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REVIEW

The role of physical activity, sedentary behaviour, diet, adiposity and body composition on health-related quality of life and cancer-related fatigue after diagnosis of colorectal cancer: a Global Cancer Update Programme (CUP Global) systematic literature review and meta-analysis

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Background: The impact of physical activity, sedentary behaviour, diet, adiposity, and body composition on health-related quality of life (HRQoL) and cancer-related fatigue among colorectal cancer survivors remains uncertain.

Methods: PubMed, Embase, and CENTRAL were systematically searched until April 2023 for relevant randomised controlled trials (RCTs) and cohort studies. Random-effects meta-analyses or descriptive syntheses were conducted depending on the number of studies. The evidence was interpreted and graded by an independent World Cancer Research Fund Expert Committee and Expert Panel.

Results: We included 31 RCTs (18 exercise, 14 diet) and 30 cohort studies (8 physical activity, 3 sedentary behaviour, 13 diet, 9 adiposity and body composition). Meta-analyses were possible for exercise RCTs that showed non-significant effects but indicative of improved HRQoL (overall four trials for global HRQoL, physical and emotional well-being) and fatigue (five trials). These studies were rated at a high risk of bias (RoB), and evidence was graded as 'very low certainty of an effect'. Descriptive synthesis of interventions to improve diet quality suggested small improvements in global HRQoL and physical well-being, but with a high RoB rating leading to a 'low certainty' grading. Evidence from RCTs on probiotics and supplements and evidence from observational studies on sedentary behaviour, and various dietary and body composition factors was generally inconsistent and too scarce to draw conclusions.

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Conclusions: Exercise and diet quality interventions might improve HRQoL and fatigue outcomes in colorectal cancer survivors. The evidence overall was limited and should be strengthened by larger, well-designed RCTs across the cancer continuum.
Key words: physical activity, diet, adiposity, quality of life, fatigue, colorectal cancer survivors

INTRODUCTION

Colorectal cancer survival rates are improving over time,[1] largely due to advances in early detection and treatment. Nevertheless, cancer survivors often encounter both short- and long-term effects due to the burden of their disease and treatment complications that can lead to fatigue and impaired quality of life (QoL). Impaired QoL may both impact[2-5] or be affected by prognosis.[6] Evidence from the World Cancer Research Fund (WCRF) Global Cancer Update Programme (CUP Global) suggests that a physically active lifestyle, adherence to a plant-based, healthy diet, and avoidance of sugary drinks and sedentary behaviour may be associated with longer overall survival after a colorectal cancer diagnosis.[7-10] Yet, the impact of these lifestyle factors, along with adiposity and body composition on health-related QoL (HRQoL) and cancer-related fatigue among colorectal cancer survivors, is not well-understood.

A previous CUP Global meta-analysis of randomised controlled trials (RCTs) of physical activity in breast cancer survivors showed that exercise, especially after primary or adjuvant treatment, improves HRQoL.[11] An independent panel of international experts convened by the WCRF concluded that the evidence supported strong-probable likelihood of causality, supporting the incorporation of exercise programmes as part of cancer care.[12] Nevertheless, differences in baseline HRQoL status among survivors of various cancer sites may exist due to differences in socio-demographic characteristics of survivors, existing comorbidities, stage at diagnosis, local and systemic treatment options, potential side-effects, and their impact on specific body functions or organs (e.g. lymphedema, stoma).

Given the lack of clarity about the potential benefits of leading a healthy lifestyle on HRQoL and fatigue during pre-, peri-, or post-treatment periods in colorectal cancer survivors,[13-16] we aimed to comprehensively assess and summarise evidence from RCTs and longitudinal observational studies on the role of diet, physical activity, adiposity, body composition, and sedentary behaviour (as lifestyle intervention target or exposure), in relation to HRQoL and cancer-related fatigue in colorectal cancer survivors. As part of CUP Global, we aimed to develop new evidence-based guidance for cancer survivors using the present findings and previous findings on cancer survival.[7-10]

MATERIALS AND METHODS

This systematic review follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[17] (Supplementary Table S1, available at https://doi.org/10.1016/j.esmoop.2025.104301). The pre-specified protocol can be found online at https://osf.io/fg6qj/, with subsequent modifications in Supplementary Text S1, available at https://doi.org/10.1016/j.esmoop.2025.104301.

Search strategy, selection criteria, data extraction, and RoB

PubMed, Embase, and CENTRAL were searched until 30 April 2023, supplemented by hand search (Supplementary Text S2, available at https://doi.org/10.1016/j.esmoop.2025.104301).

Eligible studies were RCTs (including at least 20 participants), longitudinal observational cohorts (with at least 100 participants), or pooled analyses of such studies on adult survivors of colorectal cancer or its anatomical subsites, regardless of stage or timing in relation to cancer treatment. Interventions/exposures of interest included physical activity (RCTs: any exercise programmes; observational studies: any definition of physical activity), sedentary behaviour, diet (RCTs: diet or nutrient intervention, dietary modification, and calorie restriction; observational studies: diet, foods, nutrients, dietary supplements, biomarkers of dietary intake), and measures of adiposity and body composition (RCTs: body measures modulated by lifestyle interventions; observational studies: body weight or composition). Multimodal or combined interventions were included if the combined intervention included diet and exercise programmes. We included studies where exposure(s) of interest were measured once at- or post-diagnosis or repeated longitudinally, or changes from pre-to-post diagnosis, irrespective of treatment period. Comparators were non-intervention groups and any non-exposure or reference category group. Outcomes included global/total, physical, or mental/emotional HRQoL domains and general/total cancer-related fatigue and its dimensions as estimated through any validated tool (Supplementary Table S2, available at https://doi.org/10.1016/j.esmoop.2025.104301). If multiple publications from the same study were identified, the publication with the most comprehensive results or participants was retained.

RCTs were assessed using the Cochrane risk-of-bias (RoB) tool version 2 (RoB 2).[18] Observational studies were assessed with a modified version (version dated 20 March 2024, Supplementary Table S3, available at https://doi.org/10.1016/j.esmoop.2025.104301) of the Risk of Bias for Nutrition Observational Studies (RoB-NObs) tool.[19]

Study selection, data extraction, and RoB assessment were each carried out by at least one of the CUP Global systematic reviewers and double-checked by another. Discrepancies were resolved with the review coordinator (DSMC).

For RCTs, attendance (percentage of supervised exercise session attended/completed) and adherence (objective or subjective measures of intervention targets, as defined in trials) to intervention were summarised (Supplementary Text S1, available at https://doi.org/10.1016/j.esmoop.2025.104301).

Evidence synthesis

To allow for direct comparison across outcomes and for inclusion in the meta-analyses, the scales of fatigue scores were reversed, where needed, so that higher scores consistently indicate better HRQoL and less cancer-related fatigue (Supplementary Table S2, available at https://doi.org/10.1016/j.esmoop.2025.104301). Studies of patients with metastases were analysed separately from studies of early or combined cancer stages. Trials investigating intervention effects during prehabilitation or through non-active intervention such as counselling or motivational interviewing were analysed separately from trials in other timeframes relative to diagnosis or treatment or with active or structured intervention.

Inverse variance DerSimonian—Laird random-effects meta-analyses[20] were conducted if at least three comparable studies provided sufficient information. Otherwise, a descriptive synthesis of the results was carried out.

For RCTs, the main analysis was based on the maximal follow-up time. A sensitivity analysis was carried out based on minimal follow-up time after intervention, if reported. HRQoL outcomes were analysed separately by instrument and domain because of the different QoL constructs. The results for HRQoL were expressed as weighted mean differences (MD, WMD), and weighted mean change differences (MCD, WMCD), and 95% confidence intervals (CIs). General/total cancer-related fatigue was analysed across the instruments using standardised mean differences (SMD), assuming one common cause for tiredness. Established approaches were used to impute potential missing standard deviations.[21] Meta-analyses of observational studies were possible for alcoholic drinks only and the results were reported as change in HRQoL and fatigue scores per each five drinks/week.

Variation in effect estimates attributed to between-study heterogeneity was estimated by I^2.[22] The low number of studies precluded conducting a priori specified tests for small-study effects such as publication bias[23] and subgroup analyses by physical activity frequency, intensity, type, and timing with respect to treatment, and intervention setting (Supplementary Text S1, available at https://doi.org/10.1016/j.esmoop.2025.104301). The results of both quantitative and descriptive syntheses were compared against the established reference values for minimal important differences/effect sizes to identify clinically relevant effects, where relevant (Supplementary Table S4, available at https://doi.org/10.1016/j.esmoop.2025.104301).

