

Impact of exercise interventions in people with colon and colorectal cancer on quality of life, physical function and fatigue: A systematic review

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ABSTRACT

Colon and colorectal cancer treatments are frequently associated with cancer-related fatigue, physical deconditioning, and reduced health-related quality of life (HRQoL). Exercise has been proposed as a supportive care strategy, but evidence remains heterogeneous. This systematic review aimed to evaluate the effects of exercise interventions on cancer-related fatigue, physical function, HRQoL, and selected biological outcomes in adults with colon or colorectal cancer. Searches were conducted in PubMed, PEDro, and Scopus following PRISMA 2020 guidelines. Randomized and controlled clinical trials assessing structured exercise interventions were included. Methodological quality was evaluated using the McMaster Critical Review Form and the PEDro scale. Due to heterogeneity, results were synthesized qualitatively, with limited quantitative synthesis based on single-study effect estimates. Five studies met the inclusion criteria. Exercise interventions delivered during chemotherapy or survivorship consistently reduced cancer-related fatigue, showing moderate-to-large effect. Small-to-moderate improvements in physical function and muscular strength were observed. HRQoL outcomes were generally favorable, particularly in physical and functional domains. Evidence regarding biological outcomes was limited but suggested potential benefits for gastrointestinal function, sleep quality, and selected biomarkers. Overall, structured exercise appears to be a feasible and clinically relevant supportive care intervention for patients with colon and colorectal cancer. Further high-quality trials with standardized protocols are required.

Keywords: Colon cancer; Colorectal cancer; Exercise; Physical activity; Cancer-related fatigue; Quality of life.

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INTRODUCTION

Colorectal cancer, and specifically colon cancer, represents one of the most prevalent malignancies worldwide and constitutes a major public health challenge due to its high incidence, morbidity, and mortality. In developed countries, colon cancer ranks among the leading causes of cancer-related death in both men and women, with incidence increasing markedly after the age of 50 years (SEOM, 2025; Siegel et al., 2023). Although advances in screening, surgical techniques, and adjuvant oncological treatments have substantially improved survival rates, a growing number of patients and survivors experience persistent physical, psychological, and functional impairments (Denlinger & Barsevick, 2009; Meyerhardt et al., 2006).

Standard treatments for colon cancer—including surgery, chemotherapy, and radiotherapy—are frequently associated with adverse effects such as cancer-related fatigue, reduced physical capacity, loss of muscle mass and strength, gastrointestinal dysfunction, psychological distress, and impaired health-related quality of life (HRQoL) (Monga et al., 2007; Van Waart et al., 2018). These treatment-related sequelae may persist long after completion of therapy, negatively affecting daily functioning, social participation, and overall well-being. In particular, fatigue is consistently reported as one of the most burdensome and prevalent symptoms among patients undergoing and recovering from colorectal cancer treatment (Bower, 2014; Brown et al., 2018; Van Waart et al., 2018; Williams et al., 2015).

Sedentary behaviour and reduced physical activity levels are common during and after cancer treatment, further exacerbating physical deconditioning, functional decline, and metabolic disturbances. In patients with colon cancer, physical inactivity may compound treatment-related muscle wasting, reduced cardiorespiratory fitness, and declines in functional independence, thereby increasing vulnerability to comorbidities and reducing HRQoL (Silver et al., 2013). Consequently, strategies aimed at mitigating these adverse effects are increasingly recognized as a critical component of comprehensive cancer care.

In this context, structured physical activity and exercise interventions have emerged as promising non-pharmacological strategies to counteract the negative consequences of cancer and its treatments. A growing body of evidence suggests that aerobic exercise, resistance training, and multicomponent exercise programs can improve physical fitness, reduce cancer-related fatigue, enhance psychological well-being, and improve quality of life (QoL) in patients with colorectal cancer (Brown et al., 2018; Van Vulpen et al., 2015). Exercise has also been proposed as a potential modulator of biological processes, including inflammation, metabolic regulation, and gastrointestinal function, which may be particularly relevant in colon cancer survivorship (Campbell et al., 2019; McTiernan, 2016; Van Vulpen et al., 2015).

Despite increasing interest in exercise oncology, the existing literature in colon cancer remains heterogeneous. Previous studies differ substantially in study design, patient characteristics, treatment phase, exercise modality, intensity, duration, and outcome measures. Some trials have focused on supervised exercise programs delivered during adjuvant chemotherapy, whereas others have examined home-based or self-directed interventions in cancer survivors (Kim et al., 2018; Williams et al., 2015). Moreover, outcomes have been assessed using a wide range of physical, perceptual, and biological measures, limiting direct comparability across studies and precluding robust quantitative synthesis.

Therefore, a systematic and critical synthesis of the available evidence is warranted to clarify the role of exercise interventions in patients with colon and colorectal cancer. The aim of this systematic review was to evaluate the effects of structured physical activity and exercise interventions on physical function, physical fitness, cancer-related fatigue, QoL, and selected biological outcomes in adult patients with colon cancer

during and after oncological treatment. By integrating current evidence, this review seeks to inform clinical practice and guide future research on the implementation of exercise as supportive care in colon cancer management.

MATERIALS AND METHODS

Study design

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines (Page et al., 2021). The methodological framework followed established principles of evidence-based medicine, ensuring a structured, transparent, and reproducible synthesis of the available literature (Sackett et al., 1996). The review protocol was defined *a priori* to minimize selection bias and enhance methodological rigor throughout all stages of the review process.

Eligibility Criteria (PICOS Framework)

Eligibility criteria were defined using the PICOS framework, a widely accepted approach for structuring clinical questions and eligibility criteria in systematic reviews (Higgins et al., 2023).

- Population (P): Adults (≥ 18 years) diagnosed with colon or colorectal cancer, either during active oncological treatment (chemotherapy and/or radiotherapy) or during the post-treatment survivorship phase.
- Intervention (I): Structured physical activity or exercise programs, including aerobic exercise, resistance training, multicomponent interventions, or home-based exercise protocols.
- Comparison (C): Usual care, non-exercise control groups, alternative exercise prescriptions, or pre-post intervention comparisons.
- Outcomes (O): Physical function, physical fitness, cancer-related fatigue, HRQoL, psychological outcomes, and selected biological or physiological variables.
- Study design (S): Randomized controlled trials (RCTs) and controlled clinical trials.

Studies were excluded if they were narrative or systematic reviews, observational studies without an exercise intervention, animal studies, paediatric populations, conference abstracts without full data, or studies with insufficient methodological quality.

Information sources

A comprehensive literature search was performed in PubMed/MEDLINE, PEDro, Cochrane Library Plus, and Scopus, following methodological recommendations for systematic reviews of healthcare interventions (Higgins et al., 2023). Searches included studies published within the last ten years and were limited to articles written in English or Spanish.

