opinion pieces, were focused on the paediatric population or did not directly address the topic of this review. Only publications for which the full text was freely and legally accessible were included in the core evidence synthesis. Articles were selected iteratively to ensure coverage of CRF prevalence and definition, physical function measurement, exercise efficacy, modality and dose, treatment phase, individualisation, adherence, safety, long-term outcomes, generalisability, and the relationship between fatigue and physical function. Guidelines, systematic reviews and meta-analyses were prioritised when summarising the overall evidence, while individual randomised controlled trials were used to illustrate specific clinical contexts and contrasting response patterns. Findings were synthesised narratively, with particular attention to consistency and disagreement across studies and to distinctions between association, moderation, mediation and causality.

3. Terminology and outcome measurement

A clear distinction between physical activity (PA), exercise, physical fitness and physical function is essential for interpreting outcomes in exercise oncology. Exercise represents a specific subcategory of PA that is planned, structured, and repetitive. Physical fitness encompasses attributes and capacities that enable PA performance, such as cardiorespiratory fitness, body composition and muscle strength, whereas PF refers to the ability to perform day-to-day activities requiring physical effort. Performance-based tests, such as the 6-minute walk test (6MWT), directly assess specific aspects of functional performance but should not be considered synonymous with the broader construct of PF [5,8].

According to Thanarajasingam et al. [5], PF can be assessed using multiple modalities. Clinician-reported outcomes (ClinROs) are based on clinician assessment, for example the Eastern Cooperative Oncology Group (ECOG) performance status scale. Conversely, patient-

reported outcome measures (PROs) capture patients' perceptions of their functioning. Performance outcomes (PerfOs) objectively assess performance on standardised tasks, such as 6MWT, whereas digital measures, including wearable sensors, capture real-world activity and mobility metrics. Each of these assessment modalities captures complementary aspects of PF and should not be considered interchangeable. For instance, Sada et al. [7] found no association between CRF and selected mobility capacity metrics including gait speed and static balance, while CRF was associated with poorer real-world mobility behaviours, such as greater sedentary time, a lower daily step count and shorter walking bouts. Accordingly, this review distinguishes PA, physical fitness, physical performance and PF wherever possible and interprets findings according to the specific outcome assessed.

4. Exercise and cancer-related fatigue

Exercise is widely recognised as an evidence-supported, non-pharmacological intervention for CRF both during and after active cancer treatment. Reductions in CRF have been reported across aerobic, resistance and combined exercise modalities, suggesting that potential benefits are not confined to a single type of exercise. However, much of the available evidence is derived from general cancer populations, whereas relatively few trials have specifically enrolled patients with clinically significant fatigue at baseline. This limits certainty regarding the magnitude of benefit among individuals with established CRF. Furthermore, variation in trial findings and effect magnitude may partly reflect substantial heterogeneity in cancer populations, treatment contexts, exercise interventions and fatigue assessment methods. Overall, current evidence supports exercise as a strategy for CRF management, although the magnitude of benefit and the optimal approach to exercise prescription remain uncertain [3,8].

Exercise modality may influence the magnitude of CRF response, although no single exercise type has emerged as definitively superior. A recent network meta-analysis provided low-to-moderate certainty evidence that both resistance training and yoga significantly reduced CRF compared with standard care, while relative effects differed across age groups [9]. However, findings for resistance exercise have not been consistent across outcomes and treatment settings. During chemotherapy, resistance training significantly improved lower-body strength without producing a clear reduction in fatigue, illustrating that improvements in physical fitness may not necessarily parallel changes in CRF [10]. Furthermore, exercise effects should be considered in the context of the multidimensional nature of CRF. In women undergoing anthracycline-based chemotherapy for breast cancer, an individualised aerobic

exercise programme improved physical and affective fatigue, whereas no statistically significant between-group effect was observed for cognitive fatigue [11]. Taken together, these findings suggest that several exercise modalities may reduce CRF, but current evidence does not support a universally preferred modality. The therapeutic efficacy may be influenced by treatment context, patient characteristics and the specific CRF domain assessed.