Evidence grading criteria

The CUP Global independent Expert Committee on Cancer Survivorship provided preliminary assessments on the quality of the evidence. The independent CUP Global Expert Panel graded the evidence strength as strong (subgrades: high or moderate certainty of an effect, or substantial effect unlikely) or weak (subgrades: low or very low certainty of an effect), based on pre-defined criteria including the quantity, consistency, magnitude, and precision of the summary estimates, evidence of biological gradient, the study design, RoB, and generalisability of the results (Supplementary Table S5, available at https://doi.org/10.1016/j.esmoop.2025.104301). The grading criteria for cancer survivors were recently reviewed by the Expert Committee and Panel as part of this CUP Global work area to ensure their applicability to this population.[24]

RESULTS

Figure 1 shows the flowchart of the search and Supplementary Table S6, available at https://doi.org/10.1016/j.esmoop.2025.104301, shows the excluded publications. Overall, 61 publications, 31 from RCTs and 30 from cohort studies, were included. Study details are presented in Supplementary Tables S7-S11 and S12-S15, available at https://doi.org/10.1016/j.esmoop.2025.104301, respectively.

Overall description of RCTs

Thirty-one publications from 30 RCTs were included.[25-55] Fourteen RCTs were from Europe,[25,27,29-31,33,35,38,40-42,49,52,54,55] nine from Asia,[32,34,36,44-47,51,53] six from North America,[26,28,37,39,43,50] and one from South America.[48] All had a parallel design, and six were pilot[41,43,45,50,51,54] and three were feasibility trials.[32,46,48] Three trials included only colon cancer,[26,40,41] and four only rectal cancer survivors.[35,37,38,45] Fourteen trials included individuals both with or without metastases[25,28,30,32,33,35,37,41,43,46,48,49,52-55] (percentage of metastases mostly unclear), two included only metastatic cancers,[31,42] and one did not report on cancer stage.[47] The duration of interventions ranged from 15 days[49] to 1 year.[32] The median study size was 47 participants (range 23-409).

Overall description of observational studies

Thirty publications of 13 observational studies were included.[56-85] Five studies (16 publications) were conducted in the Netherlands,[56,57,60,61,65-67,69-71,75,76,79,81,82,84] two (five publications) in Germany,[58,59,74,77,83] two (three publications) in the United States,[62,72,73] and one study each in Australia (two publications)[63,64] and Sweden.[80] One publication was a consortium from multiple countries[68] and two were of unclear location.[78,85] Eleven publications included survivors both with or without metastases,[58,59,63,64,74-77,80,83,84] wherein percentage of metastases ranged from 2.1%[76] to 57.3%.[77] Two publications included only survivors with metastases,[82,85] 13 included stage I-III,[56,57,60,61,65-71,79,81] three included stage II,[62,72,73] and one included stage II-III.[78] The median study size was 453 participants (range 138-1966).

Physical activity

Physical activity/exercise randomised controlled trials. There were 18 physical activity RCTs (18 publications, median study size 39, range 23-223) (Supplementary Table S7, available at https://doi.org/10.1016/j.esmoop.

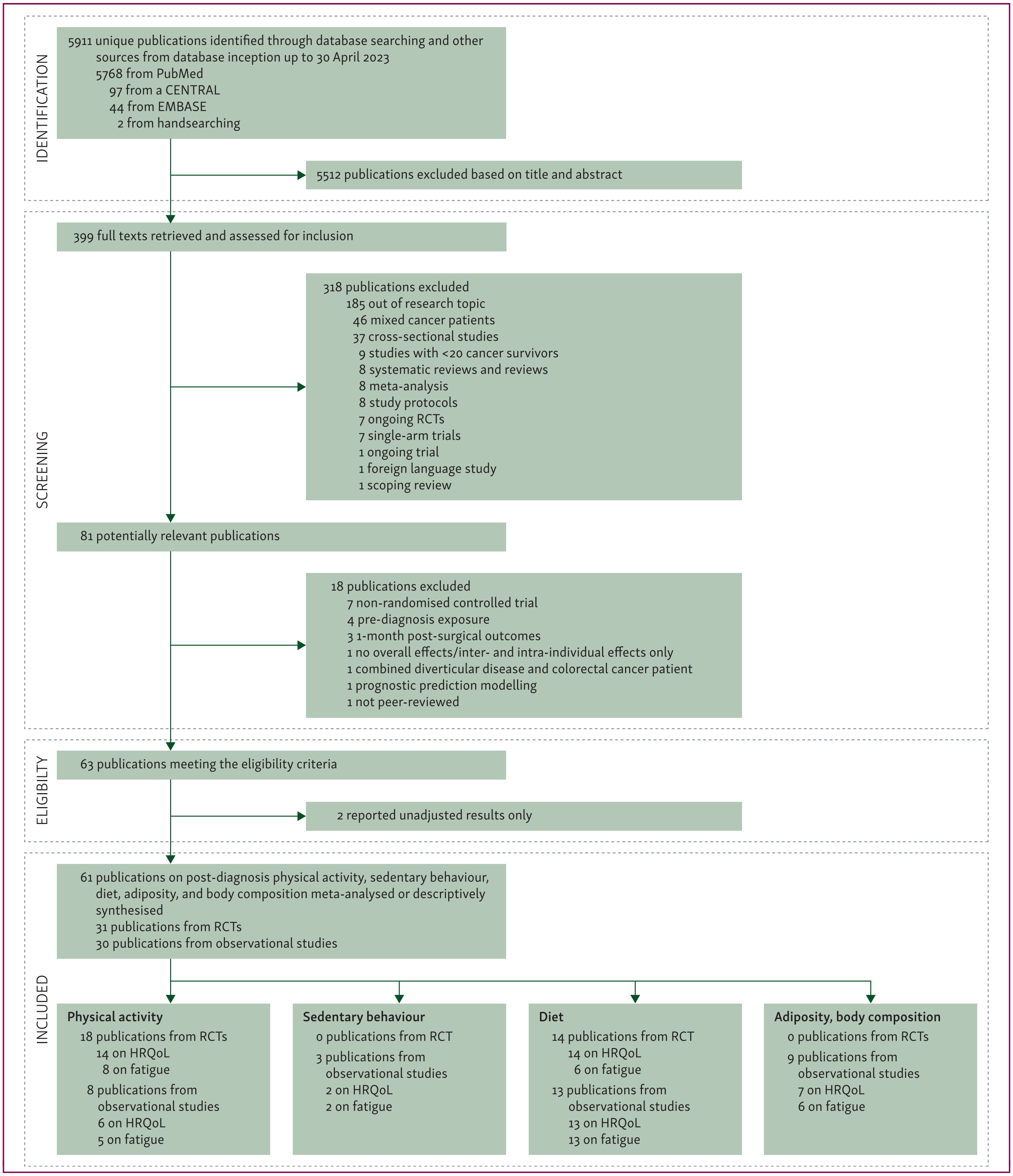

Figure 1. Flowchart of the search.
HRQoL, health-related quality of life; RCT, randomised controlled trial.