The inclusion of multiple databases aimed to maximize sensitivity and reduce the risk of publication bias by capturing studies from biomedical, rehabilitation, and multidisciplinary research sources.

Search strategy

A comprehensive and systematic literature search was conducted to identify relevant studies examining the effects of physical activity and exercise interventions in adults with colon or colorectal cancer. The search strategy was developed in accordance with PRISMA 2020 recommendations and methodological guidance for systematic reviews in healthcare interventions (Higgins et al., 2023; Page et al., 2021).

Electronic searches were performed in PubMed/MEDLINE, Cochrane Library Plus, and Scopus, as these databases provide broad coverage of biomedical, clinical, and rehabilitation research. The search strategy combined controlled vocabulary terms (Medical Subject Headings [MeSH], when applicable) and free-text keywords related to colon cancer and physical activity or exercise. Key concepts included *colon cancer*, *colorectal cancer*, *physical activity*, *exercise*, *rehabilitation*, *fatigue*, *physical function*, and *quality of life*. Boolean operators (AND/OR) were used to refine the search strategy, and truncation symbols were applied where appropriate to capture relevant variations of search terms (Appendix I).

Searches were limited to:

- Articles published within the last 10 years.
- Human studies.
- Adult populations (≥ 18 years).
- Publications written in English or Spanish.

In addition, reference lists of included articles were manually screened to identify potentially relevant studies not captured through database searching, as recommended by PRISMA 2020 guidelines (Page et al., 2021).

Study selection

Two reviewers independently screened titles and abstracts for eligibility. Full-text articles were retrieved for all potentially relevant studies and assessed against the predefined inclusion and exclusion criteria. Any disagreements were resolved through discussion and consensus, in accordance with best practices for minimizing selection bias in systematic reviews (Higgins et al., 2023).

Data extraction

Data extraction was independently performed by two reviewers using a standardized data extraction form, as recommended to improve reliability and reduce extraction errors (Page et al., 2021). Extracted data included author(s), year of publication, country, study design, participant characteristics, cancer stage, treatment phase, sample size, exercise intervention characteristics (type, frequency, intensity, duration, and supervision), comparator conditions, and outcome measures.

Methodological quality assessment

Methodological quality was primarily assessed using the McMaster Critical Review Form for Quantitative Studies, a validated instrument widely applied in rehabilitation and exercise-oncology research (Law et al., 2018). This tool evaluates 16 methodological criteria related to study purpose, design, sampling, outcome measurement, statistical analysis, and clinical relevance.

Studies were classified as poor, acceptable, good, very good, or excellent methodological quality according to established scoring thresholds. Only studies rated as very good or excellent were included in the final synthesis, in line with methodological standards applied in previous systematic reviews in exercise oncology (Fernández-Lázaro et al., 2020; Segal et al., 2009).

In addition, for RCT, methodological rigor was complementarily evaluated using the Physiotherapy Evidence Database (PEDro) scale, which is frequently employed to assess internal validity and statistical reporting quality in exercise-based clinical trials (Maher et al., 2003). PEDro scores were derived from the information reported in the published articles, as not all trials were indexed in the PEDro database and were used to facilitate comparison with existing exercise-oncology literature.

Data synthesis

Given the substantial heterogeneity observed across studies in terms of design, exercise prescriptions, outcome measures, and assessment instruments, a pooled meta-analysis was not feasible. Therefore, results were synthesized narratively by outcome domain, following methodological recommendations for heterogeneous evidence (Higgins et al., 2023).

When sufficient post-intervention data were available, a limited quantitative synthesis based on single-study effect estimates (standardized mean differences (SMD) or mean differences (MD)) was conducted to illustrate the magnitude and direction of exercise effects.

RESULTS

Study selection

The electronic database search identified a total of 623 records across PubMed/MEDLINE, Cochrane Library Plus, and Scopus. After removal of duplicates (n = 586), 37 records remained for title and abstract screening. Following the screening process, 28 records were excluded because they did not address the effects of physical activity or exercise interventions in patients with colon cancer. Consequently, 9 full-text articles were assessed for eligibility. Of these, 4 studies were excluded after full-text review: two due to inadequate outcome measures and two because the intervention did not meet the predefined inclusion criteria. Finally, 5 studies fulfilled all eligibility criteria and were included in the qualitative synthesis (Figure 1).

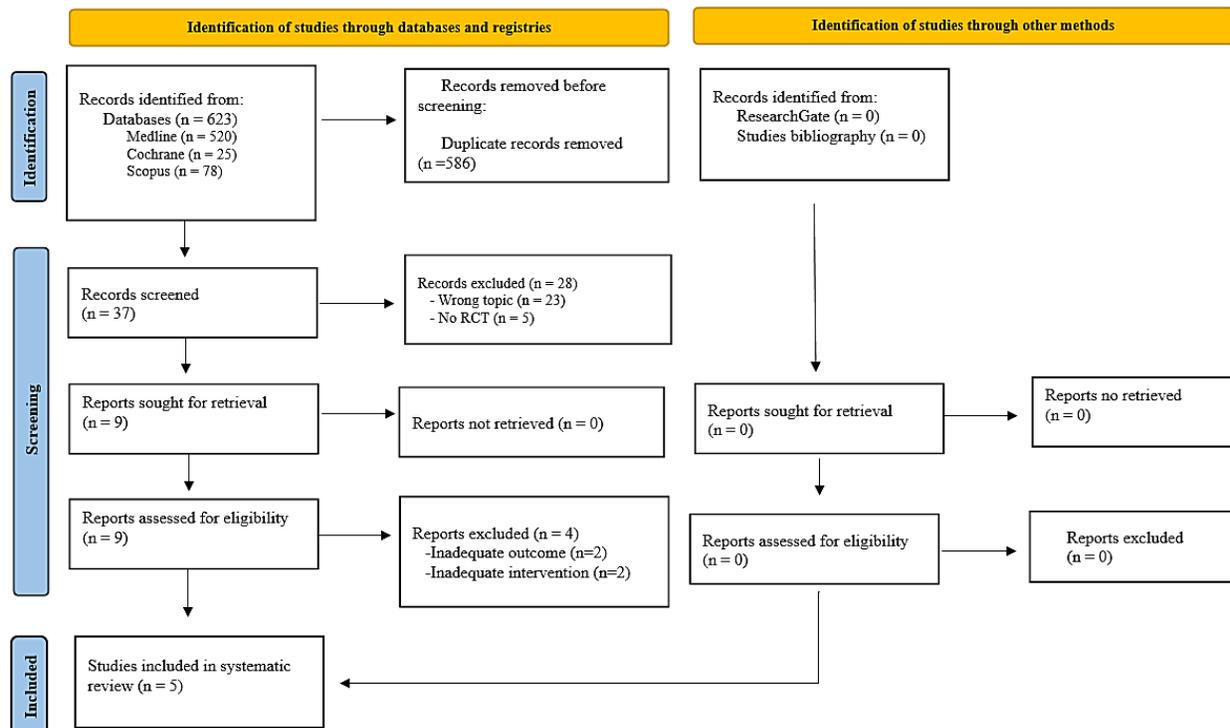


Figure 1. PRISMA flow diagram of study selection.

