An assessment of study characteristics, quality and reporting in cancer prehabilitation literature: a scoping review

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An Assessment of Study Characteristics, Quality and Reporting in Cancer Prehabilitation Literature - A Scoping Review

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Abstract

Background: Cancer and its treatment can negatively impact physical function, general wellbeing, and quality of life. An evidence-based strategy to manage this is to prescribe exercise. One approach is to prescribe exercise prehabilitation to improve pre-treatment health and function. However, current exercise prehabilitation programmes are under-researched, and the quality of their reporting has not been systematically assessed.

Objectives: This review aimed to identify the following: the characteristics of prehabilitation exercise programmes; how intensity, physical function, patient reported outcomes and treatment-related outcomes were measured; the quality of reporting and programme implementation.

Eligibility Criteria: Studies were eligible for inclusion if they reported a cancer prehabilitation exercise intervention, reported outcomes relating to physical function and patient reported outcomes, and full text copies were available in English.

Sources of Evidence: PubMed, Mednar and Scopus were screened for studies from inception until the 4th of April 2024.

Charting Methods: Exercise characteristics were extracted and manually charted in Microsoft Excel using to the Template for Intervention Description and Replication. The TESTEX (Tool for the assEssment of Study qualiTy and reporting in EXercise) framework was used to assess study quality and intervention reporting.

Results: 1495 results were retrieved, 28 of which were included. Exercise sessions lasted a mean of 42.5 ± 21.9 minutes and were completed 3.7 ± 1.3 times per week. Twenty-two studies implemented concurrent exercise, five prescribed aerobic, and one prescribed resistance. High-intensity exercise was prescribed in four studies, moderate-high in 12, seven prescribed moderate, three prescribed low–moderate, and one was low intensity. Ten studies prescribed exercise intensity using the Borg Rating of Perceived Exertion Scale, five prescribed heart rate zones, six used a set workload, and seven did not monitor intensity. A mean TESTEX score of 9.3 ± 2.3 out of 15 was achieved. The lowest scoring criterion (n = 3) related to the reporting of the exercise dose.

Conclusions: There was heterogeneity among studies regarding exercise intervention characteristics and measures of effectiveness. The overall quality of reporting was satisfactory, yet inconsistencies were apparent regarding quantifying and monitoring exercise dose, which limits the ability of researchers and clinicians to replicate, evaluate, or scale cancer prehabilitation exercise interventions, impeding evidence-based practice. As such, to be able to optimise cancer prehabilitation exercise programmes, research must first focus on improving the quality of reporting and standardising outcome measures and methods of monitoring and prescribing exercise.

Strengths and limitations of this study

- This study used a robust search strategy across multiple databases.
- The combined use of TESTEX and TiDier frameworks provides a novel assessment of the quality of reporting and exercise characteristics.
- Heterogeneity in outcomes, settings, and exercise protocols meant that meta-analysis was not feasible

Introduction

Cancer is a highly prevalent disease, with 1 in 2 people receiving a cancer diagnosis within their lifetime [1]. Therefore, minimising the burden of cancer is critical to patient wellbeing. While treatments have been developed to ameliorate the disease, reduce its severity, and improve mortality rates, they can be detrimental to physical function, well-being and quality of life (QoL) [2, 3]. It is reported that during treatment, cancer patients often experience reduced physical function and weakened immune and anti-inflammatory mechanisms, which can result in an increased risk of treatment-related toxicity and mortality [4, 5]. Consequently, developing and optimising strategies that enhance pre-treatment physical function and health are vital for managing post-treatment outcomes and preserving patient wellbeing.

A relatively new strategy is to prescribe interventions before acute treatment to physically and mentally prepare the patient (prehabilitation). This is opposed to the more commonly acknowledged

rehabilitation phase, where programmes are implemented after treatment to restore health and wellbeing [6]. Prehabilitation often features baseline and post-treatment assessments alongside programmes designed to enhance physical and psychological wellbeing, thus minimising treatment-related impairment [7, 8]. A particularly promising strategy is exercise prehabilitation, which comprises exercise-based programmes that aim to improve physical function and prepare the patient for the demands of treatment [9].

When implemented effectively, exercise prehabilitation proves highly beneficial in adults living with cancer and has been evidenced to reduce treatment complication rates, shorten hospital stays, and improve aspects of physical and psychological wellbeing [10]. Furthermore, by implementing exercises specifically designed to increase aerobic fitness and lean body mass before treatment, the risk of toxicity and the likelihood of treatment effectiveness significantly improve [11, 12]. However, the existing evidence may be threatened by a lack of adherence and no intention to treat analysis [13, 14].