2025.104301).[25-42] The intervention was combined aerobic and resistance exercise in seven trials,[25,30,33,34,40-42] aerobic exercise in two,[26,28] interval training in three,[31,35,37] walking in two,[27,38] and yoga[29] and qigong[36] in one each, while two trials did not provide further definition.[32,39] The control groups were usual care in 12 trials,[26,27,29,31,32,34-38,40,41] and waitlist controls,[28,42] attention controls,[33,39] or lower-intensity exercise[25,30] in two trials each. The intervention was supervised in six trials,[25,30,31,33,35,42] non-supervised in eight,[26-28,32,34,36,38,39] and a mixture in four.[29,37,40,41]

Intervention was group-based in 4 trials,[25,29,30,42] individualised in 11,[26-28,31-34,37-40] and mixed in 3.[35,36,41] The intervention occurred during adjuvant chemoradiotherapy and before surgery in three prehabilitation trials,[35,37,38] after surgery in one,[33] during adjuvant treatment in four,[25,30,36,40] during and/or after adjuvant treatment in two,[29,41] after adjuvant treatment in six,[26-28,32,34,39] before planned liver resection in one,[31] and during palliative chemotherapy in one.[42]

Results of meta-analyses. Seven RCTs were included in meta-analyses[26-29,34,36,41] (Figure 2, Supplementary Figures S1-S14, available at https://doi.org/10.1016/j.esmoop.2025.104301): four investigated exercise effects after treatment completion, one during treatment, one the effects of yoga after treatment, and one the effects of Baduanjin qigong during treatment. No association was observed between physical activity interventions with global HRQoL measured by the Functional Assessment of Cancer Therapy-Colorectal (FACT-C; WMD = 4.86, 95% CI −0.76 to 10.48, I^2 = 43%, 257 participants, four trials[27-29,34,38] and WMCD = 2.43, 95% CI −0.54 to 5.39, I^2 = 41%, 242 participants, four trials[26-28,34]). Physical activity interventions resulted in borderline improvements on both physical and emotional well-being as measured by FACT-C/FACT-G (WMD = 1.03, 95% CI −0.01 to 2.08, I^2 = 0% and WMD = 1.08, 95% CI 0.00-2.15, I^2 = 36%, respectively, 257 participants, four trials), but not when using WMCDs (physical: WMCD = 0.25, 95% CI −0.50 to 1.00, I^2 = 0%; emotional: WMCD = −0.03, 95% CI: −0.88 to 0.82, I^2 = 52%, 203 participants, three trials[27,28,34]). Sensitivity analyses using SMDs instead of WMDs and based on results immediately after intervention showed, in general, no intervention effects. A non-significant reduction in fatigue [combined FACT/Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F), brief fatigue inventory (BFI), Multidimensional Fatigue Inventory (MFI)] was observed (SMD = 0.25, 95% CI: −0.04 to 0.55, I^2 = 40%, 327 participants, five trials[28,29,34,36,41]).

Studies excluded from the meta-analyses. Eleven publications were descriptively reviewed, including four prehabilitation or presurgical intervention trials,[31,35,37,38] three peri-treatment,[25,30,40] and four post-treatment trials[32,33,39,42] implementing a variety of exercise programmes with different modalities or aims (Table 1). The results were generally null, except for two trials that reported improved Medical Outcomes Study Short Form 36 Health Survey (SF-36) global and mental scores after high-intensity cycling training versus usual care in survivors with metastases,[31] as well as an improvement in physical functioning score assessed by the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-C30 (EORTC-QLQ-C30) and lower physical and general fatigue as assessed by MFI in a supervised exercise versus usual care trial in colon cancer survivors undergoing chemotherapy.[40]

Adverse events. Eleven of the trials (61%) reported information on adverse events (Supplementary Table S11, available at https://doi.org/10.1016/j.esmoop.2025.104301). None reported serious exercise-related adverse events. Four reported minor adverse events, such as musculoskeletal injuries, chest or muscle pain, dizziness,

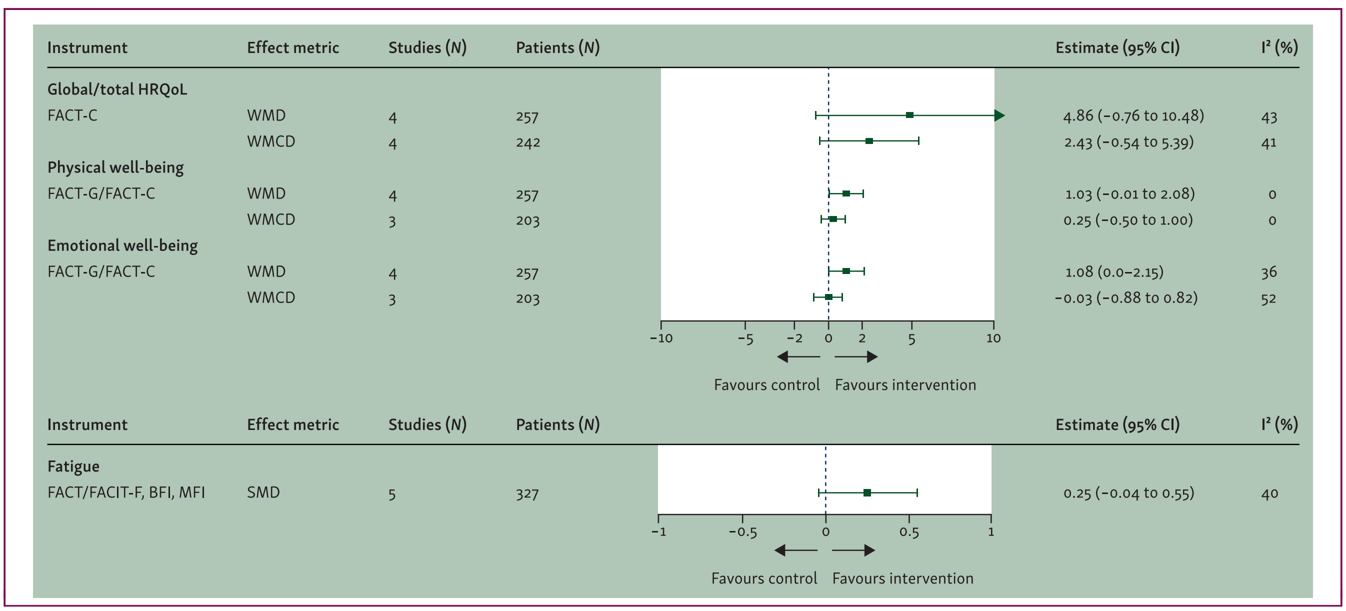

Figure 2. Summary results of meta-analyses on physical activity interventions and health-related quality of life (HRQoL) and cancer-related fatigue. To allow for direct comparison across outcomes, the scales of fatigue scores were reversed, where needed, so that higher scores consistently indicate better HRQoL and less cancer-related fatigue.

BFI, Brief Fatigue Inventory; CI, confidence interval; FACIT-F, Functional Assessment of Chronic Illness Therapy—Fatigue; FACT-C, Functional Assessment of Cancer Therapy-Colorectal; FACT-F, Functional Assessment of Cancer Therapy Scale—Fatigue; FACT-G, Functional Assessment of Cancer Therapy-General; MFI, Multidimensional Fatigue Inventory; SMD, standardised mean difference; WMCD, weighed mean change difference; WMD, weighed mean difference.

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Table 1. Characteristics and results of the descriptively reviewed randomised controlled trials of physical activity interventions and health-related quality of life (HRQoL) and cancer-related fatigue in colorectal cancer survivors

