

REVIEW ARTICLE

The impact of exercise interventions before, during, and following neoadjuvant therapies for locally advanced rectal cancer: a critical review

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ABSTRACT

Background and purpose: Neoadjuvant chemoradiotherapy (NACRT) and radiotherapy (NART) are standard treatments for locally advanced rectal cancer (LARC). However, their associated toxicities negatively affect patients' quality of life (QoL), prompting growing interest in exercise as a supportive intervention. This critical narrative review synthesised evidence on exercise interventions delivered before, during, or after NACRT/NART, with a focus on feasibility, safety, functional, psychosocial, and emerging oncological outcomes.

Materials and methods: A systematic literature search was conducted across MEDLINE, CINAHL Ultimate, and SPORTDiscus (2010–2025). Prospective studies evaluating exercise-based interventions in patients with LARC receiving NACRT or NART were included. Studies were selected using the Participants, Exposure, and Outcome framework, and methodological quality was appraised using Critical Appraisal Skills Programme checklists. Data were synthesised narratively in accordance with PRISMA reporting standards.

Results: Sixteen studies met the inclusion criteria. Interventions varied in type, intensity, supervision, and timing. Of these, nine studies ($n = 226$) were analysed quantitatively.

Feasibility outcomes varied widely across studies: Eligibility (27.1–100%), recruitment (27.5–90.0%), attendance (74.0–96.0%), attrition (0–100%). No serious adverse events were reported. Consistent improvements were observed cardiorespiratory fitness, strength, fatigue, QoL. Limited evidence suggested a potential association between post-NACRT exercise and tumour regression; however, some of these findings were not powered for oncological endpoints.

Interpretation: Exercise is a feasible and safe adjunct to treatment in LARC. Further research should explore oncological outcomes and improve representation across demographics.

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Introduction

Rectal cancer accounts for approximately one third of colorectal cancer diagnoses and is characterised by distinct anatomical, biological, and therapeutic considerations. Common presenting symptoms include rectal bleeding, altered bowel habits, abdominal pain, reduced appetite, and unexplained weight loss [1]. If left untreated, these may lead to severe complications, including mortality. In England, rectal cancer affects approximately 7486 individuals annually, with 43% of new diagnoses in those aged 75 or older [2]. Incidence is also increasing among adults under 50 years, reflecting a concerning epidemiological shift [3]. With cancer diagnoses projected to rise substantially by 2040 due to population ageing [2], evaluation of current and emerging management strategies is increasingly important.

Locally advanced rectal cancer (LARC) comprises approximately 54% of cases [4], and presents significant treatment

challenges, particularly when tumours threaten resection margins on magnetic resonance imaging. Neoadjuvant radiotherapy (NART), often combined with chemotherapy (neoadjuvant chemoradiotherapy; NACRT), is standard care and aims to downstage tumours, facilitate clear surgical margins, and reduce local recurrence [4, 5]. Despite oncological benefit, neoadjuvant treatment is associated with substantial acute and longer-term toxicities, including fatigue, sarcopenia, reduced physical fitness, impaired cardiopulmonary function, diminished quality of life (QoL), and psychological distress [6, 7]. Postoperative recovery may be further complicated by poor wound healing and anastomotic leakage, with preoperative fitness emerging as a key determinant of outcomes [8]. Consequently, prehabilitation strategies aimed at optimising functional capacity before surgery are gaining prominence. Exercise-based interventions may mitigate treatment-related physiological decline, reduce fatigue, and enhance physical and cardiovascular function [9, 10].

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A critical distinction between rectal and colon cancer lies in treatment sequencing. In the UK, colon cancer is typically managed with upfront surgical resection followed by adjuvant chemotherapy according to pathological stage, whereas rectal cancer commonly involves NART or chemoradiotherapy prior to surgery [11]. As a result, exercise interventions in colon cancer are usually delivered after completion of curative treatment with a rehabilitative or survivorship focus. In contrast, exercise delivered during neoadjuvant treatment for rectal cancer may interact with active oncological therapy and its associated physiological stressors, with important implications for feasibility, safety, and potential mechanisms of benefit.

From a radiobiological perspective, exercise may be particularly relevant during neoadjuvant therapy. Radiotherapy efficacy is strongly influenced by tumour hypoxia, a recognised contributor to radio-resistance in rectal cancer [12]). Preclinical and early-phase clinical studies suggest that aerobic exercise can transiently improve tumour perfusion and oxygenation, modulate the tumour microenvironment, and influence immune function, providing a plausible mechanistic rationale for synergy with NACRT [13, 14]. Clinically, approximately 13% of patients with LARC achieve a pathologically complete response, raising interest in non-operative management strategies in selected cases [15].

Despite growing interest, clinical implementation of exercise interventions during neoadjuvant rectal cancer treatment remains limited. Concerns regarding feasibility, safety, acceptability, and adherence persist, particularly for older patients and those with comorbidities. Additionally, heterogeneity in intervention design, frequency, duration, supervision, and outcome reporting has hindered evidence synthesis and translation into practice. During neoadjuvant therapy, patients often experience reduced autonomy due to intensive treatment schedules and symptom burden, making intervention characteristics such as exercise frequency and duration particularly relevant determinants of participation and retention.

Understanding how intervention characteristics relate to recruitment, attendance, and attrition is therefore essential to guide the development of future exercise protocols that balance potential physiological benefit with acceptability and commitment burden.

Examination of these relationships may help inform pragmatic, patient-centred trial design in an emerging and heterogeneous evidence base, rather than to infer causal effects.