Exercise dose appears to influence CRF response, although neither a universally optimal dose nor a clear linear dose–response relationship has been established. Importantly, available evidence does not support a simple assumption that greater exercise volume necessarily produces greater fatigue reduction. Consensus recommendations indicate that reductions in CRF have been observed with moderate-intensity aerobic, resistance and combined exercise performed regularly, commonly over approximately 12 weeks, although the effective frequency and duration vary according to exercise modality [8]. Consistent with the absence of a simple linear relationship, a recent dose-response network meta-analysis in breast cancer survivors suggested a non-linear, inverted U-shaped relationship between exercise dose and CRF, indicating that benefits may plateau or diminish beyond an intermediate dose range [12]. However, these findings were derived specifically from breast cancer populations and should not be interpreted as establishing a universally optimal dose. A key distinction should therefore be made between exercise doses shown to be effective in controlled clinical trials and the optimal dose for an individual patient.

Reductions in CRF appear to be influenced by a complex interplay of baseline patient characteristics and specific exercise intervention attributes. An individual patient data meta-analysis suggested that CRF response may be influenced not only by exercise modality but also by intervention delivery and duration. Greater reductions in CRF were observed with supervised exercise, and intervention duration was identified as a significant moderator, whereas exercise intensity was not significantly associated with differential fatigue response [13]. Baseline symptom burden also appears relevant. Another individual patient data meta-analysis found that patients presenting with higher baseline fatigue levels experienced greater reductions in fatigue following exercise interventions [14]. Consequently, CRF mitigation appears to be influenced not solely by modality and dose, but also by supervision, intervention duration and initial symptom burden. However, the generalisability of these moderator findings may be limited by the representation of specific cancer populations within the available trials.

5. Exercise and physical function

Exercise can improve multiple domains of physical fitness and functional performance in individuals diagnosed with cancer. In women with breast cancer, a meta-analysis of randomised controlled trials demonstrated significant improvements in muscular strength, functional exercise capacity and cardiorespiratory fitness, although the magnitude and pattern of these adaptations varied according to the treatment phase [15]. Similarly, another meta-analysis reported short-term improvements in cardiorespiratory fitness, muscular strength and walking capacity following exercise interventions across cancer populations [16]. However, gains in individual physical domains should not automatically be interpreted as an overall improvement in PF. The magnitude and clinical meaning of exercise-related benefit depend on the specific outcome assessed.

Different exercise modalities induce distinct physiological adaptations; consequently, their effects on outcomes such as muscular strength and cardiorespiratory fitness may vary. Resistance-based exercise has shown particularly consistent benefits for muscular strength, with meta-analytic evidence indicating that resistance training during chemotherapy significantly improves lower-body muscle strength [10,17]. Combined aerobic and resistance exercise programmes can concurrently target multiple domains, including muscular strength, functional exercise capacity and cardiorespiratory fitness, particularly during active treatment. However, the magnitude and pattern of adaptation are not uniform across these outcomes and may also differ according to treatment phase [15]. Thus, while specific exercise modalities may preferentially improve particular physical domains, no single modality appears to consistently enhance all aspects of physical fitness and functional performance.

Exercise-related adaptations may differ across phases of cancer care, cancer populations and specific physical outcomes. In the aforementioned meta-analysis of randomised controlled trials involving women with breast cancer [15], exercise during active treatment significantly improved muscular strength, functional exercise capacity and cardiorespiratory fitness. In the post-treatment setting, significant improvements were observed in muscular strength, fat-free mass and functional exercise capacity, whereas no significant improvement in cardiorespiratory fitness was identified. It is equally important to consider exercise outcomes across other oncological populations. In a randomised controlled trial involving patients with prostate cancer receiving androgen deprivation therapy (ADT) combined with enzalutamide, Harrison et al. [18] evaluated supervised combined aerobic and

resistance exercise. The exercise group demonstrated significant improvements in lower-body strength and 6-minute walking distance, whereas no significant between-group differences were observed in functional mobility outcomes such as the Timed Up and Go (TUG) or chair-stand test. Extending these observations to hospitalised older adults with cancer, Ferrara et al. [19] reported significant improvements in the Short Physical Performance Battery (SPPB), a composite measure incorporating balance, gait speed and chair-stand performance, as well as in knee-extension strength. These findings suggest that exercise-induced adaptations are context- and outcome-specific rather than uniform.