Furthermore, a consensus is lacking regarding the optimal approach to delivering prehabilitation, whereby programmes vary in location, and supervision status [17]. Exercise programmes are perceived as easier to implement, monitor and standardise when delivered in clinical settings, as a smaller reliance is placed on the participant's motivation to adhere [16, 17]. However, participants may be deterred by inconvenient exercise settings such as busy public gyms, and participant withdrawal is common [16,18]. Other strategies aim to enhance adherence and remove barriers like travel time and distance using home-based delivery methods (virtual/video call delivery or pre-recorded material), but safety and exercise intensity may be compromised [19,20]. Most of these home-based programmes rely on patient-reported measures of adherence. Therefore, whether sessions were completed per protocol is unknown, and the reported adherence is likely to be an inflation of actual values [21, 22]. Accordingly, the methods used for assessing and reporting adherence must be systematically assessed to understand whether adherence rate are accurate and standardised across the literature.

The optimal intensity, modality, and frequency of the exercise itself also remains unknown [23]. Aerobic programmes are evidenced to significantly improve cardiorespiratory fitness, fatigue, depression, and QoL [24]. Whereas the external load placed on the body by resistance-based programmes is theorised to induce adaptations that benefit muscular strength, bone mineral density, mobility, and body composition [25]. Yet there are arguments that concurrent programmes (combining aerobic and resistance elements) are superior and provide the benefits of both aerobic and resistance-based exercises [26].

Current guidelines for adults living with cancer comprise three 30-minute sessions of moderate-intensity aerobic exercise each week, concurrent with two sessions of resistance training at ≥60% of

their one repetition maximum (1RM) [27]. There is evidence advocating that the prescription of high-intensity interval training (HIIT) may improve cardiopulmonary fitness, muscular function and QoL in a more time-efficient manner [28]. Yet, quantifying and monitoring exercise intensity varies largely, meaning comparisons cannot be made between programmes [29]. Indeed, despite the increasing recognition of prehabilitation for people living with cancer within clinical practice guidelines, the most effective approach to prehabilitation is unknown, and the quality and characteristics of the current evidence requires assessment [30].

Currently, comparisons between different studies and programmes cannot be made due to heterogeneity in effectiveness outcomes. Gold standard techniques, like cardiopulmonary exercise testing (CPET), are validated for determining clinically significant changes in health and fitness and are highly supported across the literature [11]. However, studies often opt for non-validated methods, design their own, or use subjective measures [31]. By not using validated and objective measures, findings are open to reporter bias, measures may not accurately represent the values they are trying to assess, and discrepancies exist between perceived/reported and actual values, especially when assessing physiological variables like symptom burden or fitness levels [32, 33]. Indeed, without systematic assessment of programme implementation, evaluation and reporting, programme effectiveness cannot be identified and compared with any degree of certainty.

In summary, a consensus is lacking regarding the optimal approach to cancer prehabilitation. Furthermore, while systematic assessments of the characteristics and quality of reporting of all modalities of prehabilitation exist [34], assessments that focus specifically on exercise prehabilitation among adults living with cancer are yet to be completed. Therefore, this scoping review aimed to map the characteristics of cancer prehabilitation exercise interventions and systematically assess their quality of reporting (using a validated tool). By doing so, this review identified areas which lacked consistency, were poorly reported and therefore prevent comparison, replication and optimisation.

Aims

Cancer prehabilitation interventions are complex to design, implement and report. As such, there is a need to synthesise the evidence to understand the characteristics of such interventions and assess the quality of reporting of cancer prehabilitation exercise interventions. The aims of the current study are:

- To identify the characteristics of cancer prehabilitation exercise interventions: Frequency, intensity, time, and type of exercise, setting, part of a unimodal or multimodal intervention.
- To identify methods of measuring and assessing exercise intensity, physical function, adherence and patient reported outcomes.

- To assess the quality of reporting of prehabilitation exercise interventions.

Method

This scoping review was reported according to the Preferred Reporting Items for Systematic reviews and Meta-Analysis extension for Scoping Reviews (PRISMA-ScR) [35] and the Joanna Briggs Institute (JBI) framework [36]. The following steps were completed: **1)** Defining a review question; **2)** Refining the inclusion criteria; **3)** Creating and conducting the search strategy; **4)** Evidence screening; **5)** Data extraction; **6)** Data analysis; **7)** Presenting the results. Ethical approval was granted by the Sheffield Hallam University ethics committee (Ref: ER51277591). The search strategy and protocol were not registered.