This review therefore evaluates the feasibility, safety, and efficacy of exercise interventions delivered before, during, or after NACRT/NART in patients with LARC, focusing on functional, psychosocial, and emerging oncological outcomes. A secondary exploratory aim was to examine whether intervention frequency and duration appeared to be associated with recruitment, attendance, and attrition, in order to generate hypotheses and inform the design of future pragmatic, patient-centred exercise trials in an emerging and heterogeneous evidence base.

Objective

This critical review synthesised the current evidence base to address five objectives:

1. To evaluate the feasibility of delivering exercise interventions before, during or after NACRT/NART in LARC
2. To assess the safety and tolerability of exercise interventions in this context
3. To determine the impact of exercise on functional and fitness-related outcomes
4. To explore emerging evidence relating to tumour response or oncological outcomes.
5. To examine behavioural and psychological factors associated with adherence and retention.

By systematically integrating findings across diverse study designs, this review aims to clarify the clinical role of exercise as a complementary intervention in LARC management and to inform future research priorities.

Materials and methods

This review was designed as a critical narrative review with structured synthesis of feasibility and outcome data. Therefore, it synthesised relevant studies that incorporated exercise before or during NART or NACRT for rectal cancer, as well as during the treatment-free interval prior to surgery. As this review was based on previously published peer-reviewed studies, formal ethics approval was not required. Nonetheless, data collection and interpretation procedures adhered to ethical standards. In addition, this critical review was also conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [16]. This review was not prospectively registered on PROSPERO, given the feasibility-focused and narrative nature of the synthesis and the limited number of eligible studies, this is acknowledged as a limitation, which may increase the risk of reporting bias; however, we adhered to PRISMA guidelines to ensure transparency. A completed PRISMA 2020 checklist [17] is attached as a [Supplementary Material](#).

Inclusion and exclusion criteria

Eligibility was defined using the Participants, Exposure, and Outcome (PEO) framework [18]:

- **Participants:** Adults with LARC receiving or preparing for NART or NACRT. Randomised controlled trials (RCTs) and prospective cohort studies were included due to limited research.
- **Exposure:** Structured exercise interventions, defined as planned, repetitive bodily movement to improve or maintain health or fitness [19], delivered before, during, or after neoadjuvant treatment.
- **Outcomes:** Studies had to report at least one of:
 - Feasibility (eligibility, recruitment, attendance, retention)
 - Safety (adverse events, treatment interruptions)
 - Functional/physiological outcomes (cardiorespiratory fitness, strength, QoL) Studies focusing solely on surgical techniques, pharmacological therapies, or diet-only interventions were excluded.

Search strategy

A structured search was conducted on the 15th of July 2025, updated search on the 21st of January 2026 by two reviewers (CA and SR) independently, using MEDLINE, CINAHL Ultimate, and SPORTDiscus via EBSCOhost for publications from 2010 to 2025. Reference lists of eligible studies were also hand-searched by one reviewer CA. The study selection was completed by the two reviewers, and the process is detailed in an adapted PRISMA flow diagram (Figure 1), with study characteristics presented in Table 1. Data extraction undertaken by one reviewer (CA). This approach was necessitated by resource constraints and is acknowledged as a limitation.

The search used Boolean operators across three thematic blocks:

- rect* cancer OR rect* neoplasm OR LARC OR LARC AND
- resistance training OR aerobic exercise OR aerobic training OR physical activity OR exercise OR physical exercise

AND

- NACRT OR NART OR short course NART OR long course NACRT

Quality assessment

Evaluating the methodological quality of included studies is essential for robust literature reviews [20]. Methodological quality was assessed using the Critical Appraisal Skills Programme (CASP) checklists appropriate to study design. Studies were not excluded based on quality due to the limited number of studies and the focus on feasibility; rather, appraisal findings regarding, relevance, reliability, validity, and applicability informed interpretation of the evidence. Domains evaluated included sample size calculations, randomisation methods, blinding, baseline group similarity, dropout rates, adherence, outcome measure validity, and pre-specified outcomes. CASP tools are recognised for their reliability in assessing bias in cohort studies and RCTs.

Studies were graded as low, moderate, or high quality. Sample representativeness, disease progression stage, and participant homogeneity (age, body mass index, ethnicity) were also considered. Quantitative feasibility analysis was performed using IBM SPSS version 29 (SPSS Inc., Chicago, IL, USA).