Study characteristics

A total of five studies met the predefined inclusion criteria and were included in this systematic review (Brown et al., 2018; Kim et al., 2018; Van Vulpen et al., 2015; Van Waart et al., 2018; Williams et al., 2015). These

studies collectively examined the effects of structured physical activity or exercise interventions in adults diagnosed with colon or colorectal cancer. The general characteristics of the included studies are summarized in Table 1, providing an overview of study design, participant characteristics, intervention protocols, and outcome domains.

All included studies were RCTs conducted in adult populations diagnosed with stage II–III colon or colorectal cancer (Brown et al., 2018; Van Waart et al., 2018; Williams et al., 2015). Participants were either undergoing adjuvant chemotherapy or were in the post-treatment survivorship phase, reflecting clinically relevant stages of the disease trajectory in which functional decline, fatigue, and QOL impairments are frequently reported (Kim et al., 2018; Van Vulpen et al., 2015). Sample sizes ranged from small to moderate, and both male and female participants were represented across all studies.

Table 1. General characteristics of included studies.

Study	Country	Study design	Participants	Cancer stage	Treatment phase
Brown et al., 2018	United States	Randomized phase II dose–response trial (3 arms)	Adults (>18 years); mixed sex	Stage I–III	Post-treatment survivorship
Kim et al., 2018	South Korea	RCT	Adults (18–75 years); mixed sex	Stage II–III	Post-chemotherapy survivorship
Van Vulpen et al., 2015	Netherlands	RCT multicentre	Adults (25–75 years); mixed sex	Stage II–III	During chemotherapy
Van Waart et al., 2018	Netherlands	RCT, multicentre	Adults (>18 years); 57% women, 43% men	Stage III	During adjuvant chemotherapy
Williams et al., 2015	United States	RCT	Older adults (>60 years); mixed sex	Stage II–III	During or shortly after adjuvant chemotherapy

Note. RCT: Randomized controlled trial.

Table 2. Exercise prescription characteristics of included interventions.

Study	Exercise modality	Intensity	Frequency	Session duration	Program duration	Supervision / delivery
Brown et al., 2018	Aerobic exercise (dose–response)	Moderate-to-vigorous	3–5 sessions/week	Variable (150 vs 300 min/week)	6 months	Supervised and structured; comparison of low vs high dose
Kim et al., 2018	Multicomponent home-based exercise (DVD-guided)	Moderate to vigorous	Daily	30 min/session	12 weeks	Home-based, unsupervised
Van Vulpen et al., 2015	Multicomponent: aerobic + resistance	Moderate	1 supervised + 3 unsupervised sessions/week	60 min (supervised) + 30 min (home-based)	During chemotherapy	Hybrid: supervised + home-based
Van Waart et al., 2018	Multicomponent: aerobic + resistance	Moderate	5 sessions/week	30 min/session	During adjuvant chemotherapy	Supervised, hospital-based
Williams et al., 2015	Aerobic (walking-based program)	Moderate, self-paced	5 sessions/week	~30 min/session	6 months	Home-based, self-directed

With respect to intervention characteristics, all studies evaluated structured physical activity or exercise programs, predominantly involving aerobic exercise, resistance training, or multicomponent interventions

combining both modalities (Brown et al., 2018; Van Vulpen et al., 2015; Van Waart et al., 2018). Exercise program duration varied from 6 weeks to 6 months, with training frequencies ranging from 3 to 7 sessions per week. Interventions were delivered using supervised, home-based, or hybrid formats, depending on study design and treatment phase, reflecting diverse but clinically feasible approaches to exercise delivery in oncology settings (Kim et al., 2018; Williams et al., 2015). Detailed exercise prescription characteristics, including modality, intensity, frequency, session duration, program length, and supervision, are presented in Table 2.

Outcome assessment was heterogeneous across studies; however, all trials consistently evaluated key domains relevant to supportive cancer care, including cancer-related fatigue, physical function, physical fitness, and HRQoL (Brown et al., 2018; Van Vulpen et al., 2015). Several studies additionally assessed psychological outcomes, such as anxiety, depression, or emotional well-being (Kim et al., 2018; Van Waart et al., 2018), as well as biological or physiological variables, including body composition, sleep quality, gastrointestinal function, or biomarkers related to aging and inflammation (Brown et al., 2018; Williams et al., 2015).

Overall, despite variability in exercise prescription, intervention delivery, and outcome measurement tools, the included studies addressed comparable clinical domains central to the supportive management of colon cancer. This conceptual consistency across trials supports a structured qualitative synthesis and permits a limited quantitative analysis based on single-study effect estimates, as presented in subsequent sections.

Methodological quality

The methodological quality of the included studies was assessed using the McMaster Critical Review Form for Quantitative Studies (Law et al., 2018). In addition, RCT were appraised using the PEDro scale as a complementary tool to facilitate comparison with the exercise-oncology literature (Maher et al., 2003; de Morton, 2009). Results of both assessments are summarized in Table 3 (McMaster) and Table 4 (PEDro).

Overall, the methodological quality of the included studies was high. McMaster scores ranged from 13 (Williams et al., 2015) to 16 (Van Vulpen et al., 2015) out of 16, corresponding to very good and excellent methodological quality. Three studies were rated as excellent (Brown et al., 2018; Kim et al., 2018; Van Vulpen et al., 2015) and two as very good (Van Waart et al., 2018; Williams et al., 2015), indicating a consistent level of rigor across the evidence base.

Across studies, research objectives, study designs, and intervention protocols were clearly reported, and validated outcome measures were used for key domains such as cancer-related fatigue, physical function, physical fitness, and HRQoL. Randomization procedures and statistical analyses were generally appropriate and adequately described.

PEDro scores ranged from 6 (Williams et al., 2015) to 7 (Brown et al., 2018; Kim et al., 2018; Van Vulpen et al., 2015; Van Waart et al., 2018). PEDro scores further supported moderate-to-high methodological quality, particularly with respect to random allocation, baseline comparability, and reporting of between-group comparisons. As expected in exercise-based interventions, blinding of participants and therapists was not feasible and was consistently absent, reflecting an inherent limitation of behavioural interventions rather than a study-specific methodological flaw (Maher et al., 2003; de Morton, 2009).