Author, year Country	Intervention and comparator details	Timeframe Time point	Int *n*/Ctrl *n*	Cancer site Stage	Global/total HRQoL score				Physical/functional HRQoL score			Emotional/mental HRQoL score			Total cancer-related fatigue		
					EORTC QLQ-C30	FACT-G	FACT-C	SF12/36	EORTC QLQ-C30	FACT-G	SF12/36	EORTC QLQ-C30	FACT-G	SF12/36	EORTC QLQ-C30	MFI	FACIT-F FACT-F
Prehabilitation																	
Morielli, 2023[37] Canada	High-intensity interval/ moderate-to-vigorous training versus usual care	Prehabilitation before surgery 5-6 weeks	18/18	Rectum II-IV	$P =$ 0.56[a]	—	—	—	$P =$ 0.051[a]	—	—	$P =$ 0.028[a]	—	—	$P =$ 0.28[a]	—	—
Loughney, 2021[35] UK	High-intensity aerobic interval training versus usual care	Prehabilitation before surgery 9 weeks	17/16	Rectum II-IV	$P =$ 0.668[a]	—	—	—	$P =$ 0.782[a]	—	—	$P =$ 0.132[a]	—	—	$P =$ 0.603[a]	—	—
Moug, 2019[38] UK	Moderate-intensity walking programme versus usual care	Prehabilitation before surgery 13-17 weeks	24/24	Rectum M0	—	—	—	—	—	—	—	—	—	—	−6.6 (−21.7 to 8.5)[a]	—	—
Metastases only																	
Dunne, 2016[31] UK	High-intensity cycling interval training versus usual care	Prehabilitation before liver resection 4 weeks	20/18	CRC CRLM	—	—	—	$P =$ 0.028[a]	—	—	$P =$ 0.102[a]	—	—	$P =$ 0.037[a]	—	—	—
Zimmer, 2018[42] Germany	Supervised programme (endurance/resistance/ balance training) versus written standard recommendations	After treatment 12 weeks	17/13	CRC IV	—	$P =$ 0.28[a]	—	—	—	$P =$ 0.51[a]	—	—	$P =$ 0.41[a]	—	—	—	—
Active control																	
Ax, 2022[25] Sweden	High-intensity versus low-to-moderate intensity	During treatment 18 months	11/12	CRC II-IV	[b]	—	—	—	[b]	—	—	[b]	—	—	[b]	—	—
Demmelmaier, 2021[30] Sweden	High-intensity versus low-to-moderate intensity	During treatment 6 months	11/12	CRC II-IV	1.3 (−9.7 to 12.3)	—	—	—	—	—	—		—	—		1.1 (−3.4 to 5.5)	−2.4 (−9.2 to 4.5)
Insufficient format of data to allow meta-analysis																	
Houborg, 2006[33] Denmark	Mobilisation, strength training of extremities, and aerobic training versus activities not increasing muscular strength or aerobic capacity	After surgery 30 days	60/59	CRC Dukes' type: A-D	[b]	—	—	—	—	—	—	—	—	—	—	—	—
Van Vulpen, 2016[40] The Netherlands	Supervised exercise versus usual care	During treatment 36 weeks	17/16	Colon M0	−2.6 (−15.7 to 10.6)	—	—	—	**12.3 (3.3 to 21.4)**	—	—	−5.1 (−16.0 to 5.9)	—	—	−5.5 (−20.8 to 9.9)	**−2.7 (−5.2 to −0.1)**	—
Non-active intervention																	
Pinto, 2013[39] USA	Home-based moderate intensity (telephone counselling support) versus contact control	After treatment 12 months	20/26	CRC I-III	—	—	0.1 (−6.9 to 7.1)[c]	—	—	—	−0.3 (−8.0 to 7.5)[c]	—	—	—	—	—	0.5 (−3.0 to 4.1)[c]
Ho, 2020[32] China	Moderate-to-vigorous intensity (motivational support to increase from 30 to 60 min/5 days a week) versus usual care (± diet)	After treatment 24 months	111/112	CRC I-IV	—	−1.1 (−4.0 to 1.9)	−0.7 (−4.4 to 3.0)	—	—	—	0.2 (−1.7 to 2.1)	—	—	−1.2 (−3.3 to 0.80)	—	—	—

Results are reported as unstandardised mean difference (95% confidence interval), unless otherwise specified. *P* values are reported when no other measure of effect was provided. Empty cells indicate effects not investigated by authors.
Black: Trivial/ not significant/ non-evaluable effect.
Dark green: Clinically relevant positive effect; **Light green**: Small positive effect.
CRC, colorectal; CRLM, colorectal liver metastasis; Ctrl, control; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-C30; FACIT-F, Functional Assessment of Chronic Illness Therapy—Fatigue; FACT-C, Functional Assessment of Cancer Therapy-Colorectal; FACT-F, Functional Assessment of Cancer Therapy Scale—Fatigue; FACT-G, Functional Assessment of Cancer Therapy-General; Int, intervention; MFI, Multidimensional Fatigue Inventory; SF-12/36, Medical Outcomes Study Short Form 12/36 Health Survey.
[a]Mean/median change difference.
[b]Assessed but not formally analysed.
[c]Difference between counselling and control, no difference between supplements and control, effect not reported but narratively described.

and treatment-related side-effects in the intervention group[25,30,35,38]; two reported adverse events in the control group[29,42]; and five reported no adverse events.[26,31,37,40,41]

RoB. Attendance was reported as good-to-excellent in 5[31,32,37,40,42] of the 10 supervised/mixed trials. Adherence was reported as good-to-excellent in 8[26-28,34,35,38,40,41] (62%) of the 13 RCTs reporting results (44% across all trials) (Supplementary Table S8, available at https://doi.org/10.1016/j.esmoop.2025.104301).

All studies had an overall high RoB. Most studies[25,27,29,31-35,37,38,40-42] (67%) had low RoB regarding the randomisation process, while the majority had some concerns regarding deviations from intended interventions (61%; mainly non-adherence to assigned intervention), and selection of the reported result[25-31,33-37,40-42] (78%). Over half of the studies had high RoB regarding missing outcome data[25-27,29-31,33,37,38,41,42] (56%) (overall percentage of missing outcome data ranged from 7.9% to 38.4%) and measurement of the self-reported outcome[25-27,29,30,32,34,36,39,40,42] (61%), which were the main reasons for the overall high RoB in these studies (Supplementary Figure S15, available at https://doi.org/10.1016/j.esmoop.2025.104301).

Physical activity observational studies. Eight publications (five studies)[56-63] investigated longitudinal moderate-to-vigorous-intensity[56] or light-intensity[60] physical activity; longitudinal recreational physical activity[63]; pre-to-post-diagnosis change in physical activity[58] or recreational physical activity[62]; and pre-to-post-surgery change in moderate-to-vigorous physical activity[61] (Supplementary Tables S12 and S13, available at https://doi.org/10.1016/j.esmoop.2025.104301). Studies utilised validated[56-62] or reliability-tested[63] questionnaires to assess physical activity. The low number of studies per association precluded any meta-analysis. Studies generally showed that longitudinally higher physical activity based on repeated measures and pre-to-post diagnosis or post-diagnosis increased physical activity were associated with better global HRQoL. The few studies on physical activity decreases compared with no changes did not observe any differences. Associations with physical functioning scores were similar with those of global/total HRQoL scores but associations with emotional/mental scores were less clear and mostly null or of trivial magnitude. Longitudinally increased physical activity and pre-to-post diagnosis improvements in physical activity were associated with less general/total fatigue and its dimensions, the latter not as pronounced. These associations were not mediated through body mass index (BMI).[57]

RoB. Most studies had critical[56,58,61-63] and one had serious RoB due to confounding. Four studies (five publications)[58,59,61-63] had critical and one[56] had serious RoB due to departures from intended exposures. All studies had serious RoB in selection of participants into the study and outcome measurement. One study (two publications)[58,59] had serious RoB due to exposure misclassification, and another[62] had serious RoB due to missing data (Supplementary Figure S16, available at https://doi.org/10.1016/j.esmoop.2025.104301).

Evidence conclusions on physical activity. The evidence conclusions were based on RCTs. The observational studies

Alcohol consumption (5 drinks/week)	Instrument	Studies (N)	Patients (N)	Estimate (95% CI)	I² (%)
Global/total HRQoL					
Total alcohol	EORTC QOL-C30	3	3535	0.57 (−0.06 to 1.21)	81
Beer	EORTC QOL-C30	3	3535	0.27 (−0.31 to 0.86)	58
Liquor	EORTC QOL-C30	3	3535	−0.34 (−1.20 to 0.52)	0
Wine	EORTC QOL-C30	3	3535	1.43 (−0.14 to 3.00)	90
Physical functioning					
Total alcohol	EORTC QOL-C30	3	3535	−0.31 (−1.29 to 0.67)	94
Beer	EORTC QOL-C30	3	3535	0.23 (−0.20 to 0.66)	36
Liquor	EORTC QOL-C30	3	3535	0.15 (−0.88 to 1.18)	59
Wine	EORTC QOL-C30	3	3535	1.16 (−0.09 to 2.24)	87
Emotional functioning					
Total alcohol	EORTC QOL-C30	3	3535	0.30 (−0.19 to 0.79)	68
Beer	EORTC QOL-C30	3	3535	0.20 (−0.38 to 0.78)	49
Liquor	EORTC QOL-C30	3	3535	−0.18 (−0.78 to 0.43)	0
Wine	EORTC QOL-C30	3	3535	1.16 (−0.15 to 1.61)	74
Fatigue					
Total alcohol	EORTC QOL-C30	3	3535	0.95 (0.17–1.73)	81
Beer	EORTC QOL-C30	3	3535	0.72 (0.31–1.14)	0
Liquor	EORTC QOL-C30	3	3535	−0.23 (−0.25 to 0.79)	0
Wine	EORTC QOL-C30	3	3535	1.94 (0.13–3.76)	92

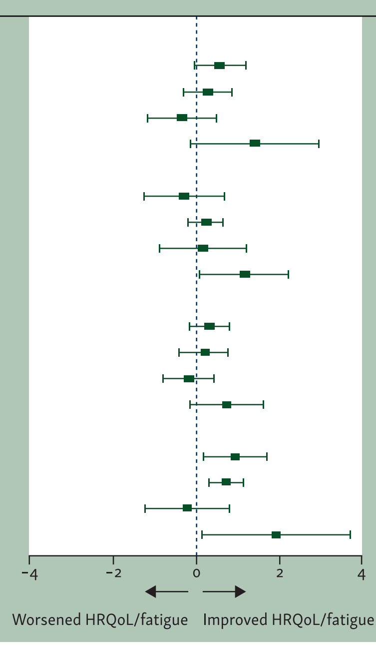

Figure 3. Summary results of meta-analyses on alcohol consumption and health-related quality of life (HRQoL) and cancer-related fatigue. To allow for direct comparison across outcomes, the scales of fatigue scores were reversed, where needed, so that higher scores consistently indicate better HRQoL and less cancer-related fatigue. CI, confidence interval; EORTC-QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-C30.

were reviewed but did not influence the conclusions. The evidence of a beneficial effect of physical activity on total, physical, and emotional HRQoL and cancer-related fatigue was graded as very low certainty (Figure 3, Supplementary Table S14, available at https://doi.org/10.1016/j.esmoop.2025.104301).