The maintenance of exercise-induced adaptations remains less certain than their immediate post-intervention effects. Brooks et al. [16] highlighted a distinct contrast in this regard: while cardiorespiratory fitness, muscular strength and walking capacity improved immediately following exercise interventions, the durability of these gains differed at subsequent follow-up. Improvements in walking capacity remained statistically significant, whereas gains in cardiorespiratory fitness and muscular strength were no longer significant. Although the certainty of evidence for these follow-up outcomes was rated as low to very low, these findings suggest that immediate improvements in physical fitness and functional performance do not necessarily translate into sustained benefits over time. The durability of exercise-induced adaptations may therefore be outcome-specific.

6. Linking cancer-related fatigue and physical function

Although CRF and PF are closely related, they represent distinct clinical constructs. The strength and nature of their association appear to vary according to the specific functional domain evaluated and the measurement methodology used. A retrospective analysis by Marker et al. [2] demonstrated that higher levels of CRF were associated with poorer performance on the 6-Minute Walk Test (6MWT), gait speed, Timed Up and Go (TUG), and 30-second sit-to-stand tests. Changes in CRF were also associated with changes in several objective measures of physical function. In contrast, Sada et al. [7] found that higher CRF was associated with greater sedentary time, fewer daily steps and shorter walking bouts, while no significant associations were observed with selected mobility-capacity measures, including gait speed and static balance. Taken together, these findings indicate that the relationship between CRF and physical functioning varies across functional domains and assessment approaches. CRF and PF should therefore be regarded as related but distinct outcomes whose association is multidimensional and measurement-dependent.

Improvement in physical capacity may represent one potential pathway contributing to reductions in CRF, although a direct causal pathway has not been conclusively established. In an analysis investigating potential mediators of exercise effect in cancer survivors after chemotherapy, improvements in cardiorespiratory fitness were found to mediate the effect of exercise on physical fatigue, whereas no such mediation was demonstrated for general fatigue. Handgrip strength and 30-second chair-stand performance were also associated with lower fatigue levels, but were not identified as significant mediators [20]. An important limitation is that the proposed mediator and fatigue outcomes were assessed at the same time point, preventing definitive establishment of their temporal sequence and causal direction. Thus, exercise-induced improvements in physical capacity may represent one pathway through which exercise influences CRF, but current evidence remains insufficient to establish a single or universal causal mechanism.

Improvements in physical fitness and functional performance do not necessarily coincide with reductions in CRF. In a randomised controlled trial involving multiple myeloma survivors, a 6-month tailored aerobic and resistance exercise programme produced significant improvements in muscular strength, whereas no significant between-group reduction in fatigue was observed [21]. A similar dissociation was observed in patients with prostate cancer receiving androgen deprivation therapy combined with enzalutamide. A 16-week supervised aerobic and resistance exercise programme improved lower-body strength and 6-minute walking distance and attenuated deterioration in cardiorespiratory fitness, yet no significant between-group improvement in fatigue was observed [18]. Conversely, other trials have reported concurrent improvements in physical outcomes and fatigue [11,19]. A different response pattern was observed by Ulrich et al. [22]. Although overall between-group differences in the 6MWT and SPPB were not statistically significant, fatigue remained stable in the exercise group while deteriorating in the standard-care group. Taken together, these findings indicate that CRF and physical outcomes do not consistently change in parallel following exercise, and improvement in one domain should not be assumed to imply a corresponding improvement in the other.

Overall, PF and CRF represent related yet distinct outcomes of exercise interventions. The observed divergence between these constructs may reflect multiple contributing factors, including systemic inflammation, treatment-related toxicities, sleep disturbances, psychological factors, the multidimensional nature of CRF and differences in outcome measurement. Consequently, improvements in objective physical outcomes, such as muscular

strength or 6MWT performance, should not be assumed to correspond directly to reductions in CRF, and vice versa.