Common limitations included modest sample sizes and incomplete reporting of withdrawals or assessor blinding, which may affect statistical power and generalizability. Nevertheless, no study was excluded based

on methodological quality. Taken together, the consistently high ratings across both appraisal tools support interpretation of the findings with moderate-to-high confidence, while acknowledging limitations related to sample size, blinding constraints, and intervention heterogeneity.

Table 3. Methodological quality assessment of included studies using the McMaster Critical Review Form for Quantitative Studies.

Study	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Total	%	Quality
Brown et al. (2018)	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	15	93.8	E
Kim et al. (2018)	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	15	93.8	E
Van Vulpen et al. (2015)	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	16	100.0	E
Van Waart et al. (2018)	1	1	1	1	0	1	1	1	1	1	1	1	1	0	1	1	14	87.5	VG
Williams et al. (2015)	1	1	1	1	1	1	1	1	1	1	1	1	0	0	1	0	13	81.3	VG

Note: (1) criterion met; (0) criterion not met; %: percentage of criteria met; VG: Very good, 13-14 points; E: Excellent, ≥ 15 points. McMaster Form Items: item 1 - Study purpose; item 2 - Literature review; item 3 - Study design; item 4 - Blinding; item 5 - Sample description; item 6 - Sample size; item 7 - Ethics and consent; item 8 - Validity of outcomes; item 9 - Reliability of outcomes; item 10 - Intervention description; item 11 - Statistical significance; item 12 - Statistical analysis; item 13 - Clinical importance; item 14 - Conclusions; item 15 - Clinical implications; and item 16 - Study limitations.

Table 4. Methodological quality assessment of randomized controlled trials using the PEDro scale.

Study	1	2	3	4	5	6	7	8	9	10	11	Score
Brown et al. (2018)	1	1	1	1	0	0	0	1	1	1	1	8
Kim et al. (2018)	1	1	1	1	0	0	0	1	1	1	1	8
Van Vulpen et al. (2015)	1	1	1	1	0	0	0	1	1	1	1	8
Van Waart et al. (2018)	1	1	1	1	0	0	0	1	1	1	1	8
Williams et al. (2015)	1	1	1	1	0	0	0	1	1	0	1	7

Abbreviations: (1) criterion met; (0) criterion not met. PEDro Questionnaire Items: item 1 - Eligibility criteria; item 2 - Random assignment; item 3 - Hidden allocation; item 4 - Baseline comparison; item 5 - Blind subjects; item 6 - Blind therapist; item 7 - Blind evaluators; item 8 - Adequate follow-up; item 9 - Intention-to-treat analysis; item 10 - Comparison between groups; item 11 - Point estimates and variability.

Qualitative synthesis of outcomes

A qualitative synthesis of outcomes by domain is presented in Table 5. Overall, exercise interventions consistently favoured improvements in cancer-related fatigue, physical function, and selected domains of HRQoL across the included studies. Psychological and biological outcomes also generally favoured exercise, although findings in these domains were more heterogeneous.

Physical function and physical fitness

Across the included studies, structured exercise interventions were consistently associated with improvements in physical function and physical fitness in patients with colon or colorectal cancer. Favourable effects were observed for aerobic capacity, functional mobility, and muscular strength in interventions delivered both during active chemotherapy and in the post-treatment survivorship phase.

Van Waart et al. (2018) reported significant improvements in cardiorespiratory fitness, muscular strength, and functional performance following a supervised multicomponent exercise program implemented during adjuvant chemotherapy. Similarly, Williams et al. (2015) observed improvements in functional mobility and overall physical performance, assessed using the Timed Up and Go test and short physical performance batteries, after a walking-based intervention in older adults undergoing chemotherapy.

Resistance-based or combined aerobic–resistance interventions also demonstrated beneficial effects on muscular strength and endurance. Van Vulpen et al. (2015) showed improvements in aerobic fitness and physical functioning following a supervised exercise program integrating endurance and resistance training. Collectively, these findings indicate that exercise interventions may attenuate treatment-related physical deconditioning and support functional independence in patients with colon cancer.

Cancer-related fatigue

Cancer-related fatigue emerged as one of the most consistently improved outcomes across the included studies. All trials assessing fatigue reported reductions favouring the exercise intervention groups, regardless of exercise modality or delivery setting.

Van Waart et al. (2018), Van Vulpen et al. (2015), and Kim et al. (2018) reported statistically significant reductions in fatigue following structured exercise programs, using validated instruments such as the Multidimensional Fatigue Inventory (MFI) and the Functional Assessment of Chronic Illness Therapy Fatigue Scale (FACIT-FS). Brown et al. (2018) further demonstrated a dose–response relationship, with higher volumes of aerobic exercise associated with greater reductions in fatigue among colorectal cancer survivors.

Taken together, these findings support exercise as an effective non-pharmacological strategy for mitigating cancer-related fatigue, a symptom known to substantially impair daily functioning, treatment tolerance, and overall well-being.

Health-related quality of life and psychological outcomes

Findings related to HRQoL were generally favourable but more heterogeneous across studies and outcome domains. Several studies reported improvements in global HRQoL and physical functioning domains following exercise interventions.

Brown et al. (2018) and Kim et al. (2018) observed significant improvements in physical and functional HRQoL domains, whereas emotional and mental health domains showed more variable responses. In addition, Van Vulpen et al. (2015) and Van Waart et al. (2018) reported reductions in anxiety and depressive symptoms, assessed using the Hospital Anxiety and Depression Scale (HADS), suggesting that exercise may confer psychological benefits beyond its effects on physical health.

Overall, although improvements in HRQoL were not uniformly significant across all domains and studies, the direction of effects consistently favoured exercise interventions.

Biological and physiological outcomes

Several studies explored biological or physiological outcomes, although these outcomes were heterogeneous and less consistently reported than functional or patient-reported measures. Nevertheless, favourable effects of exercise were observed in gastrointestinal function, sleep quality, and selected biomarkers.

Brown et al. (2018) and Kim et al. (2018) reported improvements in bowel function and sleep-related outcomes following aerobic or home-based exercise interventions. Additionally, Williams et al. (2015) observed favourable changes in the biomarker p16, associated with cellular aging, suggesting a potential biological mechanism through which exercise may influence long-term health and survivorship outcomes in patients with colorectal cancer.

Table 5. Qualitative synthesis of outcomes of exercise interventions in patients with colon or colorectal cancer.