Inclusion Criteria

The eligibility of identified studies was assessed according to the following criteria: **1)** participants were ≥18 years of age living with any type or stage of cancer; **2)** interventions featured a prehabilitation exercise programme of any modality. Studies featuring rehabilitation were eligible, providing that the results and protocols of the prehabilitation phase could be separated; **3)** outcomes measured physical function, patient-reported or treatment-related; **4)** full-text articles were available in English.

Search Strategy

A final search of PubMed, Scopus, Mednar and the reference lists of relevant studies was completed on the 4th of April 2024. The search strategy (described in supplementary material 1) was applied to identify articles containing titles, abstracts and keywords that included pre-defined search terms relating to cancer, prehabilitation, exercise, physical function and patient-reported outcomes.

Evidence Screening

The retrieved articles were exported to Covidence (an online system for storing and sorting articles) for eligibility screening (Covidence systematic review software, Veritas Health Innovation, Melbourne, Australia. Available at www.covidence.org). Initial screening of titles and abstracts identified relevant articles (SW). Full-texts were screened and inclusion was confirmed/denied (SW). An independent assessor (AM) completed calibration checks for eligibility and data extraction in 10% of the retrieved studies [37]. No discrepancies occurred during the calibration. The number of articles at each stage of the screening process and the reasons for exclusion were tracked using the PRISMA flow chart (supplementary material 2) [38].

Data Extraction and Analysis

Data were manually extracted from Covidence and collated and tabulated to include aspects of the TIDieR framework (Microsoft Excel) [39]. Information relating to the characteristics of the exercise intervention was extracted from each study (modality, intensity, frequency and duration). Data was also extracted regarding adherence, adverse events, recruitment/eligibility criteria, and sample sizes. Guided by the American College of Sports Medicine (ACSM) definitions, exercise modality was divided into the following categories [40]:

1) Aerobic: exercise that continuously requires the contraction of all major muscle groups in a rhythmic nature. This type of exercise relies on aerobic metabolism.
2) Resistance: exercise that requires the muscle to contract against an external resistance such as free weights, resistance bands, or one's body weight.
3) Concurrent: programmes comprising components of resistance and aerobic exercise.

Programme settings were categorised into centre-based, home-based and a combination of centre and home-based sessions. Centre-based programmes took place in locations designated for exercise participation (e.g., hospitals, community centres, gyms, or leisure centres). Home-based programmes were completed either in the participant's dwelling or the surrounding outdoor environment (e.g., walking around a local park). Further subgroups were created to separate supervised and unsupervised programmes. Supervision could be completed in either setting via face-to-face or remote/digital observation.

Information about the methods used to assess effectiveness were also extracted. For example, measures of physical function included $\dot{V}O_2$ max, grip strength, 6MWT scores, and body composition. Patient-reported outcomes featured subjective measures like the EORTC-QLQ-C30. Treatment-related outcomes included length of hospital stay, complication grade, and hospital readmissions.

Following data extraction, all included studies were scored against the Tool for the assEssment of Study qualiTy and reporting in EXercise (TESTEX) criteria [41]. TETSEX comprises 15 items that assess how interventions were conducted, monitored, assessed, analysed and reported [41]. If the criterion is satisfied, then a score of one is given; if not satisfied or insufficient information is reported, then a score of 0 is given. TESTEX scores were tabulated and displayed graphically. Descriptive analysis was completed to determine the mean exercise frequency, intensity, programme duration and TESTEX scores achieved. Differences in TESTEX scores were assessed depending on exercise modalities and settings, thus identifying potential disparities in the quality of implementation and reporting of each

strategy. Therefore, it can be determined whether setting and modality impact factors like adherence and safety (incidence of adverse events).

Patient and Public Involvement Statement

There was no patient or public involvement in this study.

Results

1495 articles were retrieved, 80 were duplicates, and 1352 were deemed irrelevant based on their titles. Sixty full texts were screened, 28 of which were eligible for inclusion (supplementary material 2).

Characteristics of the included cancer exercise prehabilitation studies are presented in Table 1 (supplementary material 3), and selected TiDieR characteristics of the exercise programmes are presented in Table 2 (supplementary material 4). TESTEX scores are displayed graphically and categorised by exercise modality (Figure 1) and setting (Figure 2).