Exercise impact in rectal cancer management

figure 1: Adapted PRISMA flow diagram

Exact duplicates automatically removed by EBSCOhost

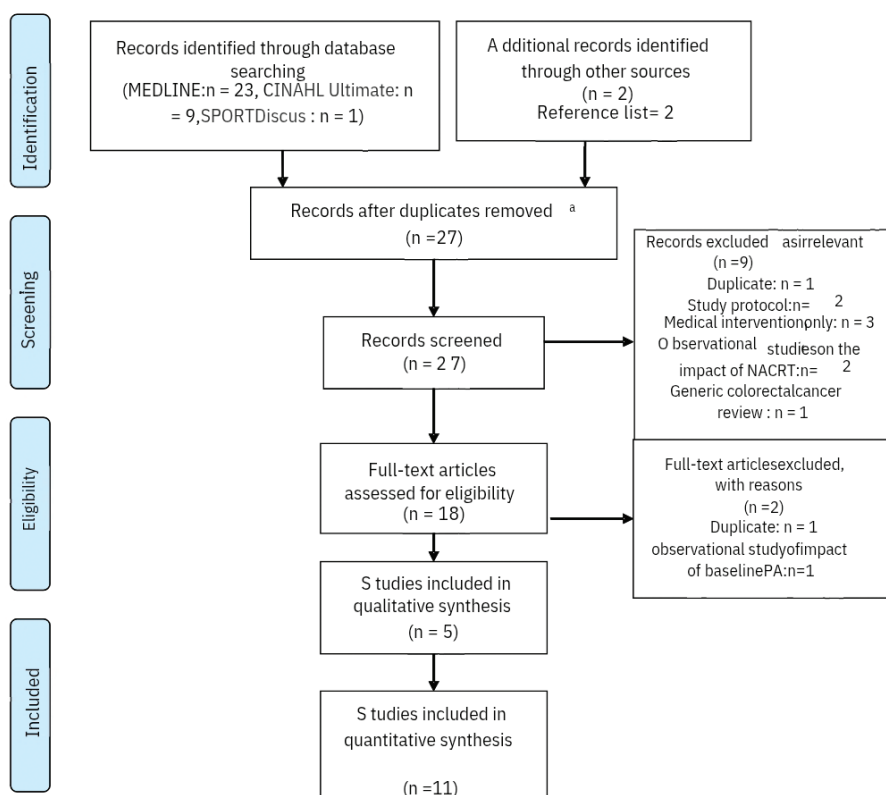


Figure 1. Adapted PRISMA flow diagram.

Table 1. Characteristics of included studies.

Authors (year) and study Design	Sample size (n)	Gender (M:F)	Age (mean)	Population	Setting and Supervision	Timing (Pre/ During/Post NACRT)	Outcome measures	Intervention (Duration and Intensity)	Adverse events	Key results	CASP Grade
Morielli et al. (2016) Phase I single-group feasibility study	18	12:6	57.5	Adults (Stage II–III rectal cancer) receiving NACRT; ECOG ≤ 2; able to walk unaided	Cross Cancer Institute, Edmonton, Canada. Supervised + unsupervised aerobic sessions	During and Post	VO ₂ max, QoL, sleep, anxiety, adherence	6 weeks, 3 times per week supervised aerobic (moderate intensity, RPE 12–14), ~45 min/session; post-NACRT: ≥ 150 min/week unsupervised	None serious	Feasible with strong adherence; QoL improved	Moderate
Morielli et al. (2016) Motivation Descriptive TPB sub-study	18	12:6	57.5	Same cohort as above; included based on completion of NACRT and aerobic programme	Same cohort. Supervised HIIT + post-NACRT unsupervised with motivational themes	During and Post	TPB constructs, motivation, barriers, benefits	Same as above	None serious; mild fatigue, diarrhoea	Enjoyable, motivational support key to post-NACRT adherence	Moderate
Morielli et al. (2018) Adherence pilot study	18	12:6	57.5	Same cohort as above; subset selected for adherence analysis; inclusion based on programme completion	University of Alberta, Canada.	During and Post	Adherence metrics, TPB predictors	Same protocol as above	None serious; diarrhoea common	Adherence linked to gender, mental health, baseline PA	Moderate
Morielli et al. (2021) Phase II RCT (EXERT Trial)	36	24:12	57 ± 12	Stage II/III rectal cancer undergoing NACRT; able to tolerate HIIT; cleared for post-treatment aerobic follow-up	Edmonton, Canada. Supervised HIIT + unsupervised aerobic	During and Post	VO ₂ peak, pCR, toxicity, completion	6 weeks during NACRT: 3x/week supervised HIIT (treadmill), intervals at 85% VO ₂ peak, 25–30 min/session; post-NACRT: ≥ 150 min/week unsupervised aerobic	No serious issues	pCR ↑ in exercisers (56% vs 18%); feasible and safe	High
Moug et al. (2019) -REx Trial, 2-arm RCT	48	31:17	65.9	Rectal cancer patients aged > 60 scheduled for surgery post-NACRT; ambulatory and community dwelling	NHS Glasgow. Remote supervised walking prehabilitation	Before, During and Post	QoL, step count, sit-to-stand, depression	13–17 weeks walking programme; daily steps increased approx. 3000; intensity moderate (MET 10); unsupervised, session duration variable (self-paced)	None serious	Strong feasibility, adherence, QoL improvement	High
Moug et al. (2020) Sub-analysis of REx Trial	44	28:16	66.8	Subset of REx Trial patients with Pre-/post-abdominal CT scans; inclusion based on full body imaging	Subgroup with CT-based TPI analysis	Before and During	Muscle mass (TPI), sarcopenia	Same graduated walking protocol as above	None serious	Muscle mass ↑ in intervention group; TPI protective effect	High
Mast et al. (2025) 3-arm RCT feasibility trial	3	Unreported	Unreported	Adults with locally advanced rectal cancer undergoing NACRT; eligible for structured hospital exercise post-treatment	Radboud UMC Netherlands. Hospital-based aerobic (ExPR), AE+RE vs control	During and Post	VO ₂ max, tumour response, toxicity	5 weeks. ExPR: 5x/week supervised cycling at CPET-based intensity, 30–40 min/session; AE+RE: 2x/week mixed exercise + 1x/week home, approx. 60 min/session	Minor fatigue, back pain	VO ₂ max ↑; tumour response ≥ 70%; reduced toxicity	Low
Piroux et al. (2022) 3-arm RCT feasibility study	18	13:5	62.0	Rectal cancer patients completing radiotherapy; medically stable and cleared for exercise by oncology team	Brussels. HIIT, resistance, usual care arms	During	QoL, fatigue, cognition, sleep	5 weeks, 3x/week supervised sessions. HIIT: ≥ 85% HRmax intervals, approx. 30–35 min/session; RES: moderate-load circuits, approx. 40 min/session	Diarrhoea, fatigue; no withdrawals	Attendance 88–92%; comparable improvements; RES ↑ social wellbeing	Moderate–High
Felipe et al. (2019) Single-arm pilot	12	3:9	61 ± 7	Stage II–III rectal cancer patients mid-NACRT; cognitively able to participate in education sessions and park-based activity	Madrid. Community-delivered exercise education	During	VO ₂ peak, QoL, HADS, fitness tests	5 weeks, 6 sessions total (1–2x/week), approx. 60 min/session; moderate-to-vigorous group-based aerobic/resistance/ flexibility	None serious; 1 dropout	VO ₂ peak ↑, MVPA ↑, depression ↓	Low
Brunet et al. (2021) Feasibility trial (not delivered)	10 referred, 0 enrolled	n/a	n/a	Intended: Adults with rectal cancer scheduled for NACRT and surgery at Ottawa Hospital; eligible for supervised trial	Ottawa Hospital, Canada. Planned supervised	During	Recruitment and feasibility barriers	Planned: 12 weeks, 3x/week supervised aerobic + resistance at 60–75% HRR, ~45–60 min/session (not delivered)	Not delivered	Study infeasible; eHealth and hybrid models recommended	Low