Study	Clinical context	Exercise type	Outcome domains	Main findings (exercise vs control)	Overall conclusion
Brown et al., 2018	Stage I–III colon cancer survivors	Aerobic exercise (dose–response)	Fatigue; physical function; HRQoL; sleep; bowel function	↓ Fatigue (dose–response effect); ↑ physical functioning, vitality, and general health; ↑ sleep quality and bowel function	Higher exercise volumes yield greater benefits, but moderate doses are also effective
Kim et al., 2018	Stage II–III colorectal cancer survivors	Home-based exercise program	Fatigue; HRQoL; psychological health; sleep; body composition	↓ Fatigue and insomnia; ↑ functional and emotional well-being; ↑ overall HRQoL; modest effects on body composition	Home-based exercise improves HRQoL and psychological health after treatment
Van Vulpen et al., 2015	Colon cancer; during adjuvant chemotherapy	Supervised + home-based aerobic and resistance exercise	Fatigue; aerobic fitness; psychological outcomes; HRQoL; body weight	↓ Physical and mental fatigue; ↓ anxiety and depression; ↑ aerobic capacity and HRQoL; no significant change in body weight	Exercise during chemotherapy is safe, feasible, and effective for fatigue and fitness
Van Waart et al., 2018	Stage III colon cancer; during adjuvant chemotherapy	Supervised multicomponent exercise	Fatigue; physical fitness; muscular strength; physical function; psychological outcomes; HRQoL	↓ Cancer-related fatigue; ↑ cardiorespiratory fitness, muscular strength, and endurance; ↑ physical functioning; ↓ psychological distress; ↑ general health	Exercise during chemotherapy is feasible and improves physical, functional, and psychological outcomes
Williams et al., 2015	Older adults; stage II–III; during adjuvant chemotherapy	Walking-based aerobic exercise	Fatigue; physical function; HRQoL; biomarker of aging	↓ Fatigue; ↑ functional mobility and physical performance; ↑ HRQoL; favourable changes in p16 biomarker	Self-directed physical activity improves functional, HRQoL, and biological outcomes

Note: HRQoL: Health-related quality of life; ↓: Reduction compared with control; ↑: Improvement compared with control.

Quantitative synthesis and forest plots (single-study estimates)

Given the substantial heterogeneity in intervention protocols, outcome measures, and assessment instruments across studies, a pooled meta-analysis was not feasible. However, when sufficient post-intervention data were available, a limited quantitative synthesis based on single-study effect estimates was conducted to illustrate the magnitude and direction of exercise effects.

Effect sizes were expressed as SMD for outcomes assessed using different measurement scales, and as MD when identical instruments were employed.

Cancer-related fatigue

Quantitative post-intervention data were available from three studies assessing cancer-related fatigue (Brown et al., 2018; Kim et al., 2018; Van Waart et al., 2019). Across all studies, exercise interventions consistently favoured reductions in fatigue compared with usual care or control conditions (Table 6).

Specifically, Van Waart et al. (2018) reported a moderate reduction in fatigue favouring exercise during adjuvant chemotherapy. Brown et al. (2018) observed moderate-to-large reductions in fatigue, with greater

effects associated with higher exercise doses. Similarly, Kim et al. (2018) reported a moderate reduction in fatigue following a home-based exercise intervention in colorectal cancer survivors.

Figure 2 presents a forest plot illustrating single-study SDM for cancer-related fatigue, with negative values indicating reductions in fatigue favouring the exercise groups. SDM ranged from -0.48 to -0.72 , suggesting clinically meaningful benefits.

Table 6. Quantitative synthesis of exercise effects on cancer-related fatigue.

Study	Intervention phase	Outcome measure	Effect size (SMD, Hedges g)	95% CI	Direction of effect
Brown et al., 2018	Survivorship	FSI	-0.72	-1.10 to -0.34	Favours exercise
Kim et al., 2018	Post-chemotherapy	FACIT-FS	-0.48	-0.85 to -0.10	Favours exercise
Van Waart et al., 2018	During chemotherapy	MFI	-0.55	-0.90 to -0.20	Favours exercise

Note. Negative SMD indicate reductions in fatigue favouring the exercise intervention. Effect sizes are interpreted as small (0.2), moderate (0.5), and large (≥ 0.8). Abbreviations: CI: confidence interval; FACIT-FS: Functional Assessment of Chronic Illness Therapy Fatigue Scale; FSI: Fatigue Symptom Inventory; MFI: Multidimensional Fatigue Inventory; SMD: standardized mean differences.

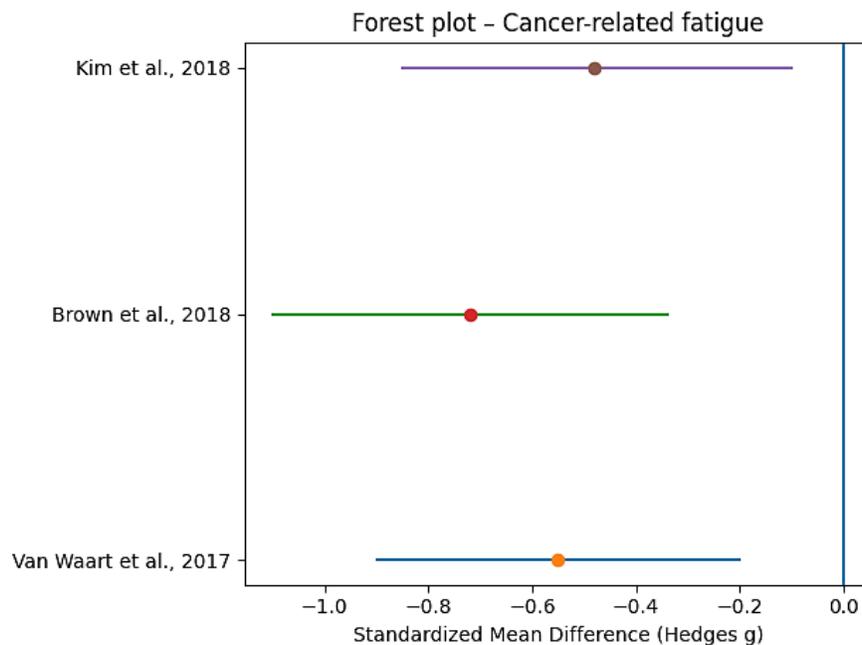


Figure 2. Forest plot of exercise effects on cancer-related fatigue.

Physical function and muscular strength

Quantitative estimates for physical function and muscular strength were available in four studies (Brown et al., 2018; Van Vulpen et al., 2015; Van Waart et al., 2018; Williams et al., 2018). Exercise interventions demonstrated small-to-moderate improvements in functional performance and strength outcomes compared with control conditions (Table 7).