Study and Participant Characteristics: Eight randomised control trials (RCTs) (30.8%) [42-49] and one non-randomised control trial compared prehabilitation to usual care conditions (50). Five studies (11.5%) compared participant responses to different exercise programmes [51-55], one study (3.9%) compared home and centre-based settings (56), and 13 studies (50%) compared pre- to post-measures from a single intervention [57-69]. Study characteristics (supplementary material 3) were heterogeneous in all variables, including sample size, cancer site, treatment types, and inclusion criteria. A total of 1540 participants were included across the 28 studies. Eight studies recruited rectal/colorectal cancer patients [43, 45, 51, 52, 54, 57, 65, 69]. Two studies focused on breast cancer [56, 68], and two studies recruited participants with oesophageal/gastro-oesophageal cancer [42, 50]. Lung cancer was the focus of five studies [46, 48, 58, 61, 64], three focused on prostate cancer [49, 55, 63] and two on bladder cancer [47, 53]. Urological and pancreatic cancer were featured in one study each [44, 66]. The remaining four studies included multiple or unspecified cancer types [59, 60, 62, 67].Twenty studies recruited participants scheduled to receive surgery. The remaining eight studies included combined-treatment programmes: surgery and chemotherapy (n = 3) [42, 56, 59], surgery and chemo-radiotherapy (n = 4) [43, 50, 57, 66], and chemo-radiotherapy and hematopoietic cell transplantation (n = 1) [67].

Health, Functionality, and Co-morbidity Status: Participant recruitment criteria were inconsistent. Six studies (21.4%) specified that participants must possess the capacity to exercise or complete physical assessments, and 23 studies (82.1%) excluded participants with co-morbidities or conditions that may preclude or contraindicate exercise participation (supplementary material 3). Validated scale-based criteria for co-morbidity status included a World Health Organisation (WHO) status lower than 1 (n = 1) [50], the absence of a heart condition classified as class III or IV according to the New

York Heart Association (n = 1), and an American Society of Anaesthesiologists (ASA) health status grading scale <4 (n = 1) (52) or <3 (n =2) [53, 54]. The ability to complete a CPET assessment was required for participation in five studies [42, 43, 58, 60, 69], one of which required a baseline CPET $\dot{V}O_2$ at the ventilatory anaerobic threshold (VAT) of <11 mL/kg/min [43]. One study required participants to achieve a veterans-specific activity questionnaire (VSAQ) score of ≤7 METs [43].

Outcome measures: Twenty-seven studies (96.4%) assessed physical function, comprising 33 unique measures (supplementary material 4). Six-minute walk tests were the modal physical function related outcome measure (n = 14) [45, 46, 49, 51, 52, 54, 55, 58, 61, 62, 65-68]. Eight studies used CPETS, which generated values of $\dot{V}O_2$ at the anaerobic threshold (AT), $\dot{V}O_2$ Max, and O_2 pulse [42-44, 54, 59, 61, 67, 69]. Assessments of muscular strength, power, and endurance included grip strength dynamometry (n = 6) [42, 48, 62, 64, 66, 68], and sit-to-stand tests (n = 4) [48, 62, 64, 66]. Nineteen studies included patient-reported outcomes featuring 23 unique measures. The most frequently used measures were the EORTC-QLQ-C30 (n = 6) [42, 48, 55, 62, 64, 65] and the 36-Item Short Form Survey (SF-36) (n = 6) [46, 51-53, 65, 68]. Twelve studies reported treatment-related outcomes, which featured 18 different measures. The modal measure of treatment success was the duration of post-treatment hospital stays (n = 6) [43, 46, 49, 50, 64, 65]. Four studies used the Clavien-Dindo classification of post-treatment complications severity (n = 4) [43, 46, 50, 51].

The programme duration, exercise modality, session frequency and session length varied across the included studies (supplementary material 4). The mean programme duration was 6.36 ± 5.01 weeks. The most frequently prescribed modality was concurrent exercise (n = 22, 78.6%), followed by aerobic (n = 5, 17.9%) and resistance (n = 1, 3.6%). The mean length of each exercise session was 42.50 minutes (SD = 21.92), prescribed for an average of 3.60 days a week (SD = 1.32). Eleven (39.3%) studies were centre-based [43, 44, 50, 53-55, 57, 58, 61, 65], 12 (42.86%) were home-based [45-49, 51, 52, 59, 64, 66-68], and five (17.9%) were home and centre-based [42, 56, 60, 62, 63]. High-intensity exercise was prescribed in four studies (14.3%), moderate-high in 12 (42.9%), seven prescribed moderate (25%), three prescribed low–moderate (10.7%), and one was low intensity (3.6%). Ten studies monitored and prescribed exercise intensity using the Borg Rating of Perceived Exertion Scale (35.7%), five prescribed heart rate zones (17.9%), six used a set workload (21.4%), and seven did not monitor intensity (25%).