(Continued)

Table 1 (Continued). Characteristics of included studies.

Authors (Year) and Study Design	Sample Size (n)	Gender (M:F)	Age (Mean)	Population	Setting and Supervision	Timing (Pre/ During/Post NACRT)	Outcome measures	Intervention (Duration and Intensity)	Adverse events	Key results	CASP Grade
West et al. (2015) Non-Randomised Controlled interventional pilot	39	27:12	64 (Ex); 72 (Control)	Patients with locally advanced rectal cancer completing NACRT; eligible for post-NACRT cycling based on CPET clearance	UK. CPET-Supervised structured cycling sessions	Post	VO ₂ LT, VO ₂ peak, step count	6 weeks, 3x/week CPET-responsive cycling (threshold and peak VO ₂), approx. 40 min/session	None serious	VO ₂ LT improved in exercisers; reversed NACRT fitness decline	High
Loughney et al. (2017) Non-Randomised Controlled pilot	39	27:12	64 (Ex); 72 (Control)	Same cohort as above; subset with valid accelerometry data; inclusion based on consent and fitness screening	UK. Same cohort as West 2015	Post	PAL, sleep metrics, EE, MET	Same as above	None serious	Sleep efficiency ↑; High MET recovery in exercise group	High
West et al. (2019) Mechanistic exploratory study	35	26:9	64.8 (Ex); 70.2 (Control)	Patients with MRI-defined threatened margins post-NACRT; included if eligible for prehabilitation and MRI follow-up	UK. As above. MRI-defined margin-threatened cases	Post	TRG, VO ₂ LT, CPET, tumour regression	Same as above	None serious	Tumour regression ↑ in exercisers (OR 8.5); VO ₂ restored	High
Loughney et al. (2021) (EMPOWER Trial) Multicentre RCT	33	26:7	64 ± 10.4	Adults with rectal cancer post-ACRT, margin-threatened disease, CPET cleared	UK. 5 NHS sites; supervised post-NACRT programme	Post	VO ₂ LT, HRQoL, PA, interviews	9 weeks, 3x/week supervised CPET-responsive programme; progressive intervals; 40 min/session	1 pre-syncope; no serious	VO ₂ LT ↑; psychological resilience ↑ Post-NACRT VO ₂ at AT ↓ significantly in all participants	High
Singh et al. (2018) Feasibility study	10	7:3	54.6 ± 14.1	Adults with localised rectal cancer undergoing NACRT; medically stable and willing to attend supervised sessions	Perth, Australia. Resistance + aerobic programme during CRT	During	Muscle strength, QoL, DXA lean mass, fatigue	10 weeks; 2x/week supervised resistance + aerobic at 60–80% HRmax, approx. 60 min/session; plus 2x/week unsupervised aerobic (30–45 min)	None serious	Muscle strength ↑, ASM loss ↓; QoL preserved	Moderate
Heldens et al. (2016) Prospective single-arm pilot	13 (9 completed)	11:2	59.1 ± 19.7	Adults with locally advanced resectable rectal cancer receiving NACRT; no contraindications to moderate exercise	Maastricht, Netherlands. Outpatient supervised programme	During	Muscle strength, 6MWT, fatigue, SF-36	9–17 weeks, 2x/week supervised moderate-intensity aerobic + resistance (Borg 13–14), 45–60 min/session	None serious	Leg ↑39.2%, arm ↑34.9%, fatigue stable slight ↑ 6MWT; feasible with high satisfaction	Moderate

QoL: Quality of Life; SF-36: Short-Form 36 Health Survey; EQ-5D-5L: EuroQol 5 Dimensions, 5 Levels; HADS: Hospital Anxiety and Depression Scale; FACIT-F: Functional Assessment of Chronic Illness Therapy-Fatigue; FACT-G: Functional Assessment of Cancer Therapy-General; CES-D: Center for Epidemiologic Studies–Depression Scale; ESS: Epworth Sleepiness Scale; ISI: Insomnia Severity Index; PSQI: Pittsburgh Sleep Quality Index; MFI: Multidimensional Fatigue Index; TPB: Theory of Planned Behaviour; HIIT: high-intensity interval training; 6MWT: 6-minute walk test; DXA: Dual-energy X-ray Absorptiometry; CRT: Neoadjuvant chemoradiation treatment

