REVIEW

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Does Exercise Improve Health-Related Quality of Life of Colorectal Cancer Survivors? A Systematic Review and Meta-Analysis

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Abstract

Introduction: Early diagnostic and treatment advances have resulted in prolonged cancer survivorship. Therefore, exercise intervention in survivorship management is essential for enhancing cancer survivors' health-related quality of life (HRQoL). **Objective:** The systematic review and meta-analysis in this study aimed to explore the effect of exercise intervention on health-related quality of life of colorectal cancer survivors. **Methods:** The current study followed guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 (PRISMA 2020) to identify relevant literature. Comprehensive searches were conducted using EBSCOhost, Web of Science (WOS), Scopus, Science Direct, and PubMed. The inclusion criteria included are randomised control trials studies written in English, with no restrictions for the time of publication that reported the effects of exercise intervention on health-related quality of live among colorectal cancer survivors. Meta-analysis was conducted by pooling the mean and standard deviation of post-intervention scores across randomised control trial studies using a random effects model. **Result:** A total of 467 articles were identified but only seven articles were randomised control trials (RCT) (n = 7) with PEDro scores ranging from 6 to 9 showing good internal validity were included in the review. The results of the meta-analysis of pooled data from six RCTs studies on HRQoL showed no significant effect of exercise intervention on HRQoL in the intervention group compared to control group [SMD = 0.25; 95% CI; –0.0, 0.51; Z = 1.88; p = 0.06; I^2 = 30.8%]. **Conclusion:** This meta-analysis provides key insights into the effect of exercise on the health-related quality of life (HRQoL) of colorectal cancer (CRC) survivors. Therefore, more experimental studies should be carried out with rigorous methodology to evaluate the effectiveness of exercise interventions before it is recommended as a routine activity in post-treatment management for CRC survivors.

Keywords: health-related quality of life (HRQoL)- colorectal cancer survivors- exercise

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Introduction

Globally, the incidence and mortality rate for colorectal cancer (CRC) continues to rise. According to the World Health Organisation (WHO), colorectal cancer (CRC) is the third and second most prevalent form of cancer diagnosed in men and women, respectively, with more than 1.8 million new cases and 880,792 deaths [1].

Fast escalations in CRC incidence and mortality rates have been reported in Eastern Europe, Asia, and South America. In contrast, this rate is declining in developed countries, such as the United States of America, Australia, New Zealand, and several Western European countries, due to early detection [2]. It is postulated that CRC affliction will increase by 60% to more than 2.2 million new cases and 1.1 million deaths by 2030 [3].

Early diagnostic and treatment advances, combined with the aging and rising global population, have resulted in steep rises in cancer survivorship. Therefore, the post-treatment period is crucial, owing to the significant mental and physical health implications of diagnosis and therapy [4]. Furthermore, good post-treatment management

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is necessary for enhancing the survivors' health and quality of life. Although there are numerous examples of survivorship programs, there are still no universal guidelines concerning their implementation [5].

Current research suggests that certain key factors such as physical exercise must be included in survivorship programs, substantially improving the health-related quality of life among CRC survivors [6]. This exercise may significantly reduce the short- and long-term consequences of cancer therapies, such as fatigue, psychological issues, and loss of physical fitness, which subsequently improve the health-related quality of life among CRC survivors [7].

Colorectal cancer survivors' health-related quality of life (HRQoL) improves to a comparable level or better than the general population after treatment. However, persistent physical and psychological complaints related to cancer and its treatment, such as decline in physical fitness [8], fatigue [9], and depression [10] can have a negative impact on CRC survivors' HRQoL for up to ten (10) years after diagnosis [11]; therefore, more attention must be given to the HRQoL of this population [12].

Notably, CRC survivors with identical illness and treatment features might have diverse HRQoL, suggesting that other factors such as modifiable lifestyle factors (e.g., diet and physical activity) may potentially impact their HRQoL directly or indirectly [5]. Previously, less was known about the role of physical activity intervention after cancer treatments among CRC survivors. Nevertheless, increase in exercise is recommended for these survivors to improve their fitness and patient-reported outcomes [13].

A longitudinal population-based study concluded a positive association in moderate-to-rigorous physical exercise of at least 150 min per week increased level of HRQoL among CRC survivors. This finding has been further corroborated in other observational studies [14-20], where a significant improvement of HRQoL scores has been reported among CRC survivors that engage in physical activity.

In a systematic review, Eyl et al. [21] supported the findings that HRQoL is associated with physical activity among long-term CRC survivors. However, this evidence is limited, as it only involved cross-sectional and observational studies. In addition, there are systematic reviews and meta-analysis of randomised controlled trials (RCT) that showed significant improvement in physical fitness, function, quality of life, reduced fatigue, and depression in patients with cancer survivors after exercise intervention [5, 14, 22]. These reviews of randomised control trials involved samples with various cancer type diagnoses, thus resulting in limited evidence regarding the effects of exercise intervention, specifically on HRQoL of CRC survivors survivors.