Sedentary behaviour

Sedentary behaviour observational studies. Three publications (two longitudinal cohorts)[56,57,64] were included. One studied accelerometer-based sedentary behaviour[56] and another on the same population investigated television viewing.[64] Higher accelerometer-measured sedentary behaviour was associated with worse global and physical EORTC-QLQ-C30 scores.[56] Higher self-reported television viewing was statistically significantly associated with worse total, physical, and emotional FACT-C scores.[64] The association of accelerometer-measured sedentary behaviour and general/total fatigue [EORTC-QLQ-C30, Checklist Individual Strength (CIS)], and subjective and activity dimensions (CIS)[56] was partially mediated by BMI and handgrip strength[57] (Supplementary Tables S15 and S16, available at https://doi.org/10.1016/j.esmoop.2025.104301).

RoB. The two studies[56,64] had critical or serious RoB due to confounding, serious RoB in participant selection, moderate RoB in the classification of exposures, serious or critical RoB due to departures from intended exposures, low RoB due to missing data, serious RoB due to outcome measurement, and some concerns regarding selection of reported results (Supplementary Figure S17, available at https://doi.org/10.1016/j.esmoop.2025.104301).

Evidence conclusions on sedentary behaviour. The quality of evidence was graded as very low certainty owing to very limited data and high RoB (Figure 3, Supplementary Table S17, available at https://doi.org/10.1016/j.esmoop.2025.104301).

Diet

Dietary randomised controlled trials. Thirteen RCTs (14 publications[32,43-55]) pertained to dietary and lifestyle patterns, probiotic use, and dietary supplements. Control groups were mostly usual care or placebo. The low number of studies per association precluded any meta-analysis. The results were descriptively reviewed (Table 2, Supplementary Table S9, available at https://doi.org/10.1016/j.esmoop.2025.104301).

Dietary/nutritional interventions. Four trials (five publications[32,43,44,52,55]) were dietary and nutritional interventions, including one 2 $\times$ 2 factorial dietary and physical activity trial,[32] one personalised nutrition intervention,[44] one web-based dietary intervention pilot and feasibility trial,[43] and one three-arm trial with an individualised dietary counselling for regular food-based therapeutic diet based on dietary deficits, a high protein liquid supplement, and a control arm (two publications, investigating outcomes assessed at 3 months[55] and a median 6.5 years after intervention[52]). Except for a study on web-based diet counselling aimed at increasing whole grains, vegetables, and fish and decreasing alcohol, soft drinks, and processed meat that showed no intervention effects,[43] the other trials showed small to trivial improvement in global HRQoL scores favouring dietary interventions. Only the personalised nutrition trial reported large effects but in a population with suspected malnutrition.[44] With respect to the domains of the HRQoL score, the results on physical and emotional/mental health scores largely reflected those of global HRQoL scores, but with attenuated effects. In addition, the personalised nutrition intervention[44] and the long-term individualised dietary counselling[52] reported improved general/total fatigue scores, but no effect was observed in the web-based diet counselling study.[43]

Probiotic/symbiotic interventions and HRQoL. Five trials (five publications[45,47,49,51,53]) tested different probiotic/symbiotic interventions compared with placebo or no intervention (Table 2), of which only the microbial cell preparation (MCP) plus omega-3 trial[47] consistently resulted in clinically relevant effects of better global, physical, and emotional/mental HRQoL scores and less fatigue. The use of lactic acid bacteria plus fermentable fibres only resulted in better global HRQoL but not physical or emotional score.[49]

Dietary supplements interventions and HRQoL. Five trials (six publications[46,48,50,52,54,55] investigated different dietary supplement interventions compared with placebo or usual care (Table 2), of which the creatine monohydrate supplementation trial showed small but clinically relevant higher global and emotional HRQoL scores,[54] and the Korean red ginseng trial[46] that reported on 11 dimension-specific fatigue scores and indicated better but mostly statistically non-significant scores compared with placebo (9/11 95% CIs crossing null) (Supplementary Figure S18, available at https://doi.org/10.1016/j.esmoop.2025.104301).

Adverse events. Seven of the 13 trials (54%) reported information on adverse events (Supplementary Table S9, available at https://doi.org/10.1016/j.esmoop.2025.104301). In the *Lactobacillus plantarum*[45] and Lacidofil®[51] trials, adverse effects were similar across groups. The MCP and omega-3 fatty acid intervention significantly improved chemotherapy side-effects.[53] The Korean red ginseng trial reported similar proportions of adverse events across groups but higher proportion of severe neutropenia in the intervention group.[46] The probiotic/symbiotic trial reported no adverse events.[49] The creatine monohydrate supplement trial reported no complaints in the intervention group.[54] The kefir trial reported increased gastrointestinal complaints and constipation in the intervention group.[53]

RoB. Adherence to the allocated interventions was not reported or not evaluable in the dietary and lifestyle patterns and probiotic trials. In the supplement trials, when reported, adherence was $\geq$85% (Supplementary

Table 2. Characteristics and results of the randomised controlled trials of diet/nutrition interventions and health-related quality of life (HRQoL) and cancer-related fatigue in colorectal cancer survivors