Ten studies (35.7%) implemented exercise as the sole prehabilitation strategy. The remaining 18 studies (64.3%) prescribed exercise as the main component of a multimodal programme (supplementary material 4). Among the multimodal programmes, BCTS were implemented in 11 studies [47-49, 52, 57-59, 64, 66-68], nutritional counselling in eight [42, 43, 45, 46, 51, 53, 54, 66],

relaxation and anxiety relief in five [45, 46, 51, 53, 54], psychological counselling in one [42], and smoking cessation in one [43].

Figure 1 shows the total TESTEX scores for each study included in this review, categorised according to exercise modality. The mean total TESTEX score was 9.32 ± 2.29 (Fig 1). The lowest scoring criteria related to the reporting of exercise dose, volume and intensity, which was met by three studies [42, 59, 67]. Two studies, that both implemented concurrent exercise [42, 48] received the highest TESTEX score (14 points). The lowest score (6 points) was achieved by one aerobic exercise-based study [57] and one resistance-based [56]. When comparing modalities, the greatest mean score was received by concurrent exercise protocols (M = 9.59, SD = 2.24), followed by aerobic exercise (M = 8.80, SD = 2.39). Only one study prescribed resistance exercise and scored six points.

Figure 2 shows the TESTEX scores for each study based on the setting in which the programme was delivered. Home-based programmes received a mean total TETSEX score of 8.90 ± 2.08 (Fig.2). Centre-based programmes received a mean of 10.36 points (SD = 2.20), and the combined centre and home-based programmes achieved a mean score of 9 (SD = 3.16). The lowest-scoring studies (6 points) featured centre-based elements, one being completed in a clinical centre and the other including home and centre-based components [56, 57].The highest-scoring studies (14 points) were completed in either home-based only or home and centre-based settings [42, 48].

Adherence and Adverse Events: Across all 28 studies, nine met the TESTEX criteria for adherence (≥85% adherence) [43, 48, 53, 54, 59, 62-64, 68]. All of which implemented concurrent exercise. Satisfactory adherence (≥85% adherence rate) was achieved in 40% (n =2) of the studies implemented in centre and home-based settings [62, 63]. The adherence criterion was also met by 27.3% of centre-based studies (n = 3) [43, 53, 54] and 33.3% of home-based studies (n = 4) [48, 59, 64, 68]. Methods for assessing adherence were researcher-reported completion rates (n = 7) [43, 44, 50, 53, 58, 61, 69], participant-reported completions rates (n = 16) [42, 45-49, 51, 52, 56, 59, 60, 62-64, 68] and smartwatch-derived accelerometry (n = 2) [66, 67]. The protocols of 18 studies included adverse events as an outcome. No serious adverse events were reported, but two studies reported non-serious exercise-related events, one reporting nine [64], the other reporting six events [48].These events included muscle pain, foot pain, knee pain, and the exacerbation of pre-existing musculoskeletal conditions.

Discussion

The importance of prehabilitation for improving post-treatment outcomes is becoming increasingly recognised within cancer care [70]. However, the optimal approach remains unknown due to

heterogeneity in exercise characteristics and a lack of systematic assessment regarding the quality of reporting [71]. Accordingly, this review aimed to identify the exercise characteristics and quality of reporting of cancer exercise prehabilitation programmes, thus highlighting areas that lack consistency and quality.

What is the quality of reporting of prehabilitation exercise interventions?

Across all 28 included studies, the average TESTEX quality score was 9.32 ± 2.29, below the minimum 'satisfactory' score of 10 [41]. However, this threshold is not explicitly defined, and when interpreting TESTEX scores in cardiovascular rehabilitation, a score above 9 is considered 'good' [72]. Indeed, the mean quality of studies in the present review is similar to that achieved in other clinical contexts such as the rehabilitation of patients with Parkinson's disease [73]. Furthermore, the average quality achieved in the present review exceeds that of exercise programmes prescribed for adults with Multiple Sclerosis where a systematic review reported a mean TESTEX score of 7.5 [74]. However, these studies focused on rehabilitation and may have different quality standards. It should also be noted that the quality of the included studies varied depending on characteristics like modality, setting and the specific TESTEX criteria being assessed.