Data extraction and analysis

Data from eligible studies were extracted using a standardised IBM SPSS template, capturing:

- Study design, country, sample size, and demographics
- Exercise intervention details (mode, intensity, frequency, supervision)
- Eligibility rate, attendance/adherence rate, and dropout rates
- Physical activity/fitness outcomes (such as, VO₂max, heart rate reserve, target maximal heart rate, 6-minute walk test, muscle mass)
- Safety incidents and adverse events
- Psychosocial outcomes (QoL, fatigue, motivation)

Data synthesis and exploratory analyses

Data were synthesised narratively, grouping findings into themes: feasibility and adherence, safety, functional and fitness

outcomes, psychosocial effects, predictors of adherence, and oncologic/tumour-related outcomes. This was due to substantial clinical and methodological heterogeneity across studies, including variation in intervention timing, modality, intensity, supervision, and outcome measures [21, 22]. To complement narrative synthesis and support future protocol development in exercise oncology, limited exploratory quantitative analyses were undertaken using study-level aggregated data explicitly reported in the included studies. Specifically, Pearson's correlation coefficients were calculated to examine linear associations between prescribed exercise frequency (sessions per week), intervention duration (number of weeks), and feasibility outcomes including recruitment, attendance, and attrition. These analyses were conducted for hypothesis-generating purposes only and were not intended to establish causal relationships. This approach is consistent with prior methodological work in feasibility research and complex intervention development, where exploratory analyses of aggregated trial-level data have been used to inform intervention design in emerging [23, 24].

Standardised 95% confidence intervals were reported, with an alpha value of 0.05 for statistical significance.

Results

Database search

The database search yielded 25 abstracts after removing duplicates ($n = 8$) MEDLINE (23 studies), CINAHL Ultimate (9 studies), and SPORTDiscus (1 study). Reference screening added two studies [25, 26]. After title and abstract screening, nine studies were excluded for reasons including duplication ($n = 1$), protocol/methodological papers ($n = 2$), general colorectal cancer focus without rectal cancer subgroup ($n = 1$), observational studies without exercise interventions ($n = 2$), or non-exercise medical interventions ($n = 3$). Eighteen studies underwent full-text review, with two further excluded for duplicated data or observational design. Sixteen studies, involving 226 participants with LARC receiving or recovering from NACRT, were included in the final synthesis. Study selection is summarised in the PRISMA flow diagram (Figure 1), and study characteristics are presented in Table 1.

Eleven studies used interventional designs, including four RCTs or pilot RCTs. Studies spanned seven countries (England, Scotland, Australia, Netherlands, Canada, Belgium, Spain) and included inpatient and home-based interventions across NACRT, post-NACRT, or pre/postoperative phases. Nine studies implemented exercise thrice weekly, four twice weekly, with durations ranging from 5 weeks [27–29] to 17 weeks [30, 31]. Most delivered exercise during chemoradiotherapy, with one study [26] specifying post-radiotherapy sessions. Study characteristics are summarised in Table 1. Although three of the included studies were rated as low quality according to CASP [27, 29, 32] their inclusion did not materially alter findings significantly.

Patients' characteristics

Patient characteristics are detailed in Table 2. Two studies [29, 32] lacked demographic data due to poor recruitment. Among the remaining studies, mean or median age and sex distribution were consistently reported, with a male-to-female ratio of approximately 2.4:1 across the studies. Reporting of Body Mass Index (BMI) and ethnicity was inconsistent, with one study omitting BMI [7] and another not reporting female representation [26].

Feasibility outcomes

Feasibility outcomes were synthesised descriptively at the individual study level and are presented in Table 3. Recruitment rates varied widely across studies, reflecting differences in eligibility criteria, timing relative to neoadjuvant therapy, and recruitment settings. Studies embedding exercise delivery within routine clinical care or providing supervised sessions generally reported higher recruitment and retention than those relying solely on self-directed or home-based programmes.

Attendance and adherence were reported using heterogeneous metrics, including proportion of prescribed sessions attended, weekly exercise minutes achieved, or categorical adherence thresholds. Direct comparison across studies was therefore not possible.

Eligibility and recruitment

Eligibility rates varied widely across studies, ranging from 27.1 [33] to 100% [30], reflecting differences in inclusion criteria, clinical pathways, and recruitment settings. Of the 417 eligible individuals, 226 were enrolled, yielding an overall recruitment rate of 54.2%.

Recruitment ranged from 27.5 to 90% across studies. Recruitment challenges were common, with two studies terminating early due to insufficient enrolment [29, 32]. Studies integrating exercise delivery within routine oncology care or offering supervised sessions tended to achieve higher recruitment.

Attendance and adherence

Adherence was reported using heterogeneous metrics, including proportion of prescribed sessions attended, weekly exercise minutes achieved, or categorical adherence thresholds. Despite this variability, attendance was generally high, ranging between 74.0 and 96.0% across studies. Supervised hospital-based interventions demonstrated the highest adherence (91% in Loughney, West [33]; 98% in West, Astin [9]). Home-based programmes showed more variable adherence, though the REX trial [30] achieved 75% adherence with weekly telephone support. Predictors of adherence included younger age, female sex, marital status, higher baseline motivation, and fewer gastrointestinal side effects [34].

Exercise-based intervention attrition rates

Attrition rates again varied widely across studies (0–100%), averaging 32.5% (SD = 29.3%), with primary reasons including treatment-related toxicity, disease progression, and logistical barriers such as travel distance [9, 35]. No study reported attrition attributable to exercise-related harm.