Furthermore, a meta-analysis of exercise interventions for colorectal cancer patients reported that there was strong evidence for the effects of short-term exercise on the physical fitness, but no evidence found on the quality of life of colorectal colorectal cancer patients [6].

Meanwhile, Kraemer and colleagues in their systematic review and meta-analysis of randomised control trials studied the effect of home-based and supervised intervention on functional capacity and quality of life of colorectal colorectal cancer patients concluded that the exercise intervention can modify the quality of life if the adherence rate is above 80% [23]. A meta-analysis carried out on the RCT studies involved exercise intervention for post-treatment CRC survivors concluded physical exercise improves aerobic power, metabolism, and tumour biomarkers but no effect on the quality of life [24].

Thus, the systematic reviews and meta-analysis of RCT on the effects of exercise intervention on the quality of life, particularly on CRC survivors, remain unclear. Therefore, this review aims to review systematically and analyse available RCT studies to ascertain the effects of exercise intervention towards the quality of life of CRC survivors after treatment. Another goal of the research is to establish the effects of exercise and QoL, which may lead to the discoveries of insights on the outcomes on HRQoL of CRC survivors through reviewing individualised physical activity intervention in this systematic review.

Materials and Methods

Study Design

This meta-analysis was conducted following the Preferred Reporting Items for Systematic Review and Meta-Analyses guidelines [25].

Search Strategy

This systematic review utilised five electronic databases, namely, EBSCOhost, Web of Science (WOS), Scopus, Science Direct, and PubMed. These databases identified the relevant sources for analysis in the review. The following databases were searched systematically, with no restrictions with respect to time, restricted to only journal articles published in English. The leading search terms included were "colorectal cancer survivor," "colorectal carcinoma survivor," "colon cancer survivor," "rectal cancer survivor," "colorectal neoplasm survivor," "colon neoplasm survivor," "rectal neoplasm survivor," "physical activity," "exercise," "quality of life," "health-related quality of life," and "well-being." These keywords were taken from previous studies [5, 6], which had been verified by experts involved in this study: public health specialist (ZI) and colorectal surgeon (ZA). All search terms were truncated and adapted for each database where necessary.

Inclusion-Exclusion Criteria

Initially, the PICOS criteria [26] (Table 1) were selected as the eligibility criteria. Additionally, specific inclusion

Table 1. Eligibility Criteria for Inclusion of Studies in Systematic Review According to the PICOS (Population, Intervention, Comparator, Outcomes And Study Design) Criteria.

Components	Feature
Population	Colorectal cancer survivors
Intervention	Exercise
Comparator	CRC survivors not enrolled in exercise intervention
Outcomes	Health-related quality of life
Study design	Randomized controlled trials

criteria included: 1) studies were RCT, preliminary or feasibility RCTs involving exercise intervention in CRC survivors published in the English language; 2) adults (>18 years old) with the diagnosis of colorectal cancer (all types of colorectal cancers); 3) examining the exercise of CRC survivors as the independent variable regardless of: i) duration (short-term or long term); ii) all types of exercise performed; iii) reported as an estimate of total energy expenditure (e.g., calories per kilogram per week (cal/kg/wk) or minutes per week (min/wk) or METs per week (METs/wk) or moderate to vigorous physical activity (MVPA); and iv) results are related to the QoL (e.g., global scores from validated QoL questionnaires, or scores from various questionnaires focused on the variables such as fatigue, depression, anxiety, and sleep that have a direct impact on the HRQoL of CRC survivors). Meanwhile, the specific exclusion criteria consisted of: 1) studies including other types of cancer; and 2) studies that lack specific information regarding the intervention's duration, intensity, and duration of exercise.

Data Extraction

After searching the previously specified databases, an assessment was carried out to search for any duplicate documents. The titles and abstracts of the carefully chosen articles were screened independently based on the PICOS and specific inclusion/exclusion criteria by three researchers (NJ, NH, and ZIA). If any of the above exclusion criteria were discovered during this screening step, the record will be excluded; otherwise, it will be included while awaiting analysis after the full reading of the included records.

Next, the full texts of the identified articles were retrieved and reviewed (using a structured form to abstract information about the articles (author's names, year of publications and study design), characteristics of the study population [e.g., type of colorectal cancer (rectal or colon), sample size, stage of cancer, age, time since diagnosis], characteristics of the intervention and control (e.g., type, program length, frequency and duration), outcome measures and results were extracted independently by three reviewers (NJ, NH and ZIA); disagreements were discussed until consensus is achieved or a third independent reviewer is requested for their opinion (SA and ZI). The final step involved utilising the PEDro scale to assess the methodological quality; those who received a score of four or higher were chosen. Meta-analysis was carried out by Meta-analysis was carried out by (IHB).

Study Quality Assessments

Three reviewers (NJ, NH, and ZIA) independently assessed the included studies' quality using the Physiotherapy Evidence Database (PEDro) scale [23]. The PEDro scale consists of eleven items, which range from 1 to 10 (except for the first item). In addition, the final score ranged from fair to good and fair to substantial, respectively. A higher score indicated that the study had greater validity [27].