TESTEX adherence criteria (≥85% achieved according to the study's criteria) were reportedly met by nine studies. It is accepted by researchers and healthcare providers that adherence is mediated by the setting in which the exercise is delivered [75]. Thus, it is vital to understand whether a relationship between setting and adherence exists within the literature [16]. Fifty percent of studies that delivered exercise in centre and home-based settings, and 33.33% of those delivered in home-based settings met adherence criteria, greater than that achieved in a solely centre-based setting (30%). Respectively, it could be assumed that removing the need to travel and offering participants flexibility in exercise settings increases adherence [14].

However, adherence measures were unstandardised, comprising attendance rates, completion per protocol, exercise diary tracking, and step counts. Indeed, only 16 % of home-based and none of the home and centre-based programmes used objective measures and instead relied on self-reported attendance and exercise completion. Meanwhile, 70% of centre-based programmes used objective attendance measure or completion reported by the researcher. Similarly, a significant disadvantage of home-based interventions is that adherence is difficult to control [16]. Therefore, the finding that a greater proportion of supervised exercise programmes (37.5%) met adherence criteria compared to unsupervised programmes (25%) is not surprising. Indeed, when exercise is unsupervised, a greater reliance is placed on the individual's motivations, and behavioural factors become more potent mediators of adherence [16, 76]. It must also be considered that unsupervised studies rely on

participant-reported adherence rates. Therefore, as self-reported measures are known to be an inflation of actual values, it is possible that actual adherence was lower than the rates reported [77].

Another outcome that used self-reported measures in home-based settings was the incidence of adverse events, where some studies relied on participants to report the occurrence of any exercise-related events themselves. In the context of cardiovascular treatment, comparisons between the number of events reported by patients and healthcare professionals indicated that patients often did not report an event or underestimated its severity [78]. Hence, the same misreporting could be expected in the present review, explaining why of the 18 studies that met TESTEX criteria for reporting adverse events, only two studies reported any incidences occurring. Additionally, the lack of adverse events may also be attributed to the fact that 23 studies specified that participants must be free from contraindications or conditions that preclude exercise. The ACSM list of contraindications includes hypertension, anaemia, and recent strokes [40]. Yet, individuals living with these conditions are at the highest risk of treatment-related complications and have the greatest need for prehabilitation [79]. Similarly, five studies required participants to be able to complete a CPET, thus preventing lower functioning and more at-risk patients from participating, despite them being most in need of prehabilitation. Accordingly, by excluding these individuals, the reporting of adverse events may not be a true representation of the incidences that occur in a real-world setting and many patients are denied the opportunity to receive prehabilitation [80].

Concurrent with findings from Engel et al., [34] detailed descriptions of the intervention content were lacking and when looking specifically at exercise interventions, the reporting of the exercise dose and volume was poor. Indeed, the lowest scoring TESTEX criteria related to the reporting and monitoring of the exercise duration and intensity, meaning that the exact exercise dose and energy expenditure could only be determined for three studies. All three of these studies monitored participants using wearable technology that measured heart rate and accelerometry data. Importantly, if the exercise dose is poorly reported and monitored, it cannot be determined whether the stimulus was sufficient to induce beneficial adaptations, enhance physical function and improve patient-reported outcomes [81]. Alternatively, if the dose is too intense, recovery is compromised, and patients are at risk of injury or illness [82]. Accordingly, for the balance between adaptation and recovery to be understood and optimised, programmes must report objective and valid measures of the type, intensity and volume of exercise completed in each session.

What are the characteristics of cancer prehabilitation exercise interventions?

The characteristics of the exercise programmes were heterogeneous and unstandardised. Most studies implemented concurrent exercise (78.6% of studies), 17.9% prescribed aerobic exercise, and 3.6%

were resistance-based. The highest mean quality was achieved by concurrent exercise protocols (9.64 ± 2.22), which scored marginally higher than aerobic exercise (8.60 ± 2.30).