Exploratory associations between intervention characteristics and feasibility metrics

To inform future trial design, exploratory analyses examined associations between intervention characteristics and feasibility outcomes using study-level aggregated data explicitly reported in individual publications; these are summarised in Table 4. A moderate positive association was observed between intervention duration and attrition ($r = 0.433$), suggesting that longer programmes may be associated with increased participant withdrawal during neoadjuvant treatment. A weak negative association was observed between prescribed exercise frequency and recruitment ($r = -0.263$), indicating that higher-frequency prescriptions may pose a barrier to initial participation.

No clear association was observed between intervention characteristics and session attendance. These findings were not statistically significant and are reported for hypothesis-generation only, to inform future research rather than to support causal interpretation.

Safety and tolerability

No serious adverse events attributable to exercise participation were reported. Safety monitoring methods varied across studies. Supervised interventions commonly employed pre-session symptom screening, real-time monitoring by qualified professionals, and predefined criteria for exercise modification or cessation. Home-based interventions primarily relied on participant self-report with clinical follow-up contact and escalation pathways when required. No studies reported exercise-related interruptions to neoadjuvant therapy or delays to surgery. Minor symptoms (fatigue, skin irritation, gastrointestinal discomfort) occurred but did not cause withdrawals or treatment interruptions. Real-time monitoring (such as, Borg scale, CPET titration, physiotherapist supervision) ensured safety.

Intervention modalities and delivery

Exercise modalities included:

- **Aerobic Training:** Walking, cycling, or treadmill-based, ranging from moderate to high-intensity interval training (HIIT) [25, 28].
- **Resistance Training:** Used in five studies, standalone or combined with aerobic exercise [26, 28].
- **Multicomponent Education-Led Programmes:** Community-based exercise education showed promising adherence and QoL improvements [27]. Supervised hospital-based [7, 33], remote, or hybrid delivery models ensured fidelity and flexibility.

Impact on functional capacity and fitness

Cardiorespiratory fitness (VO_2AT) declined during NACRT but improved post-exercise interventions, with gains of 2.1–2.9 ml/kg/min in trials [7, 33]. The 6-minute walk test and step counts showed positive trends (+69m in [30]). Resistance training improved leg (+39%) and arm strength (+35%) [31] and muscle mass (+16 mm^2/m^2 [36]). However, Heldens, Bongers [31] and West, Loughney [7] found that some preoperative improvements were not maintained postoperatively, with three participants in the Heldens, Bongers [31] trial experiencing declines to below baseline levels.

Psychosocial and behavioural outcomes

Seven studies reported psychosocial benefits, including improved QoL, reduced fatigue, and lower depression scores [33, 35]. Participants enjoyed exercise more than expected ($p = 0.003$), citing enhanced self-esteem and physical function. Predictors of positive psychosocial response included younger age, female sex, and fewer treatment-related side effects. Motivation commonly declined after NACRT, highlighting the need for tailored behavioural support [34].

Oncological and tumour-related outcomes

Three studies reported oncologic outcomes. West, Astin [9] found improved tumour regression grading ($p = 0.02$) post-aerobic intervention, although this analysis was exploratory and the original study was not powered for oncological endpoints. R Morielli, Usmani [37] reported a higher pathological complete response rate (39% vs. 12%, $p = 0.020$) in the exercise group. Mast et al. [29] did not report oncological outcomes for rectal cancer due to recruitment limitations. Overall, evidence for oncological benefit remains preliminary but suggests potential biological relevance warranting further investigation.

Discussion and conclusion

This critical review synthesised evidence from 16 studies evaluating the feasibility, safety, and efficacy of exercise interventions delivered during or around NART and NACRT for patients with LARC. Collectively, the findings indicate that exercise interventions are generally feasible and safe in this population, with consistent benefits for physical function and QoL. However, substantial heterogeneity in study design, intervention characteristics, and outcome reporting continues to limit definitive conclusions and highlights important priorities for future research.

Most studies included in this review were of high methodological quality per CASP assessments but were limited by small sample sizes, typical of feasibility trials, constraining statistical power and generalisability [38]. The largest RCT [30], with 49 participants, was underpowered for definitive conclusions on efficacy.

In addition, the lack of reporting on ineligible participants in most studies impedes understanding of barriers to inclusion and limits refinement of intervention accessibility. Future studies should ensure transparent reporting of inclusion barriers to enhance inclusive intervention design.

Across studies, feasibility outcomes demonstrated both promise and challenge. Recruitment rates ranged from

Table 2. Cumulative sex characteristics of included studies.

Patient characteristics	Minimum	Maximum	Mean	Std. deviation	Skewness	
					Statistic	Std. error
Male	0	31	15.80	11.361	0.135	0.687
Female	0	17	7.33	5.568	0.436	0.717

Table 3. Feasibility metrics across included studies.

Study	Eligibility rate (%)	Recruitment rate (%)	Attrition rate (%)	Adherence/attendance rate (%)	Decline rate (%)
Morielli, Usmani [35]	71.11	56.25	22.22	74.00	43.75
Morielli, Boulé [25]	63.90	27.48	63.89	82.00	73.00
Moug, Mutrie [30]	100.00	61.54	16.67	75.00	38.46
Mast, Gootjes [29]	Unreported	14.29	0	Unreported	85.71
Piroux, Reyckler [28]	86.96	90.00	0	92.00	10.00
Felipe, Alejo [27]	82.14	52.17	16.67	89.00	Unreported
Brunet, Price [32]	85.70	50.00	100.00	Unreported	Unreported
West, Loughney [7]	Unreported	Unreported	10.26	96.00	Unreported
Loughney, West [33]	27.08	48.72	34.21	91.00	51.28
Heldens, Bongers [31]	Unreported	65.00	30.77	95.70	33.33
Singh, Galvão [26]	Unreported	66.67	30.00	77.00	25.00

approximately 56–65% in single-centre studies [31, 35] and higher success in multicentre trials [33]. In contrast, poor recruitment reported by Brunet, Price [32] despite a year-long recruitment period, stemmed from logistical issues such as transport and lack of clinical integration. Overall, these findings suggest that feasibility is strongly influenced by how closely exercise delivery aligns with routine clinical care. However, addressing logistical barriers, such as transportation and referral pathways, is essential to optimise real-world implementation [7, 26, 31, 33, 39].