7. Potential mechanisms linking exercise, CRF and physical function

CRF is a multifactorial symptom with a complex aetiology. Proposed mechanisms include physiological processes such as anaemia, systemic inflammation, dysregulation of the hypothalamic–pituitary–adrenal axis and circadian rhythms, muscle loss, and physical deconditioning, as well as psychological and behavioural factors including reduced self-efficacy, psychological distress and lower participation in daily activities [4]. The interaction of these mechanisms may contribute to substantial heterogeneity in the presentation and severity of CRF and may partly explain interindividual differences in response to exercise. Accordingly, exercise is likely to influence fatigue through several interacting biological, physical and psychosocial pathways rather than through a single universal mechanism.

Cancer and its treatments, particularly chemotherapy, may contribute to reductions in skeletal muscle function and cardiorespiratory fitness, thereby increasing the relative effort required to perform daily activities. Chemotherapy-related skeletal muscle dysfunction may involve several cellular processes, including mitochondrial dysfunction, oxidative stress and disruption of the balance between muscle protein synthesis and degradation. These alterations may contribute to muscle wasting, reduced strength and impaired functional capacity, potentially promoting sarcopenia and physical deconditioning [6]. Exercise may counteract some of these impairments by improving muscular strength, cardiorespiratory fitness and body composition. Increased physical capacity may reduce the relative physiological demand of everyday activities, while improvements in self-efficacy may further contribute to lower perceived fatigue [4]. Thus, improved physical capacity represents a plausible pathway linking exercise with both better physical functioning and reduced physical fatigue, although this causal pathway has not been definitively established.

The impact of exercise on CRF may extend beyond improvements in physical capacity and involve inflammatory, behavioural and psychosocial pathways. Elevated inflammatory markers have been observed in cancer survivors, suggesting that chronic inflammation may contribute to the pathogenesis of CRF. Exercise may in turn modulate inflammatory signalling through several mechanisms, potentially including improvements in body composition and reduced release of pro-inflammatory adipokines from visceral adipose tissue. In addition, acquiring new skills and achieving physical activity goals may enhance self-confidence and

self-efficacy, reduce psychological distress and positively influence sleep quality [4]. These mechanisms are likely to interact, and their relative contribution to CRF reduction may vary between individuals.

8. From general recommendations to individualised exercise prescription

Existing exercise guidelines provide a useful foundation for designing an appropriate exercise programme for an individual with cancer; however, they should be regarded as a starting point rather than a universally optimal prescription. The ACSM consensus recommendations presented by Campbell et al. [8] provide evidence-informed FITT parameters (frequency, intensity, time and type) associated with beneficial outcomes, rather than doses that are necessarily optimal for all individuals with cancer. Similarly, updated clinical guidelines recommend aerobic, resistance or combined exercise for reducing fatigue but do not identify a single universally superior exercise modality, dose, intensity or duration [3]. Accordingly, guideline-based recommendations should not be treated as fixed prescriptions, and doses shown to be effective should not be considered synonymous with individually optimal doses. Exercise prescription should instead consider the target outcome, cancer and treatment context, baseline fatigue and physical capacity, as well as individual symptoms, tolerance and preferences.

Assessing baseline symptom burden and functional status is important when tailoring exercise interventions to individual patient needs. An individual patient data meta-analysis by Buffart et al. [14] examined whether baseline characteristics moderated exercise effects in patients during and after cancer treatment. Patients with higher baseline fatigue tended to experience greater reductions in fatigue following exercise interventions, while those with poorer baseline physical function demonstrated greater improvements in physical function. These findings suggest that individuals with greater baseline impairment may derive greater benefit from exercise, although this should not be interpreted as a universal response pattern. Baseline assessment may therefore help establish intervention priorities, target outcomes, appropriate starting levels and the anticipated response to exercise. Accordingly, CRF and physical function should be assessed before exercise prescription and used to help inform an individualised programme rather than relying solely on general recommendations.