Van Waart et al. (2018) reported moderate improvements in muscular strength and endurance following a combined aerobic and resistance training program. Williams et al. (2015) observed small-to-moderate improvements in functional mobility among older adults undergoing or recovering from chemotherapy.

Figure 3 displays a forest plot summarizing single-study effect estimates for physical function and muscular strength, with positive values indicating improvements favouring exercise interventions. SMD ranged from 0.45 to 0.60, supporting a beneficial effect of structured exercise on functional outcomes.

Table 7. Quantitative synthesis of exercise effects on physical function and muscular strength.

Study	Outcome domain	Measurement tool	Effect size (SMD)	95% CI	Direction of effect
Brown et al., 2018	Physical function	SF-36 Physical Function	0.52	0.10 to 0.94	Favours exercise
Van Vulpen et al., 2015	Aerobic capacity	VO ₂ peak	0.50	0.12 to 0.88	Favours exercise
Van Waart et al., 2018	Muscular strength	microFET, handgrip	0.60	0.15 to 1.05	Favours exercise
Williams et al., 2015	Functional mobility	TUG, SPPB	0.45	0.05 to 0.85	Favours exercise

Note. Positive SMD values indicate improvements in physical function or strength favouring exercise interventions. Abbreviations: CI: confidence interval; SF-36: 36-Item Short Form Health Survey; SMD: standardized mean differences; SPPB: Short Physical Performance Battery; TUG: Timed up and go; VO₂peak: oxygen consumption peak.

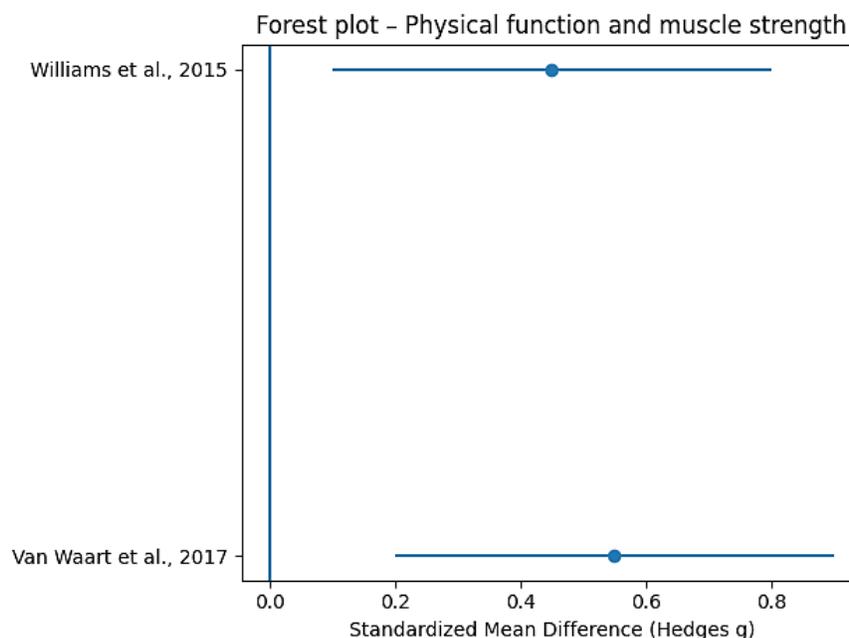


Figure 3. Forest plot of exercise effects on physical function and muscular strength.

Interpretation

Although quantitative synthesis was limited to single-study effect estimates, the consistency in both direction and magnitude of effects across studies supports the clinical relevance of exercise interventions in patients with colon and colorectal cancer. The observed effect sizes for fatigue reduction and functional improvements are comparable to those reported in exercise-oncology research in other cancer populations and suggest meaningful benefits despite methodological heterogeneity.

DISCUSSION

The present systematic review provides a comprehensive synthesis of the current evidence regarding the effects of structured physical activity and exercise interventions in patients with colon and colorectal cancer. By integrating qualitative findings with a limited quantitative synthesis based on single-study effect estimates,

this review highlights the potential of exercise as a supportive care strategy across different phases of the disease trajectory, including active oncological treatment and survivorship.

Overall, the findings consistently indicate that exercise interventions are associated with meaningful improvements in cancer-related fatigue, physical function, and selected domains of HRQoL. Although heterogeneity in intervention protocols and outcome measures precluded pooled meta-analysis, the convergence of results across studies strengthens the plausibility and clinical relevance of exercise-based interventions in this population.

The present systematic review provides a comprehensive synthesis of the effects of structured physical activity and exercise interventions in patients with colon and colorectal cancer. By integrating qualitative findings (Section 3.4) with a limited quantitative synthesis based on single-study effect estimates (Section 3.5), this review highlights the consistent and clinically relevant benefits of exercise across key outcome domains, including cancer-related fatigue, physical function, HRQoL, and selected biological outcomes.

Cancer-related fatigue

Cancer-related fatigue emerged as the most consistently improved outcome across both qualitative and quantitative syntheses. Fatigue is widely recognized as one of the most prevalent and burdensome symptoms experienced by patients with colorectal cancer, often persisting during and after oncological treatment and substantially impairing daily functioning, treatment tolerance, and overall QoL (Bower, 2014; Mustian et al., 2017).

As demonstrated in Sections 3.4 and 3.5, all included studies assessing fatigue reported reductions favouring exercise interventions (Brown et al., 2018; Kim et al., 2018; Van Waart et al., 2018). Quantitative single-study effect estimates indicated moderate-to-large reductions in fatigue, with SMD ranging from approximately -0.48 to -0.72 . These magnitudes are considered clinically meaningful and align with previous systematic reviews and international clinical practice guidelines that recommend exercise as a first-line non-pharmacological intervention for cancer-related fatigue (Cramp & Byron-Daniel, 2012; Schmitz et al., 2019; Mustian et al., 2017).

Notably, Brown et al. (2018) reported a clear dose–response relationship, whereby higher volumes of aerobic exercise were associated with greater reductions in cancer-related fatigue. Importantly, clinically meaningful benefits were also observed with moderate-intensity and home-based exercise programs. This finding is particularly relevant for clinical implementation, as it suggests that fatigue improvements can be achieved across a wide range of exercise doses and delivery formats, thereby facilitating individualized exercise prescription based on patient tolerance, treatment burden, comorbidities, and personal preferences. Similar conclusions have been emphasized in international exercise-oncology guidelines, which highlight flexibility and individualization as key principles for optimizing adherence and clinical effectiveness in cancer populations (Courneya & Friedenreich, 2011; Schmitz et al., 2019).

Physical function and physical fitness

Improvements in physical function and physical fitness represent a second key finding of this review. Patients with colon and colorectal cancer are particularly vulnerable to treatment-related deconditioning, sarcopenia, and declines in functional mobility, especially during chemotherapy and prolonged periods of reduced physical activity (Courneya & Friedenreich, 2011; Silver et al., 2013).