Adherence and attendance were generally favourable, particularly in supervised interventions, and were often supported by positive patient experiences. Participants frequently reported greater enjoyment than anticipated and perceived benefits in self-esteem, physical function, and QoL [34]. These findings align with broader colorectal cancer literature, including a systematic review by Singh, Hayes [40], who reported an average adherence rate of 86% in colorectal cancer exercise trials. Nevertheless, treatment-related fatigue, gastrointestinal symptoms, and motivational decline following NACRT remained important barriers, particularly in unsupervised programmes.

The Colon Health and Life-Long Exercise Change (CHALLENGE) trial Courneya Kerry, Vardy Janette [41] provides valuable contextual insight into how behavioural support may mitigate such barriers. Although conducted in colon cancer survivors following adjuvant chemotherapy, CHALLENGE demonstrated that a theory-driven, behaviourally supported exercise programme could sustain adherence over several years, despite ongoing fatigue and deconditioning. These findings reinforce that exercise prescriptions require more than generic advice; structured behavioural strategies, supervision, and

follow-up are central to long-term engagement. While CHALLENGE is not directly transferable to rectal cancer populations undergoing neoadjuvant therapy, it offers an important benchmark for intervention quality and implementation.

Rejection rates across the studies were substantial, ranging from 10 to 85.7% [28, 29], reflecting treatment burden, emotional distress, and competing clinical demands. Exploratory analyses in this review suggested a moderate association between longer intervention duration and higher attrition, alongside a weak negative association between prescribed exercise frequency and recruitment. Although these analyses were hypothesis-generating and not statistically inferential, they provide a rationale for considering intervention burden as a modifiable design feature. During neoadjuvant treatment, when many aspects of care feel externally controlled, overly intensive or inflexible exercise prescriptions may exacerbate perceived burden and deter participation.

Mode of delivery also appeared influential. Supervised hospital-based programmes were associated with higher attendance and greater improvements in cardiorespiratory fitness compared with unsupervised approaches [7, 42]. However, home-based and remote interventions demonstrated acceptable feasibility in several studies [27, 36], suggesting that hybrid delivery models may offer a pragmatic balance between effectiveness and accessibility. Such models may be particularly relevant for patients facing transport challenges or treatment-related fatigue.

Safety outcomes across the included studies were consistently reassuring. Except for Felipe, Alejo [27], which did not report safety outcomes, no serious exercise-related adverse events were identified. This aligns with wider oncology exercise literature reporting low adverse event rates during neoadjuvant therapy [43, 44]. Minor events such as transient fatigue, musculoskeletal discomfort, or presyncope were infrequent and did not result in withdrawal [31, 33]. However, approaches to safety monitoring varied considerably, ranging from passive self-report to structured clinician-led assessment using instruments such as patient or reported version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE) [29]. This heterogeneity limits comparability and highlights the need for standardised safety reporting in future trials.

Table 4. Impact of exercise duration and frequency on recruitment rate, attendance, and attrition.

Feasibility Measures	Correlation study	Intervention duration	Intervention frequency
Recruitment rate	Pearson correlation	-0.029	-0.263
	Sig. (2-tailed)	0.941	0.529
Attrition rate	Pearson correlation	0.433	0.071
	Sig. (2-tailed)	0.212	0.855
Attendance	Pearson correlation	-0.382	-0.067

Exercise interventions were associated with consistent improvements in physical function and QoL. Gains in cardiorespiratory fitness, including increases in ventilatory threshold of 2.1–2.9 ml/kg/min, were reported in several studies [7], alongside attenuation of treatment-related functional decline and ameliorate physical and functional decline [7, 25, 26, 35]. However, meta-analytic evidence from Zhang [45] found no significant improvements in functional capacity as measured by the 6-minute walk test (6MWT), underscoring the potential influence of intervention timing. Zhang [45] found no significant improvement in 6-minute walk distance, suggesting that outcome sensitivity and intervention timing may influence observed effects. Prehabilitation prior to NACRT remains underexplored, with only one study addressing this phase [30] despite evidence that physical activity declines during neoadjuvant treatment [6, 46] and that higher baseline activity levels are associated with improved tumour downstaging [8, 47].

Emerging evidence also suggests a potential oncological role for exercise. Two studies reported significantly greater tumour regression among patients undertaking structured exercise following NACRT, representing the first human data in rectal cancer to suggest that exercise may augment tumour response [9, 25]. While these findings are preliminary and include post hoc analyses not powered for oncological endpoints, they are biologically plausible. Preclinical and early clinical studies indicate that exercise may improve tumour perfusion, modulate immune activity, and reduce hypoxia, mechanisms directly relevant to radiotherapy efficacy [13, 14, 48, 49]. Further mechanistic investigation is warranted.