The higher quality of reporting and greater research focus on concurrent programmes has led to findings that concurrent exercise reduces hospital stay durations, cardiorespiratory fitness, full body strength, and muscular capillarisation [83, 84]. Similarly, concurrent exercise is theorised to enhance psychosocial outcomes, like diminishing feelings of distress, anxiety, and depression [59]. Contemporary evidence suggests that enhanced psychosocial outcomes occur as exercise improves the efficiency of depression-related biomarker clearance (e.g., cortisol and pro-inflammatory cytokines) and anti-neurodegenerative chemical regulation in the hypothalamic-pituitary-adrenal axis [85]. As a result, depleted levels of the neurotransmitters responsible for negative mental states circulate, and self-esteem, pain and depressive symptoms improve [86, 87]. Alternative theories suggest that the aerobic component of exercise elevates post-session serotonin, a neurotransmitter that mediates mental state [88]. For example, regular walking was reported to increase serotonin, improve sleep quality, and reduce feelings of fatigue among breast cancer patients [89]. Nonetheless, as concurrent exercise programmes tend to prescribe a higher volume of aerobic than resistance components, the benefits of resistance exercise are unoptimised.

The justification for prescribing higher volumes of aerobic exercise within concurrent programmes may be that the ability of aerobic exercise to enhance cardiopulmonary fitness is vital to Anaesthetists, as cardiorespiratory function limits a patient's ability to withstand anaesthesia and surgery [90]. Aerobic exercise is also evidenced to improve $\dot{V}O_2$ Max, lean body mass and cancer-related fatigue [91-93]. Additionally, regular aerobic exercise may aid in regulating tumour vasculature remodelling thus enabling tissues to form structures that mirror healthy models and augmenting perfusion and oxygenation properties [94]. Subsequently, treatment tolerance, energy availability, and immune function increase [95]. Nonetheless, it must be noted that robust evidence is lacking concerning cancer prehabilitation, and research efforts have hitherto prioritised rehabilitation [96]. Moreover, while aerobic exercise elicits many beneficial responses, musculoskeletal adaptations are potentially limited and predominantly occur in response to the weight-bearing aspects of the exercise [97].

Contrariwise, resistance exercise stimulates muscle synthesis, consequently enhancing physical function, muscular strength, and insulin sensitivity [98]. Previous research states that resistance-based programmes improve post-treatment limb strength, muscle mass, contractile force, and bone density [99]. Subsequent improvements, particularly in muscle mass, are also hypothesised to improve survival [100]. Other observed adaptations occur in response to resistance exercise-induced muscular contractions, which regulate the release of interleukin-6 (IL-6) and other cytokines [101] which could

be anti-tumorigenic [102]. Yet, while resistance exercise appears to be a potent mediator of muscular conditioning, research is scarce and poorly reported.

Most studies implemented moderate (n = 7) or moderate to high (n = 12) intensity exercise. However, the most common method for monitoring and prescribing intensity was RPE, which is subjective in nature and at risk of bias from feelings of psychological distress, cancer-related pain, and fatigue [103]. Indeed, while validated in healthy populations, there is little evidence to support the use of RPE amongst cancer patients, and treatments like chemotherapy or radiotherapy to the chest and cancer-related medications may impact the perception of physical exertion [104, 105]. Attempts to validate RPE among patients on beta-blockers are inconclusive [106] as bet-blockers reduce tissue perfusion and cardiac output, thus distorting perceptions of physical exertion [107]. Therefore, as beta-blockers are frequently prescribed among those living with cancer to regulate blood pressure and HR and to block tumorigenesis and metastasis, it can be argued that RPE values do not truly represent exercise intensity [108, 109]. Subsequently, while most studies reported implementing a moderate to high-intensity exercise, the lack of objectivity means that the actual intensity is unknown.

Notably, for beneficial adaptations to occur, the exercise intensity must be at a sufficient level to induce an oxidative stress response and catalyse adaptations in the body that defend against future physical stress [81, 110]. For example, Nichols et al. [81] implemented a cardiac rehab intervention among 70 patients but observed no improvements in $\dot{V}O_2$ Max, concluding that the peak values of 46–54% of heart rate reserve observed during the exercise were insufficient to cause beneficial adaptations and were likely an overestimation of the intensity achieved throughout the session. Accordingly, for exercise prehabilitation to be optimised, studies must systematically and objectively measure and report exercise intensity, thus ensuring that the correct stimulus for adaptation is provided.

Across the included studies, 74 unique outcome measures were reported. As such, the extensive range and the poor detail in which measures were described inhibit comparison and data synthesis. Hence, without a core set of outcomes, the efficacy and effectiveness of cancer prehabilitation programmes are not well-understood [111]. Common outcome measures included 6MWT and CPET scores, which assessed physical function in 14 and eight studies, respectively. The CPET is the ‘gold standard’ tool for evaluating functional capacity, exercise limitations, and clinical responses [112, 113]. Hence, CPET scores often inform the intensity and modality of exercise protocols [114]. However, while CPET and 6MWT assessments provide outcomes relating to physical function, they are not validated among populations with comorbidities or advanced-stage cancers and cannot detect changes in complex physiological processes [115, 116]. For example, physiological symptoms like cachexia require assessment via alternative means, often biomarker analysis or body composition imaging

[117, 118]. For this reason, it must be considered whether exercise programmes can truly be optimised if complex physiological outcomes are not being assessed at a mechanistic level.