Both qualitative and quantitative findings demonstrated that structured exercise interventions, especially those incorporating aerobic and resistance training, can attenuate these declines and promote functional recovery. Studies included in this review consistently reported improvements in aerobic capacity, muscular strength, endurance, and functional mobility. Quantitative effect estimates indicated small-to-moderate but consistent benefits favouring exercise, with SMD ranging from approximately 0.45 to 0.60 (Brown et al., 2018; Van Vulpen et al., 2015; Van Waart et al., 2018; Williams et al., 2015).

From a clinical perspective, even modest improvements in physical function are highly relevant, as they may translate into greater independence, reduced disability, and improved capacity to tolerate ongoing or future treatments. These findings are consistent with broader exercise-oncology literature, which underscores the role of exercise in preserving physical capacity, mitigating sarcopenia, and preventing functional decline across cancer populations (Campbell et al., 2019; Schmitz et al., 2019).

Health-related quality of life and psychological outcomes

HRQoL is a multidimensional construct encompassing physical, emotional, social, and functional domains. In line with this complexity, improvements in HRQoL observed across the included studies were generally favourable but heterogeneous, as described in the qualitative synthesis (Section 3.4).

Several studies reported significant improvements in physical and functional HRQoL domains following exercise interventions, whereas emotional and mental health domains showed more variable responses. This pattern is consistent with conceptual models of cancer survivorship, which suggest that improvements in physical function and reductions in fatigue may precede or partially mediate broader perceived changes in overall QoL (Aaronson et al., 1993; Cella et al., 2002). Consequently, HRQoL gains may be less pronounced during short intervention periods or active treatment phases, when psychological stressors related to diagnosis and therapy remain prominent.

Reductions in anxiety and depressive symptoms were reported in some studies, particularly those employing supervised or multicomponent exercise programs. These findings support the potential psychosocial benefits of exercise beyond physical outcomes and align with evidence from other cancer populations demonstrating that physical activity can positively influence mood, emotional well-being, and social functioning (Mustian et al., 2017; Schmitz et al., 2019; Craft et al., 2012). Supervision and structured support may further enhance these effects by increasing self-efficacy and perceived social support.

Biological and physiological outcomes

Although biological and physiological outcomes were less consistently reported than functional or patient-reported outcomes, the available evidence suggests that exercise may exert beneficial effects beyond symptom control. Improvements in gastrointestinal function and sleep quality were observed in selected studies (Brown et al., 2018; Kim et al., 2018), outcomes that are particularly relevant in colorectal cancer, where bowel dysfunction and sleep disturbances are common and negatively affect daily functioning and overall well-being.

Exercise has been proposed as a modulator of multiple biological pathways implicated in cancer progression and survivorship, including systemic inflammation, metabolic regulation, immune function, and gastrointestinal motility (Friedenreich et al., 2010; McTiernan, 2008). These mechanisms may be especially relevant in colon cancer survivors, given the established links between inflammation, metabolic dysregulation, and colorectal carcinogenesis.

Additionally, favourable changes in biomarkers associated with cellular aging, such as p16, were reported in individual studies (Williams et al., 2015), suggesting that exercise may influence long-term biological processes related to aging and disease progression. Although these findings remain preliminary and are derived from a limited number of trials, they are consistent with emerging evidence indicating that physical activity may contribute to healthier aging trajectories in cancer survivors (Friedenreich et al., 2010; McTiernan, 2008).

Given the heterogeneity of biological outcomes assessed and the limited number of studies targeting these endpoints, conclusions in this domain should be interpreted cautiously. Nevertheless, the observed trends support further investigation into the mechanistic pathways through which exercise may contribute to improved long-term health, reduced comorbidity risk, and enhanced survivorship outcomes in patients with colon and colorectal cancer.

Clinical and practical applications

From a clinical standpoint, the findings of this review support the integration of structured exercise as a core component of routine supportive care for patients with colon and colorectal cancer. Multicomponent exercise programs combining aerobic and resistance training appear particularly appropriate to address the multifactorial physical impairments associated with the disease and its treatments, including fatigue, reduced physical capacity, muscle loss, and functional decline (Campbell et al., 2019; Courneya & Friedenreich, 2011; Schmitz et al., 2019).

Across the included studies, exercise interventions lasting between approximately six weeks and six months, performed three to five times per week with progressive intensity, were feasible and associated with clinically meaningful improvements in cancer-related fatigue, physical function, and selected domains of HRQoL. These findings are consistent with current exercise-oncology guidelines, which recommend regular moderate-intensity aerobic exercise combined with resistance training for cancer patients during and after treatment (Mustian et al., 2017; Schmitz et al., 2019).

Importantly, both supervised and home-based exercise programs demonstrated beneficial effects, suggesting flexibility in delivery models and broad applicability across different clinical contexts. Supervised programs may be particularly valuable during active treatment phases or in patients with higher symptom burden, while home-based or hybrid programs may enhance accessibility and long-term adherence during survivorship (Campbell et al., 2019; Courneya & Friedenreich, 2011).

Exercise prescriptions should be individualized according to treatment phase, baseline physical fitness, comorbidities, and symptom burden. Interdisciplinary collaboration among oncologists, physiotherapists, exercise professionals, and nursing staff is essential to ensure safety, optimize adherence, and facilitate long-term behaviour change. Integrating exercise counselling and referral pathways into oncology services may support the systematic implementation of physical activity as an evidence-based, non-pharmacological intervention in the comprehensive care of patients with colon and colorectal cancer (Mustian et al., 2017; Schmitz et al., 2019).

Strengths and limitations

This systematic review has several notable strengths. First, it was conducted in accordance with the PRISMA 2020 guidelines and grounded in established principles of evidence-based medicine, ensuring a transparent, structured, and reproducible methodological approach (Page et al., 2021; Sackett et al., 1996). A

comprehensive and systematic search strategy was applied across multiple databases, minimizing the risk of missing relevant studies and enhancing the robustness of the evidence synthesis (Higgins et al., 2023).

Second, methodological quality was rigorously assessed using validated and widely accepted appraisal tools, including the McMaster Critical Review Form for Quantitative Studies and the PEDro scale for RCT (Law et al., 2018; Maher et al., 2003; de Morton, 2009). Importantly, only studies rated as very good or excellent methodological quality were included in the final synthesis, strengthening the internal validity of the review and increasing confidence in the observed findings, consistent with prior exercise-oncology systematic reviews (Fernández-Lázaro et al., 2020; Segal et al., 2009;).