The relevance of survivorship evidence from colon cancer must be interpreted cautiously. The CHALLENGE trial [41] demonstrated a statistically significant improvement in 5-year disease-free survival, corresponding to a 28% reduction in recurrence risk, establishing exercise as a disease-modifying intervention in colon cancer. However, rectal cancer management differs fundamentally, particularly in the UK, where NART or chemoradiotherapy is standard [11]. These differences have implications for feasibility, safety, and the mechanisms through which exercise may exert benefit, reinforcing the need for rectal cancer-specific trials rather than extrapolation from survivorship cohorts.

Intervention modality also warrants consideration. The HIIT has emerged as a time-efficient and tolerable option during NACRT, offering comparable or superior cardiorespiratory benefits relative to moderate-intensity continuous training [25, 28]. Resistance training remains underrepresented despite evidence of benefits for muscle mass and strength, outcomes particularly relevant for sarcopenia and cachexia prevention [26, 36].

Finally, the evidence base is limited by under-representation of women, ethnic minority groups, older adults, and patients with multimorbidity. Only 4% of participants in a large UK feasibility study were non-Caucasian [30], limiting generalisability. No studies evaluated exercise during NART alone, despite its relevance for frail patients [50]. Future research should therefore prioritise inclusive, pragmatic trial designs informed by successful large-scale exercise oncology studies in related populations.

The CHALLENGE trial [41] demonstrated the feasibility of delivering a structured, behaviourally supported exercise intervention across six countries in 889 colon cancer survivors, achieving sustained adherence, and improvements in cardiorespiratory fitness. Addressing these gaps will be essential to ensure equitable and scalable integration of exercise into rectal cancer care.

In summary, exercise interventions appear feasible and safe for many patients with LARC undergoing neoadjuvant treatment, with meaningful benefits for physical function and QoL. Future research should prioritise adequately powered, inclusive trials with standardised reporting, mechanistic endpoints, and patient-centred intervention design to clarify the role of exercise as a supportive and potentially treatment-modifying therapy in rectal cancer.

Future research directions

- Evaluate exercise during NART for feasibility and efficacy in frail populations
- Investigate optimal intervention timing (e.g. pre-NACRT or post-radiotherapy)
- Develop inclusive recruitment strategies for more diverse populations
- Explore barriers (such as, fatigue, motivation) through qualitative research
- Replicate findings on exercise enhancing tumour response
- Ensure transparent reporting of eligibility and participation metrics

Limitations

This review has several methodological limitations that should be considered when interpreting the findings. Firstly, study screening and study selection were conducted independently by two reviewers, which strengthened methodological rigour and reduced the risk of selection bias. However, data extraction and synthesis were undertaken by a single reviewer due to resource constraints. While this approach is commonly adopted in feasibility-focused narrative reviews, it may introduce a degree of interpretive bias, and future reviews would benefit from duplicate data extraction.

Secondly, the review protocol was not prospectively registered on PROSPERO. While protocol registration is recommended to enhance transparency and reduce the risk of reporting bias, this review was conceived as a feasibility-focused critical narrative synthesis within an emerging and heterogeneous evidence base. Nonetheless, the absence of prospective registration should be acknowledged as a limitation. To mitigate this risk, the review adhered closely to PRISMA reporting standards, and a completed PRISMA 2020 checklist is provided as supplementary material.

Thirdly, substantial clinical and methodological heterogeneity across included studies precluded meta-analysis. Heterogeneity was evident in intervention timing (before, during, or after neoadjuvant therapy), exercise modality, intensity, frequency,

duration, level of supervision, and outcome measurement. As a result, findings were synthesised narratively, and comparisons across studies should be interpreted with caution.

Fourthly, exploratory analyses examining associations between intervention characteristics (exercise frequency and intervention duration) and feasibility outcomes were based on aggregated study-level data rather than individual participant data. These analyses were undertaken to generate hypotheses and inform future trial design, not to infer causality. The small number of studies, inconsistent reporting of feasibility metrics, and a lack of adjustment for potential confounders limit the interpretability and generalisability of these findings.

Fifthly, reporting of adverse events and safety monitoring varied across studies. Although no serious exercise-related adverse events were reported, differences in monitoring approaches, ranging from active supervision with structured symptom screening to reliance on participant self-report, may have resulted in under-reporting of minor adverse events, particularly in home-based interventions.

Finally, the included studies were characterised by relatively small sample sizes and limited demographic diversity, with under-representation of older adults, individuals with significant comorbidity, women, and ethnically or socioeconomically diverse populations. These factors limit the generalisability of findings and highlight the need for inclusive, adequately powered rectal cancer-specific exercise trials embedded within routine clinical care.

Conclusion

The findings of this study consistently support exercise, particularly aerobic and resistance modalities, is feasible, safe, and beneficial for LARC patients undergoing NACRT, improving function and potentially tumour response. Small samples, demographic biases, and lack of NART-specific studies limit generalisability. Rectal cancer-specific trials are required to define optimal exercise prescription during neoadjuvant therapy and to further explore potential interactions with radiotherapy response. Inclusive recruitment, better reporting, and clinical integration are essential to optimise exercise in rectal cancer care.

Implications for rehabilitation

Exercise can safely enhance health and function in LARC management but remains underutilised. Future interventions should target diverse populations, including women, ethnic minorities, and older adults, to ensure equitable benefits.

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Disclosure statement

The authors report no conflict of interest.

Data availability statement

Data were derived from published studies listed in the references.

Ethics declarations & trial registry information

This article has been conducted in an ethical and responsible manner.

Authors' contributions

CA and JS contributed to the conceptualisation and design of this review. CA performed the qualitative and quantitative analysis. CA drafted the manuscript. All authors reviewed, edited and approved the final manuscript.

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