Individualisation is an important component of patient-centred exercise prescription and may be understood as an ongoing, iterative process of adapting an intervention to changes in clinical status and exercise response. In a recent systematic review and meta-analysis, only

approximately 49% of studies adequately reported how exercise was individualised [23]. The most common approach involved adjustment based on objective baseline assessments, whereas pre-session and inter-session modifications were used less frequently. Individualisation based on subjective clinical reasoning and adjustments made between exercise sessions were associated with greater reductions in fatigue, although these findings do not establish the superiority of any single individualisation strategy. People with cancer may experience fluctuations in symptom burden, treatment tolerance and psychological well-being. Exercise prescription should therefore remain adaptable both at programme initiation and throughout the intervention, with repeated reassessment used to guide progression and modification.

Supervised exercise, conducted under the guidance of a qualified professional, may enhance intervention effectiveness, although the evidence is not entirely conclusive. An individual patient data meta-analysis by van Vulpen et al. [13] found that supervised exercise was associated with greater reductions in CRF. Supervision may also support improvements in some physical function outcomes, although the overall superiority of supervised over unsupervised exercise has not been conclusively established [8]. Potential benefits of supervision include closer symptom monitoring, appropriate progression or regression of exercise, technical guidance and behavioural or motivational support. However, supervised programmes may also increase practical barriers related to time, travel and accessibility. The level and format of supervision should therefore be individualised according to clinical status, physical capacity, previous exercise experience, safety considerations and patient preferences.

The timing of exercise initiation should be considered within the context of the treatment continuum rather than viewed as universally optimal at a single time point. A systematic review comparing earlier and later initiation found no significant differences in fatigue, walking capacity, cardiorespiratory fitness, quality of life or physical activity outcomes [24]. Evidence also suggests that the pattern of exercise-related adaptation may differ according to treatment phase. In breast cancer populations, exercise performed during active treatment and after treatment produced different patterns of change, particularly in fat-free mass and cardiorespiratory fitness [15]. These findings suggest that the treatment phase may influence which physical outcomes are most responsive to exercise. Accordingly, exercise timing should remain flexible and responsive to treatment phase, clinical status and individual readiness rather than being determined by a fixed chronological threshold.

9. From efficacy to real-world effectiveness: adherence and maintenance

Beyond the initial design of an exercise programme, its practical implementation and sustained adherence are important determinants of real-world effectiveness. Adherence appears to be influenced by a combination of clinical, behavioural, psychological and environmental factors, with relevant predictors differing between active treatment and post-treatment periods. During active treatment, higher adherence was associated with previous exercise behaviour, motivation, programme location and fewer physical limitations. In the post-treatment period, adherence was associated with previous adherence, family or social support, trainer feedback and exercise-related knowledge and skills. Comparisons across studies are complicated by substantial heterogeneity in how adherence is defined and measured. Available evidence does not support a single consistent profile of patients who are more likely to adhere; rather, adherence appears to reflect the interaction of multiple personal, clinical and programme-related factors [25].

Achieving meaningful population-level benefits from exercise interventions requires consideration of both initial uptake and sustained participation. In the MASCOT trial, the uptake rate was approximately 57%, with a median attendance of around 75%, while time and travel were identified as important barriers to participation [21]. These findings illustrate that the real-world effectiveness of exercise depends not only on whether an intervention can produce benefit under trial conditions, but also on its accessibility, feasibility, participation burden and compatibility with everyday life. Moreover, individuals who enrol in exercise trials may differ from the broader oncology population in motivation, health status or willingness to exercise. Consequently, benefits observed among trial participants may not translate directly to all people with cancer.

Maintaining physical activity after completion of a structured exercise programme represents a distinct challenge from adherence during the intervention itself. In a systematic review of 18 randomised controlled trials with follow-up periods of at least 6 months, evidence regarding the long-term maintenance of increased physical activity was generally inconclusive. The review also examined behaviour change techniques (BCTs), with social support, goal setting, action planning and ongoing supervision or support identified as potentially beneficial strategies [26]. These findings suggest that the selection and implementation of BCTs may be more important than the number of techniques used. Improvements in physical activity during

a structured intervention should therefore not be assumed to persist after formal support has ended.