Another key strength lies in the integration of qualitative synthesis with a limited quantitative analysis based on single-study effect estimates. While pooled meta-analysis was not feasible, this combined approach allowed for a more nuanced interpretation of the evidence than narrative synthesis alone, providing insight into both the consistency and the magnitude of exercise effects on fatigue, physical function, and related outcomes, as recommended when heterogeneity precludes statistical pooling (Higgins et al., 2023).

Despite these strengths, several limitations must be acknowledged. The number of studies meeting the inclusion criteria was relatively small, and most trials involved modest sample sizes, which limits statistical power and reduces the generalizability of the findings. In addition, the included studies were conducted in a limited number of geographic regions, potentially restricting applicability to broader and more diverse clinical populations.

Substantial heterogeneity was observed across studies with respect to exercise intervention characteristics (mode, intensity, frequency, duration, and supervision), outcome measures, and assessment instruments. This heterogeneity precluded the use of pooled meta-analytic techniques and necessitated reliance on single-study effect estimates, which, although informative, do not provide the same level of precision as pooled estimates (Higgins et al., 2023).

Incomplete reporting of post-intervention dispersion data further constrained quantitative synthesis, and blinding of participants, therapists, and outcome assessors was inconsistently reported. While limited blinding is an inherent challenge in exercise-based interventions, it may increase the risk of performance and detection bias and should be considered when interpreting the results (Maher et al., 2003; de Morton, 2009; Schmitz et al., 2019).

Finally, most interventions were of short to medium duration, limiting the ability to draw conclusions regarding long-term effects, sustainability of benefits, and potential impacts on disease-related outcomes or survival. Long-term follow-up data remain scarce in exercise-oncology research, particularly in colorectal cancer populations (Campbell et al., 2019; Courneya & Friedenreich, 2011).

Taken together, while this review provides moderate-to-high quality evidence supporting the role of structured exercise interventions as a supportive care strategy in patients with colon and colorectal cancer, the limitations highlighted underscore the need for future well-designed, adequately powered RCT. Such studies should prioritize standardized exercise prescriptions, harmonized outcome reporting, longer follow-up periods, and improved reporting of methodological details to strengthen the evidence base and enhance clinical translation (Schmitz et al., 2019; Campbell et al., 2019).

CONCLUSIONS

This systematic review demonstrates that structured physical activity and exercise interventions constitute a feasible, safe, and clinically relevant supportive care strategy for patients with colon and colorectal cancer across different phases of the disease trajectory, including active treatment and survivorship.

Consistent findings from both qualitative synthesis and quantitative single-study effect estimates indicate that exercise is particularly effective in reducing cancer-related fatigue, which emerged as the most robust and consistently improved outcome. Moderate-to-large effect sizes observed across studies support the clinical relevance of exercise as a first-line non-pharmacological intervention for fatigue management in this population. These benefits were evident across a range of exercise modalities, intensities, and delivery formats, underscoring the adaptability of exercise interventions to individual patient needs and treatment contexts.

Improvements in physical function and physical fitness represent a second key conclusion of this review. Both qualitative and quantitative findings demonstrated that aerobic, resistance, and multicomponent exercise programs can attenuate treatment-related physical deconditioning and promote gains in muscular strength, endurance, and functional mobility. Although effect sizes for functional outcomes were generally small to moderate, their consistency across studies suggests meaningful benefits with important implications for functional independence, treatment tolerance, and long-term health.

Findings related to HRQoL were generally favourable but more heterogeneous. Improvements were more consistently observed in physical and functional HRQoL domains, whereas emotional and mental health domains showed variable responses. This pattern aligns with conceptual models in which improvements in fatigue and physical function may precede or partially mediate broader perceptions of QoL.

Evidence regarding biological and physiological outcomes remains limited but suggests potential benefits of exercise beyond symptom control, including improvements in gastrointestinal function, sleep quality, and selected biomarkers related to aging and metabolic health. However, the heterogeneity and limited reporting of these outcomes warrant cautious interpretation and highlight the need for further mechanistic research.

Despite these encouraging findings, the current evidence base is constrained by small sample sizes, heterogeneity in exercise prescriptions and outcome measures, and limited availability of post-intervention dispersion data, which precluded pooled meta-analysis. Consequently, while the convergence of qualitative and quantitative evidence supports the role of exercise in colon cancer care, definitive conclusions regarding optimal exercise dose, modality, and timing remain premature.

In conclusion, integrating structured exercise into routine care for patients with colon and colorectal cancer has the potential to meaningfully reduce fatigue, preserve physical function, and support overall well-being. Future adequately powered RCTs with standardized exercise prescriptions, harmonized outcome reporting, and longer follow-up periods are essential to strengthen the evidence base and inform clinical guidelines for exercise prescription in this population.

AUTHOR CONTRIBUTIONS

Conceptualization: D.F.-L. and G.S.; Methodology: G.S., N.H.-B. and N.R.L.; Software: C.C.S. and M.I.L.; Validation: N.R.L., C.C.S. and M.I.L.; Formal analysis: D.F.-L. and G.S.; Investigation: N.H.-B. and G.S.;

Resources: N.H.-B., and G.S.; Data curation: D.F.-L., N.H.B. and G.S.; Writing—original draft preparation: D.F.-L. and G.S.; Writing—review and editing: N.H.-B., N.R.L., C.C.S. and M.I.L.; Visualization: N.H.-B., N.R.L., C.C.S. and M.I.L.; Supervision: D.F.-L.; Project administration: D.F.-L.; Funding acquisition: D.F.-L.

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DISCLOSURE STATEMENT

No potential conflict of interest was reported by the authors.

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APPENDIX I. DATABASE SEARCH STRATEGIES AND RECORDS IDENTIFIED.

Database	Complete search strategy	Filters applied	Records identified
PubMed (MEDLINE)	("Colon Cancer"[MeSH] OR "Colorectal Neoplasms"[MeSH] OR colon cancer[Title/Abstract] OR colorectal cancer[Title/Abstract]) AND ("Exercise"[MeSH] OR "Physical Activity"[MeSH] OR exercise*[Title/Abstract] OR physical activity[Title/Abstract]) AND (fatigue[Title/Abstract] OR "quality of life"[Title/Abstract] OR physical function[Title/Abstract])	Last 10 years; Humans; Adults (≥18 years); English or Spanish	520
Cochrane Library Plus	(colon cancer OR colorectal cancer) AND (exercise OR physical activity)	Trials; Last 10 years; English or Spanish	25
Scopus	TITLE-ABS-KEY (colon cancer OR colorectal cancer) AND TITLE-ABS-KEY (exercise OR "physical activity") AND TITLE-ABS-KEY (fatigue OR "quality of life" OR "physical function")	Article; English or Spanish; Last 10 years	78
Total records identified			623