Author, year Country	Intervention and comparator details	Timeframe Time point	Int n/Ctrl n	Cancer site, stage	Global/total HRQoL score						Physical/functional HRQoL score					Emotional/mental HRQoL score					Total cancer-related fatigue		
					EORTC-QLQ-C30	FACT-G	FACT-C	FACIT-F	SF-12/36	GIQLI	EORTC-QLQ-C30	FACT-G	FACT-C	SF-12/36	GIQLI	EORTC-QLQ-C30	FACT-G	FACT-C	SF-12/36	GIQLI	EORTC-QLQ-C30	FACIT-F	BFI
Diet/nutrition																							
Wang, 2023[43] USA	Web-based counselling versus wait list	During/after treatment 24 weeks	22/20	CRC I-IV	−4.0 −13.7 to 5.7)	—	—	—	—	—	0.0 (−3.9 to 3.9)	—	—	—	—	7.2 (−4.7 to 19.1)	—	—	—	—	−4.1 (−15.8 to 7.6)	—	—
Wang, 2022[44] China	Personalised nutrition versus usual care	During/after treatment 6 months	28/28	CRC I-III	**29.8 (27.6-32)**	—	—	—	—	—	**17.6 (15.7-19.6)**	—	—	—	—	**28 (25.3, 30.7)**	—	—	—	—	**−39.3 (−41.7 to −36.9)**	—	—
Ho, 2020[32] China	Diet versus usual care (± PA)	After treatment 24 months	111/112	CRC I-IV	—	**3.1 (0.2-6)**	3.3 (−0.4 to 7)	—	—	—	—	—	—	2.6 (0.7-4.5)	—	—	—	—	0.4 (−1.6 to 2.4)	—	—	—	—
Ravasco, 2012[52] Portugal	Dietary counselling versus usual care	During treatment 6.5 years	34/26	CRC I-IV	$P < 0.002$[a,b]	—	—	—	—	—	$P < 0.002$[a,b]	—	—	—	—	$P < 0.002$[a,b]	—	—	—	—	$P < 0.002$[a,b]	—	—
Ravasco, 2005[55] Portugal	Dietary counselling versus usual care	During treatment 3 months	37/37	CRC I-IV	[c]	—	—	—	—	—	[c]	—	—	—	—	[c]	—	—	—	—	[c]	—	—
Probiotics																							
Yoon, 2021[45] Korea	*Lactobacillus plantarum* versus PBO	Post-operative 3 weeks	19/17	REC I-III	5.5 (−6.4 to 17.4)	—	—	—	—	—	2.1 (−6.9 to 11.1)	—	—	—	—	—	—	—	—	—	—	—	—
Golkhalkhali, 2018[47] Malaysia	MCP + Ω-3 versus PBO	During treatment 6 months	70/70	CRC NR	**27.7 (26.8-28.6)**	—	—	—	—	—	**16.9 (15.9-17.9)**	—	—	—	—	**11.9 (11.1-12.7)**	—	—	—	—	**−25.1 (−26.2 to −24.0)**	—	—
Theodoropoulos, 2016[49] Greece	LAB versus PBO (+ fibres)	Post-operative 6 months	38/37	CRC 0-IV	—	—	—	—	—	**6.5 (5.7-7.3)**	—	—	—	—	[c]	—	—	—	—	$P > 0.05$	—	—	—
Lee, 2014[51] Korea	Lactobacillus (Lacidofil®) versus PBO	After treatment 12 weeks	28/32	CRC II-III	—	−3.5 (−11.3 to 4.3)	1.0 (−1.1 to 3.1)	—	—	—	—	−1.0 (−30 to 1.0)	—	—	—	—	−0.5 (−2.7 to 1.7)	—	—	—	—	0.5 (−0.1 to 1.1)	—
Can, 2009[53] Turkey	Kefir versus control	During treatment 6 cycles	17/20	CRC II-IV	—	−3.1 (−11.8 to 5.6)	—	—	—	—	—	0.4 (−2.6 to 3.5)	—	—	—	—	−1.0 (−3.6 to 1.6)	—	—	—	—	—	—
Supplements																							
Kim, 2020[46] Korea	Korean red ginseng versus PBO	During treatment 16 weeks	206/203	CRC II-IV	—	—	—	2.1 (−2.9 to 7.2)	—	—	—	—	—	—	—	—	—	—	—	—	—	—	−4.4 (−9.1 to 0.3)
Ribeiro, 2017[48] Brazil	Zinc versus PBO	During treatment 4 cycles	11/14	CRC II-IV	—	—	—	7.0 (−9.7 to 23.4)	—	—	—	—	—	—	—	[c]	—	—	—	—	—	4.0 (−3.7 to 11.7)	—
Gillis, 2016[50] Canada	Whey versus PBO	Prehab 8 weeks	22/21	CRC I-III	—	—	—	—	—	—	—	—	—	—	—	—	—	—	$P = 0.3$	—	—	—	—
Norman, 2006[54] Germany	Creatine monohydrate versus PBO	During treatment 8 weeks	16/15	CRC III-IV	**5.3 (2.0-8.6)**	—	—	—	—	—	−2.5 (−5.6 to 0.6)	—	—	—	—	**6.4 (1.9-10.9)**	—	—	—	—	−4.6 (−8.9 to −0.3)	—	—
Ravasco, 2012[52] Portugal	Protein versus usual care	During treatment 6.5 years	29/26	CRC I-IV	[a,b]	—	—	—	—	—	[a,b]	—	—	—	—	[a,b]	—	—	—	—	[a,b]	—	—
Ravasco, 2005[55] Portugal	Protein versus usual care	During treatment 3 months	37/37	CRC I-IV	[c]	—	—	—	—	—	[c]	—	—	—	—	[c]	—	—	—	—	[c]	—	—

Results are reported as unstandardised mean difference (95% confidence interval), unless otherwise specified. *P* values are reported when no other measure of effect was provided.

Black: Trivial/ not significant/ non-evaluable effect.

Dark blue: Large positive effect; **Light blue**: Medium positive effect; **Dark green**: Clinically relevant positive effect; **Light green**: Small positive effect.

BFI, Brief Fatigue Inventory; CRC, colorectal; Ctrl, control; cy, cycles; EORTC-QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-C30; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; FACT-C, Functional Assessment of Cancer Therapy-Colorectal; FACT-G, Functional Assessment of Cancer Therapy-General; GIQLI, Gastrointestinal Quality of Life Index; Int, intervention; LAB, lactic acid bacteria; NR, not reported; PA, physical activity; PBO, placebo; Prehab, prehabilitation; REC, rectum; SF-12/36, Medical Outcomes Study Short Form 12/36 Health Survey.

[a]Difference between counselling and control, no difference between supplements and control, effect not reported but narratively described.

[b]Mean/median change difference.

[c]Assessed but not formally analysed.

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Table S10, available at https://doi.org/10.1016/j.esmoop.2025.104301).

Overall, 3 publications[45,51,54] had some concerns of RoB and 11 publications[32,43,44,46-50,52,53,55] had high RoB. Eight studies[32,45,46,49,50,52,54,55] had low RoB and six had some concerns[43,44,47,48,51,53] regarding the randomisation process. Six studies had high RoB in deviations from the intended intervention,[43,47-50,53] six in missing outcome data (5.9% to 58% missing in the intervention group and 0% to 42% missing in the control group of the high-risk studies),[43,46-48,50,53] and six in measurement of the outcome.[32,43,44,52,53,55] Only one study[49] had high RoB in the selection of the reported results (Supplementary Figure S19, available at https://doi.org/10.1016/j.esmoop.2025.104301).

Dietary factors observational studies. Thirteen publications (seven studies) were included.[65-77] Exposures varied greatly across publications. A meta-analysis was possible for alcohol consumption based on three studies (two publications)[65,75,76] including 3535 participants (Figure 4). The results for other exposures are descriptively reviewed (Supplementary Tables S18 and S19, available at https://doi.org/10.1016/j.esmoop.2025.104301).

Summary of evidence matrix	Global/total HRQoL	Physical HRQoL	Emotional/mental HRQoL	Cancer-related fatigue
Physical activity				
Physical activity interventions	There was a variety of studies and interventions; there was some consistency in direction of effects across studies; the meta-analyses including three to five trials indicated non-significant intervention effects based on a low number of studies with overall small magnitude of effect, and with high risk of bias			
Physical activity (prehabilitation) interventions	No meta-analysis; limited amount of evidence across three trials with mostly null results and high risk of bias			
Sedentary behaviour				
Sedentary behaviour (observational studies)	No meta-analysis; limited amount of evidence from two studies with individual results reaching statistical significance but, with an overall lack of consistency in exposure assessment (overall accelerometer based and self-reported TV watching) and high risk of bias			
Diet				
Interventions to improve diet quality	No meta-analysis; the positive effects from three trials of the four with cancer survivors of similar cancer stages were consistent but of different magnitude, and with high risk of bias		No meta-analysis; intervention effects were inconsistent across four trials, and there was a high risk of bias	
Probiotics/symbiotic interventions	No meta-analysis; limited amount of evidence across five trials investigating different probiotics/symbiotics interventions with mostly null or inconsistent results and high risk of bias			
Dietary supplements interventions	No meta-analysis; limited amount of evidence across five trials investigating different dietary interventions with mostly null or inconsistent results and high risk of bias			
Dietary and lifestyle patterns (observational studies)[a]	No meta-analysis; limited amount of evidence from three studies on different patterns with some evidence of associations but inconsistent across patterns and with critical risk of bias			
Dietary patterns (observational studies)[a]	No meta-analysis; limited amount of evidence from three studies on different patterns with mostly null or inconsistent results across patterns and with critical risk of bias			
Alcoholic drinks (total, wine, beer, liquor) (observational studies)	Meta-analyses based on three studies indicated limited evidence for HRQoL scores, and some evidence of improved fatigue scores of trivial magnitude and with high heterogeneity and critical risk of bias.			
Dietary factors (observational studies)[b]	No meta-analysis; very limited amount of evidence from only one study, with mostly null or inconsistent results and critical risk of bias			
Vitamins and fish oil supplements (observational studies)	No meta-analysis; very limited amount of evidence from only one study, with little or no evidence of effect and with critical risk of bias			
Serum 25(OH)D (observational studies)	No meta-analysis; very limited amount of evidence from only one study, with some evidence of improvement in scores but with critical risk of bias			
B-vitamin biomarkers (observational studies)	No meta-analysis; very limited amount of evidence from one pooled analysis of three studies with mostly null associations and with critical risk of bias			
Adiposity and body composition				
Body mass index (observational studies)	No meta-analysis; the evidence from seven studies was mostly null or inconsistent in the direction, and with critical risk of bias			
Waist circumference and body fat (observational studies)	No meta-analysis; very limited amount of evidence from only one study, with null results and critical risk of bias			
Skeletal muscle-related measures (observational studies)	No meta-analysis; limited amount of evidence from one to three studies, with mostly null or inconsistent results and critical risk of bias			

← Certainty of an effect for decreased score — **Conclusions key** — Certainty of an effect for improved score →

High certainty | Moderate certainty | Low certainty | Very low certainty | Low certainty | Moderate certainty | High certainty

Figure 4. Summary matrix of the evidence conclusions for physical activity, sedentary behaviour, diet, adiposity and body composition and health-related quality of life (HRQoL) and cancer-related fatigue after diagnosis of colorectal cancer.