10. Safety and generalisability

Although exercise is widely recommended in cancer care, evidence regarding potential harms remains less robust and less consistently documented than evidence supporting its benefits. A meta-analysis evaluating the harms of exercise in patients with cancer undergoing systemic treatment concluded that evidence regarding exercise-related harms remains uncertain, with adverse events reported inconsistently and often incompletely and the overall certainty of evidence rated as very low [27]. Given this uncertainty, safety assessment should form an integral part of individualised exercise prescription, with consideration of health history, comorbidities, treatment-related toxicities and other clinically relevant risk factors [8].

Across the available literature, the representation of cancer types and patient populations remains uneven. A recent umbrella review highlighted that physical activity recommendations for cancer survivors have remained largely generic and demonstrated a substantial overrepresentation of evidence derived from breast cancer populations. Because the strength and nature of the evidence vary considerably according to cancer type and outcome, findings derived predominantly from breast cancer populations should not be assumed to apply uniformly across all oncology populations [28]. In addition, participants enrolled in exercise trials may differ from the broader cancer population, as they may be more interested in exercise and have fewer comorbidities, lower levels of fatigue and psychological distress, and higher baseline quality of life [14]. Therefore, study findings should be interpreted in the context of the specific populations from which the evidence was derived.

11. Long-term effects

The durability of exercise-induced improvements is clinically important, as immediate post-intervention gains should not be assumed to persist over time [16]. In women with breast cancer who completed aerobic high-intensity interval training combined with progressive resistance exercise, total and cognitive CRF remained lower than in the usual-care group at the 2-year follow-up. Higher lower-limb strength was also observed, whereas no statistically significant between-group differences were found in cardiorespiratory fitness, handgrip strength, sedentary behaviour or moderate-to-vigorous physical activity [29]. These findings indicate that the durability of exercise-related benefits may vary substantially across outcomes.

Moreover, persistence of symptom or physical benefits should be distinguished from maintenance of physical activity behaviour after an intervention, for which longer-term evidence remains limited and inconclusive [26]. Maintenance of symptom benefit, physical fitness and functional outcomes, and physical activity behaviour should therefore be considered distinct aspects of long-term effectiveness.

12. Evidence gaps, limitations and future directions

Substantial clinical and methodological heterogeneity limits the comparability of data across exercise oncology studies. Studies vary considerably in cancer type, with breast cancer populations frequently overrepresented [8], as well as in disease stage, treatment modality and phase, and baseline levels of fatigue and physical function. Considerable variability also characterises the exercise interventions themselves, including modality, frequency, intensity, duration, supervision and individualisation. Furthermore, CRF is assessed using different instruments and operational definitions, while trials evaluate a wide range of physical outcomes, including muscular strength, cardiorespiratory fitness, 6MWT performance, TUG performance and patient-reported physical function, which capture distinct domains of fitness and functioning [3,5]. Consequently, direct comparisons across studies are challenging, complicating identification of a consistently superior exercise modality or universally optimal dose. Although this heterogeneity represents an important limitation, it also reflects the clinical diversity of cancer populations and treatment contexts.

Available evidence is considerably stronger in demonstrating that exercise can provide benefits for people with cancer than in determining which specific prescription is most appropriate for an individual patient. Important gaps also remain in the populations represented in clinical trials. The evidence base is dominated by breast cancer populations [28], while exercise trial participants may be more interested in exercise and have fewer comorbidities, lower levels of fatigue and psychological distress, and higher baseline quality of life than the broader oncology population [14]. In addition, only a small minority of trials have specifically recruited participants based on elevated fatigue at baseline, limiting direct evidence regarding exercise as a treatment for established clinically significant CRF [3]. Despite strong evidence supporting the general benefits of exercise in oncology, substantial gaps remain regarding optimal dose, direct comparisons between exercise modalities, timing, dynamic individualisation, long-term maintenance and safety in higher-risk populations.