Strengths and Limitations

A limitation in the strength of evidence is the heterogeneity of outcomes, settings, and exercise protocols. Accordingly, meta-analysis was not feasible, and comparisons between studies could not be made. Additional limitations occurred as a risk of bias assessment was not completed. The present review opted for a narrow search strategy, which included outcome measures, and thus retrieved fewer results. However, this strategy was adopted to maintain feasibility and ensure relevance to the research objectives [119]. Risk of bias assessments typically focus on the reporting of the results themselves; this did not apply to the present review. Hence, any inaccuracy in the estimated effectiveness of each study was not considered [120]. The combined use of TESTEX and TiDier frameworks is a key strength of the present review and provides a novel assessment of the quality of reporting and exercise characteristics and created a balanced and fully representative strategy for data extraction and synthesis [41].

Future Guidance

In future, research must address the heterogeneity in exercise characteristics by creating standardised programmes that optimise the beneficial effects of exercise [121]. To do so, further investigation into the role of the exercise type, intensity and frequency is needed. For example, novel evidence suggests that high-intensity interval training induces more profound improvements in $\dot{V}O_2$ Max than moderate-intensity exercise [122]. Yet, in the current review, most protocols were prescribed at a moderate to high intensity, potentially to find a balance between overload and recovery [123].

Furthermore, methods of quantifying intensity are unstandardised, poorly reported and subjective, meaning that the actual intensity achieved is ambiguous. Similarly, as there was large heterogeneity in effectiveness outcomes, programmes cannot be compared. Hence, studies should assess programme effectiveness using objective and validated measures (like HR and biomarker analysis) [111].

Indeed, while the amount of research relating to cancer exercise prehabilitation is rapidly increasing, the quality of these studies and the consistency in how they are designed, monitored and evaluated lack [124]. Therefore, areas of weakness highlighted within the current review, like methods of monitoring the exercise dose and the range and validity of the selected outcome measures used, must be addressed in order to standardise programmes and facilitate optimisation. Finally, validated frameworks, such as TESTEX or the Consensus on Exercise Reporting Template (CERT), should be used to assess the quality of reporting and implementation, therefore facilitating replication, comparison and optimisation [34, 125].

Conclusion

This scoping review describes the characteristics and quality of reporting of prehabilitation exercise interventions for adults living with cancer. Cancer prehabilitation is a relatively new concept that lacks homogeneity. Most studies implemented concurrent exercise, with only one study focusing on resistance exercise. On average, the included studies were of satisfactory quality, yet there were clear disparities between exercise modalities and settings. Large variability was seen regarding the outcome measures used and methods of prescribing and monitoring exercise dose. Furthermore, by identifying common reporting gaps and variability, this review will provide a foundation for standardised intervention design, which is essential to improving intervention quality, comparability, and effectiveness to enhance patient outcomes.

Funding Statement

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sector.

Conflicts of Interest

The authors declare there are no personal or financial conflicts of interest regarding the research presented in this article.

Contribution Statement

SW, TM-W, RC and AM conceived the study idea. SW performed the literature search, performed the data analysis, interpreted the data, and wrote the first draft of the manuscript. AM performed calibration checks. TM-W, RC, AM, LH and CD critically revised the manuscript. SW had full access to all the data, takes responsibility for the integrity and the accuracy of the data analysis, and is the guarantor. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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Figure Legends

Figure 1. ***TESTEX Quality Assessment Scores (scale 0-15) Categorised by Prehabilitation Exercise Modality***
Bars display the total TESTEX score (0-15) achieved by each study. Total scores are categorised based on exercise modality: Light grey bars) Aerobic exercise; Medium grey bars) Concurrent exercise; Dark grey bars) Resistance exercise.

Figure 2. ***TESTEX Quality Assessment Scores (scale 0-15) Categorised by Intervention Setting***
Bars display the total TESTEX score (0-15) achieved by each study. Total scores are categorised based on exercise setting: Light grey bars) Centre-based; Medium grey bars) Centre-based and Home-based; Dark grey bars) Home-based.