[a]Includes a priori- and a posteriori-defined patterns and ultra-processed foods.

[b]Energy density of diet, red meat, processed meat, sugary drinks, dietary fibre, fruits and vegetables, vegetables, fruits, vitamin D intake (foods/supplements).

Results of meta-analyses on alcohol. Total alcohol, beer, liquor, and wine consumption were not associated with global/physical/emotional EORTC-QLQ-C30 HRQoL scores, except for a positive association between wine and physical functioning ($\beta_{5\ \text{drinks/week}}$: 1.16, 95% CI 0.09-2.24, $I^2 = 87\%$). In contrast, except for liquor, consumption of any alcoholic beverage ($\beta_{5\ \text{drinks/week}}$: 0.95, 95% CI 0.17-1.73, $I^2 = 81\%$), wine ($\beta_{5\ \text{drinks/week}}$: 1.94, 95% CI 0.13-3.76, $I^2 = 92\%$), and beer ($\beta_{5\ \text{drinks/week}}$: 0.72, 95% CI 0.31-1.14, $I^2 = 0\%$) was associated with trivial reductions in fatigue (Supplementary Figures S20-S23, available at https://doi.org/10.1016/j.esmoop.2025.104301).

Results of other dietary exposures. Three studies (three publications) examined a priori-defined dietary and lifestyle patterns, namely the 2018 WCRF/AICR recommendations[67,71] and a healthy lifestyle score (HLS),[74] which included components such as diet, physical activity, body weight, and alcohol consumption, with higher scores indicating healthier habits. The associations with adherence to these patterns were inconsistent for global HRQoL, but improved physical functioning was reported. Adherence to the HLS score[74] was associated with better total fatigue score; while adherence to the 2018 WCRF/AICR recommendations[67,71] was inconsistently associated with total fatigue scores, reduced subjective and activity fatigue scores were observed. One study additionally examined the 2018 WCRF/AICR dietary sub-score[67] and found null associations with HRQoL and fatigue scores. Another study examined pre-to-post diagnosis changes in adherence to the American Cancer Society (ACS)-based dietary quality index[72] and reported inconsistent associations with HRQoL scores. One study examining ultra-processed food consumption, defined by the NOVA food-processing classification system with modifications to comply with national guidelines and the WCRF/AICR cancer prevention recommendations,[86] reported mostly non-significant associations with worse HRQoL and higher fatigue scores.[65] One study examined a posteriori-defined dietary patterns (Western, fruit and vegetables, bread and butter, high carbohydrates), generally showing null associations.[77] Three publications (one study) examined intakes of vegetables,[66] fruits,[66] dietary fibre,[66] food energy density,[65] red and processed meat,[65] sugar-sweetened beverages,[65] and vitamin D (dietary and/or supplement use),[69] with most associations being null or inconsistent across the HRQoL and fatigue scores. One pooled analysis (three studies) examined pre-to-post diagnosis changes in circulating B-vitamins,[68] with generally null results apart from the inverse associations of hydroxykynurenine ratio (an inverse functional marker of vitamin B6 status) with global and physical HRQoL scores. One study reported that higher circulating 25-hydroxyvitamin D3 (25(OH)D_3)[69] levels and non-deficient versus deficient status were associated with better global HRQoL and total and dimension-specific fatigue outcomes. Four publications (four studies) investigated use of different dietary supplements[68-70,73] with mostly null associations.

RoB. All studies had critical RoB due to confounding and serious RoB in selection of participants and in outcome measurement. Seven[65-67,71,74,76,77] and two studies[70,75] had serious and critical RoB in exposure classification, respectively. Ten publications[65-68,70-72,75-77] had critical RoB and one[73] had serious RoB due to departures from intended exposures. Four[68,69,71,74] and three[72,73,77] studies had critical and serious RoB due to missing data, respectively. One study[66] had serious RoB due to selective reporting (Supplementary Figure S24, available at https://doi.org/10.1016/j.esmoop.2025.104301).

Evidence conclusions on diet. The evidence on diet was highly fragmented across multiple dietary interventions and exposures. Evidence of an effect of dietary/nutritional interventions was graded as low certainty for global and physical HRQoL, and as very low certainty for emotional HRQoL and fatigue. Evidence for probiotics and dietary supplement interventions and all observational evidence were graded as very low certainty for all HRQoL domains and fatigue. Limited and inconsistent evidence from few studies and high likelihood of bias led to these evidence conclusions (Figure 3, Supplementary Table S20, available at https://doi.org/10.1016/j.esmoop.2025.104301).

Adiposity and body composition

Measures of adiposity and body composition in observational studies. Nine publications (nine studies)[63,78-85] reported on several adiposity and body composition measures. The low number of studies per association precluded any meta-analysis. The results were descriptively reviewed (Supplementary Tables S21 and S22, available at https://doi.org/10.1016/j.esmoop.2025.104301). Seven publications (seven studies) investigated BMI with different HRQoL and fatigue scores.[63,78-80,83-85] One of five studies investigating BMI and global HRQoL observed a longitudinal association of higher BMI and better HRQoL,[79] whereas the rest reported no associations.[63,80,83,85] When focusing on the domains, the results were conflicting in four studies in relation to physical scores.[78-80,83] No associations were reported with emotional/mental scores in two studies reporting results.[78,80] Associations with fatigue were conflicting in four studies reporting results.[79,80,83,84] One study reported lowered SF-36 vitality scores for underweight versus non-underweight and obese versus overweight patients.[78] Another study reported lower FACT-C score in patients with underweight and obesity compared with those who were normal weight and overweight, though the results were not statistically significant.[63] The only study on waist circumference reported no associations with HRQoL and fatigue scores.[79] Three publications (two studies) investigated various body fat measurements.[79,81,83] Higher body fat percentage was longitudinally associated with better global and physical HRQoL and worse fatigue

(EORTC-QLQ-C30 but not CIS) in one study.[79] No associations were reported for visceral and subcutaneous fat area with global and physical HRQoL in another study[83] and with fatigue in two studies.[81,83] Four studies examined skeletal muscle-related measures, including mid-upper arm muscle circumference,[79] skeletal muscle index,[81] skeletal muscle radiodensity,[81] and skeletal muscle mass[82,83] with mostly null associations, except for a positive association of mid-upper arm muscle circumference with physical score[79] and an association between stable or gain versus loss in percentage muscle mass and better global HRQoL and reduced fatigue.[82]

RoB. All studies had critical RoB due to confounding and due to departures from intended exposures and serious RoB due to outcome measurement. Seven studies[63,78,79,81,83-85] had serious RoB in selection of participants. Two studies[63,84] had serious RoB in exposure classification and four[78,80,82,85] had serious RoB due to missing data (Supplementary Figure S25, available at https://doi.org/10.1016/j.esmoop.2025.104301).

Evidence conclusions on adiposity and body composition. The evidence of anthropometric factors and HRQoL and fatigue outcomes was limited in quantity, mostly null and/or inconsistent, and of high likelihood of bias; as such, the evidence was judged as very low certainty of an effect (Figure 3, Supplementary Table S23, available at https://doi.org/10.1016/j.esmoop.2025.104301).