Future research should focus on identifying which exercise modalities and dose–response patterns are most effective for specific patients and outcomes, while including more diverse cancer populations and treatment contexts. Studies should concurrently assess CRF and clearly defined physical outcomes to better elucidate their interrelationships, incorporate longer follow-up periods, and improve reporting of exercise prescription, individualisation and adverse events. Further mediation studies with appropriately timed assessments are also needed to clarify whether improvements in physical capacity precede and contribute to reductions in CRF. This narrative review has several inherent limitations, including its non-systematic design, iterative and purposive literature selection, restriction to English-language publications, and inclusion of only freely and legally accessible full texts. These criteria may have resulted in the omission of relevant evidence, particularly paywalled studies, and should be considered when interpreting the conclusions.

13. Clinical and practical implications

Developing an exercise prescription should begin with an individualised baseline assessment to identify the primary domains requiring improvement, such as CRF, muscular strength, cardiorespiratory fitness, walking capacity or broader physical function. Reliance on generalised exercise programmes without consideration of individual needs may be insufficient. Exercise prescription should also incorporate the broader patient context, including personal preferences, motivation, practical barriers, access to supervision and time or travel constraints. This is particularly relevant because baseline fatigue and physical function may influence exercise response, while different clinical outcomes may show distinct patterns of improvement. Consequently, a uniform, one-size-fits-all exercise programme is unlikely to be appropriate for all patients [8,14].

An exercise programme should be directed towards clearly defined target outcomes that are regularly reassessed, allowing the intervention to be modified in response to changing patient needs. Exercise modality can be selected according to the primary clinical goal; for example, resistance training may preferentially improve muscular strength, aerobic training may target cardiorespiratory fitness, and combined training can address multiple physical domains. However, current evidence does not support a single universally superior exercise modality. Similarly, because a universally optimal exercise dose has not been established, an appropriate approach is to initiate exercise at a tolerable level and subsequently adjust the prescription according to symptoms, fatigue, exercise tolerance, functional response and

adverse effects. Supervision may enhance exercise effectiveness, but its level and format should be individualised according to clinical status, safety considerations, exercise experience, accessibility and treatment phase. Exercise prescription should therefore not be regarded as a rigid, standardised FITT formula, but as a dynamic and collaborative process guided by repeated assessment of the patient's response and evolving clinical status [8,13,23].

To accurately evaluate the effectiveness of exercise interventions, clinicians should not rely on a single parameter but should consider both symptom-based and physical outcomes. Relevant outcomes may include CRF, physical function, muscular strength, cardiorespiratory fitness and physical activity behaviour, which should be interpreted as distinct but complementary domains. Importantly, improvements in 6MWT performance, muscular strength or peak oxygen uptake ($\text{VO}_{2\text{peak}}$) do not automatically translate into reductions in CRF, just as attenuation of fatigue does not necessarily indicate improvement in objective physical performance. Furthermore, clinical success should encompass adherence, safety and long-term sustainability rather than relying solely on a single marker of exercise effectiveness [2,7,16].

14. Conclusions

Exercise represents an evidence-supported intervention for reducing cancer-related fatigue and improving multiple domains of physical fitness and functional performance in people with cancer across the cancer continuum. Although CRF and physical function are closely related, they remain distinct clinical constructs; consequently, improvements in these domains do not necessarily occur simultaneously or to the same extent.

Current evidence does not support a single universally optimal exercise modality, dose, timing strategy or supervision model. Exercise prescription should therefore be individualised according to the primary therapeutic goal, baseline fatigue and physical function, treatment context, clinical status, tolerance and patient preferences. Clearly defining the target outcome and establishing the patient's baseline status are important steps in selecting and subsequently adapting an appropriate exercise programme.

The clinical effectiveness of exercise also depends on adherence, accessibility, safety and long-term sustainability, rather than solely on short-term physiological adaptations. Future research should clarify the causal pathways linking changes in physical fitness and function

with reductions in fatigue and determine which exercise prescriptions are most effective, feasible and sustainable for specific patients and outcomes.

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