DISCUSSION

This comprehensive review systematically examined and meta-analysed interventional and observational evidence on the impact of post-diagnosis physical activity, sedentary behaviour, diet, and adiposity and body composition measures in colorectal cancer survivors on global, physical, and emotional/mental HRQoL and total cancer-related fatigue and its dimensions. Meta-analyses were possible for physical activity trials and for alcohol consumption in observational studies. Physical activity interventions showed results indicative of improved HRQoL and reduced fatigue but were graded as ‘very low certainty’. Interventional evidence from the few trials that aimed at improving diet quality suggested improvements in HRQoL but were graded as ‘low certainty’. Evidence from trials specifically on probiotics and supplement use was mostly null and were graded as ‘very low certainty’. Alcohol consumption (total, beer, and wine) was associated with less fatigue, but not with HRQoL, across a few observational studies, although there was high between-study heterogeneity leading to a ‘very low certainty’ grading. The rest of the observational evidence on other dietary exposures, sedentary behaviour, and adiposity and body composition was too inconsistent or scarce to allow strong conclusions to be reached.

Exercise has been acknowledged as beneficial for HRQoL and cancer-related fatigue in guidelines for cancer survivors.[87] In the present meta-analyses, physical activity interventions showed positive trends towards improved HRQoL and reduced fatigue, but included few and often small studies and did not provide strong evidence of an effect. Trials not included in these meta-analyses corroborated the meta-analyses’ results, while observational studies generally associated higher activity levels with only slight/trivial improvements in HRQoL and reduced fatigue. Multiple reasons could lead to this observation. Trials had small sample sizes, limiting the power of analyses, while suboptimal adherence to the interventions may bias the results towards the null. It is also possible that only patients who were physically fit were able, or agreed, to participate in the exercise trials. In contrast, less than half of the trials (43%) excluded survivors who were already exercising sufficiently (at least 150 min/week). A physical activity trial in an already physically active population leaves little room to investigate intervention effects. No screening was also done for HRQoL and fatigue scores at baseline, limiting the exclusion of patients with already good HRQoL and fatigue scores. The results of other meta-analyses on HRQoL and fatigue outcomes[13,88,89] are in line with ours, indicating positive but not significant trends towards improved HRQoL and fatigue. Other meta-analyses have reported statistically significant intervention effects for HRQoL[90] and fatigue[15,90,91] outcomes. However, these meta-analyses pooled trials irrespective of cancer stage, timeframe, and outcome tool,[90] or included behavioural physical activity promotion or multimodal interventions with physical and mental rehabilitation components.[15,91] Published meta-analyses have also shown that physical activity interventions are well tolerated in colorectal cancer survivors,[90] which is in line with our finding of minimal adverse effects of the interventions. Apart from the potential benefits on HRQoL and cancer-related fatigue, being physically active may also have beneficial effects on colorectal cancer survival.[10]

Evidence from the few dietary/nutritional interventions suggested mostly small/trivial improvements in global HRQoL. Results were similar for dietary/nutritional interventions and emotional and physical HRQoL, and fatigue outcomes. Observational evidence indicated that adherence to healthy lifestyle patterns may improve HRQoL and fatigue outcomes and following unhealthy patterns or consuming unhealthy foods may have adverse results. A commonly observed dietary change in cancer survivors is the introduction of dietary supplements after diagnosis.[92,93] In the present review, evidence from trials on use of supplements and probiotics was heterogeneous, mostly null, and without sufficient data for meta-analyses. Observational evidence on dietary supplements largely supported the null results from interventions. The observational meta-analyses on alcohol consumption showed statistically significant, but trivial effects on fatigue, with high heterogeneity and RoB concerns. Although the effects of healthy dietary and lifestyle patterns on HRQoL and fatigue outcomes were not robust, limited-suggestive evidence suggests that maintaining a healthy diet and avoiding unhealthy foods offer benefits for colorectal cancer survival.[9]

Evidence on the effect of sedentary behaviour and adiposity on quality of life among patients with colorectal cancer was limited and solely based on observational studies. The only two studies assessing sedentary behaviour suggested a detrimental association with HRQoL and fatigue. The evidence on BMI was mostly null or inconsistent across studies of cancer survivors at various stages and in relation to treatment timeframe, suggesting complex relationships. This aligns with our previous meta-analyses on overall survival, which indicated non-linear associations for BMI that follow different shapes among colorectal cancer survivors with and without metastases.[8] Evidence on other body composition measures was scarce and reported across multiple exposure and outcome measures preventing firm conclusions.

Our review underscored the urgent need for a robust evidence base in this area, including the intricate mechanisms underpinning lifestyle factors, treatment effects, and HRQoL. Physical activity has been demonstrated to enhance physical health and aspects of QoL such as muscle strength, cardiorespiratory function, and sleep quality.[88,94] Lifestyle factors, including physical activity, may reduce inflammation and change factors like insulin, insulin-like growth factor-1, leptin, ghrelin, oxidative stress, and apoptosis.[94] Evidence on diet suggests that baseline appetite loss and poorer health significantly reduce survival following CRC diagnosis.[95] Survivors may experience adverse lifestyle changes during treatment, but also healthy lifestyle could potentially augment the efficacy of cancer treatments and reduce their adverse effects,[4] contributing to better QoL outcomes.

Currently, evidence from high-quality intervention studies on which to base conclusions is lacking. Evidence was fragmented across multiple interventions and exposures, preventing firm conclusions. In the few meta-analyses carried out, the clinical heterogeneity observed between studies may mask any associations. Most trials had a high RoB, mainly due to the self-reported nature of the outcome measurement, in conjunction with non-blinded interventions such as exercise intervention, suboptimal adherence, and missing outcome data. Current RoB tools tend to automatically devalue such studies. While bias cannot be excluded, especially as the outcomes are self-reported,[96] it is important to recognise that patient-reported outcomes, such as HRQoL, are increasingly considered the gold standard for evaluating overall well-being and are highly relevant for cancer survivors and health professionals. This underscores the importance of more tailored assessment tools to accurately evaluate the quality of trials that measured patient-reported outcomes.

Given the few studies included, we were also not able to test for publication bias or conduct subgroup and meta-regression analyses. Observational studies displayed serious or critical RoB due to poor control for confounding (most studies did not adjust for baseline HRQoL, which could lead to floor/ceiling effects in participants with better scores at baseline, or control for stage and/or treatment), selection of participants, deviations from intended exposures including the possibility of reverse causation, and measurement of outcomes.

The limited evidence and generally low-certainty conclusion does not preclude benefits from maintaining a healthy lifestyle in colorectal cancer survivors in terms of QoL and fatigue, especially regarding physical activity, which has been shown to have equal or better effects on cancer-related fatigue compared with available pharmacological options.[97] Colorectal cancer survivors are at high risk of sarcopenia and malnutrition, which adversely affects both main survival outcomes[98-101] and QoL.[102,103] Having a healthy lifestyle has been shown to improve both main survival outcomes[7,9] and certain HRQoL and fatigue outcomes,[67,71,74] but adherence is low among cancer survivors.[104] Meta-analyses of lifestyle[16] or multimodal[91,105] interventions also suggest a synergistic effect of exercise with other interventions, showing improved HRQoL and reduced fatigue in cancer survivors. Even with the lack of definitive evidence, being physically active, maintaining a healthy diet, and a healthy weight and body composition could act synergistically to improve outcomes after colorectal cancer. The findings from this review are contributing to new guidance for cancer survivors being developed as part of CUP Global. This complements the existing recommendation to follow the WCRF/AICR Cancer Prevention Recommendations after a cancer diagnosis as far as possible after the acute stage of treatment.

For the development of robust evidence-based guidelines, more high-quality research from adequately powered studies investigating optimal interventions (type, frequency, duration of physical activity, and improved overall dietary and lifestyle quality) is required. Future trials focusing on improving intervention adherence and minimising attrition are essential, as these facilitate improvements in both health behaviours and outcomes.[106] Trials should also prioritise populations with suboptimal lifestyle habits, for whom intervention may have higher potential impact. Future observational studies, depending on the specific research question, should adequately control for important confounding factors such as cancer stage, treatment, comorbidities, and baseline QoL, and utilise time-varying analyses to account for potential changes during follow-up. Moreover, there is a lack of studies from countries with low and middle Human Development Index, such as those in Africa, which are facing an increasing cancer burden.[107,108] It is essential to enhance efforts to ensure that research includes diverse populations and demographics that are currently underrepresented. Finally, more research is needed to shed light on how healthy lifestyle choices can improve QoL and cancer-related fatigue across the colorectal cancer continuum.

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DATA SHARING

Only publicly available data were used in our study. Data sources and handling of these data are described in the 'Materials and methods' section. Further details are available from the corresponding author upon request.

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