Outcomes

In this review, the primary outcome is health-related quality of life (HRQoL), i.e., global quality of life (QoL), including three elements of HRQoL (physical, mental, and social status) [28], which were assessed using validated HRQoL questionnaires. Meanwhile, secondary outcomes consisted of variables that directly affect the HRQoL of CRC survivors, such as fatigue, depression, and anxiety obtained from other validated questionnaires.

Statistical Analysis

The post-intervention mean standard deviations (SDs) were used for comparisons. The analysis was carried out using the standardised mean difference (SMD) as the outcome measure. This meta-analysis study employed a random effects model that combines sampling error within study variances. The Q test and I^2 statistics was carried out to assess the variation across studies are due to heterogeneity rather than chance [29, 30]. The degree of heterogeneity was evaluated using the following values: I^2 = 0% to 29% indicates no heterogeneity; I^2 = 30% to 49% indicates moderate heterogeneity; and I^2 = 50% to 74% indicates strong heterogeneity [30]. Publication bias was conducted if the number of studies exceeds 10 in which the analysis is done using funnel plot and Egger test. The meta-analysis was performed using R version 4.2.1 [31] and the metafor package version 4.2.0 [32].

Results

Literature search and quality assessment

The initial literature search identified 467 studies, as presented in the PRISMA flow (Figure 1). A total of 452 records were screened after 15 duplicate studies were eliminated. After the screening of topics and abstracts, only one hundred and two (n = 102) records were retained for eligibility evaluation. The articles excluded were mainly attributable to their different subject areas, for instance, cancers unrelated to colorectal cancer and that comprising systematic literature review articles. Finally, only seven (7) full-text articles [33-39] were included in this review, while the others were excluded because the variables studied were inappropriate for assessment in terms of exercise or quality of life variables or that involving non-randomised control trial studies. The included studies were published between the years 2003 and 2020.

The internal validity of the chosen articles is tabulated in Table 2. All studies were randomised control trials (RCT) (n = 7) with PEDro scores ranging from 6 to 9. The mean and standard deviation of the PEDro score among the studies was 7.29 (1.28). Three studies scored 6, two studies with a score of 9, one study scored 7 and 8 each. Five studies were classified as good category (6 to 8), followed by two studies classified as excellent category (9 to 10).

General characteristics of studies

The selected general characteristics of the studies are reported, as shown in Table 3. The studies involved were published between the years 2003 and 2020, where they were mostly conducted in Western countries, such as Canada [36], United Kingdom [33], United States of

Table 2. PEDro Score

Author (Year)	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11	Total
Courneya (2003) [36]	1	1	1	1	1	0	0	1	1	1	8
Bourke (2011) [33]	1	1	1	1	1	1	1	0	1	1	9
Pinto (2013) [39]	1	1	1	1	0	1	1	1	1	1	9
Brown (2018) [34]	1	1	1	0	0	0	1	1	1	1	7
Kim (2019) [38]	1	1	1	0	0	0	0	1	1	1	6
Christensen (2019) [35]	1	1	1	0	0	0	0	1	1	1	6
Ho (2020) [37]	1	1	1	0	0	1	0	0	1	1	6

America [34, 39], and Denmark [35]; as well as Asian countries, such as Hong Kong [37] and Korea [38]. The sample size of the included studies ranged from 18 [33] to 223 [37]. The mean age of participants ranged from 55 years (Pinto et al., 2013) to 70.3 years [33]. In total, 529 patients with CRC were enrolled in the RCTs involving exercise intervention and physical activity combined with dietary intervention. Among these, controls made up of 189 CRC survivors and another 340 were given exercise intervention only [33-36, 38, 39] or combined intervention of physical activity and dietary [37]. Most of the studies (71%) reported specific stages of cancer involved in control and intervention groups [34-38], while two studies only mentioned Dukes stages A to C [33] and Stage I to III only [39]. Two studies [33, 34] only recruited all colon cancer survivors whereas other studies involved both colon and rectal cancers [35-39].

Instruments for health-related quality of life assessment

The health-related quality of life was measured using the Functional Assessment of Cancer Therapy-Colorectal questionnaire (FACT-C) in all studies retained [33-39]. Meanwhile, other questionnaires such as the Functional Assessment of Cancer Therapy-Fatigue questionnaire (FACT-F) were adopted in four studies [33, 36, 38, 39] and one study used the Fatigue Symptom Inventory [34]. In addition, Pittsburgh Sleep Quality Index (PSQI) was applied to examine sleep quality in one study [34]. The depression score in the studies was measured using the Centre for Epidemiological Studies Depression scale [36], Patient Health Questionnaire [38] and Hospital Anxiety and Depression scale [37]. Only two studies measured anxiety scores using State-Trait Anxiety Inventory [36] and Hospital Anxiety and Depression Scale (HADS) [37], respectively.

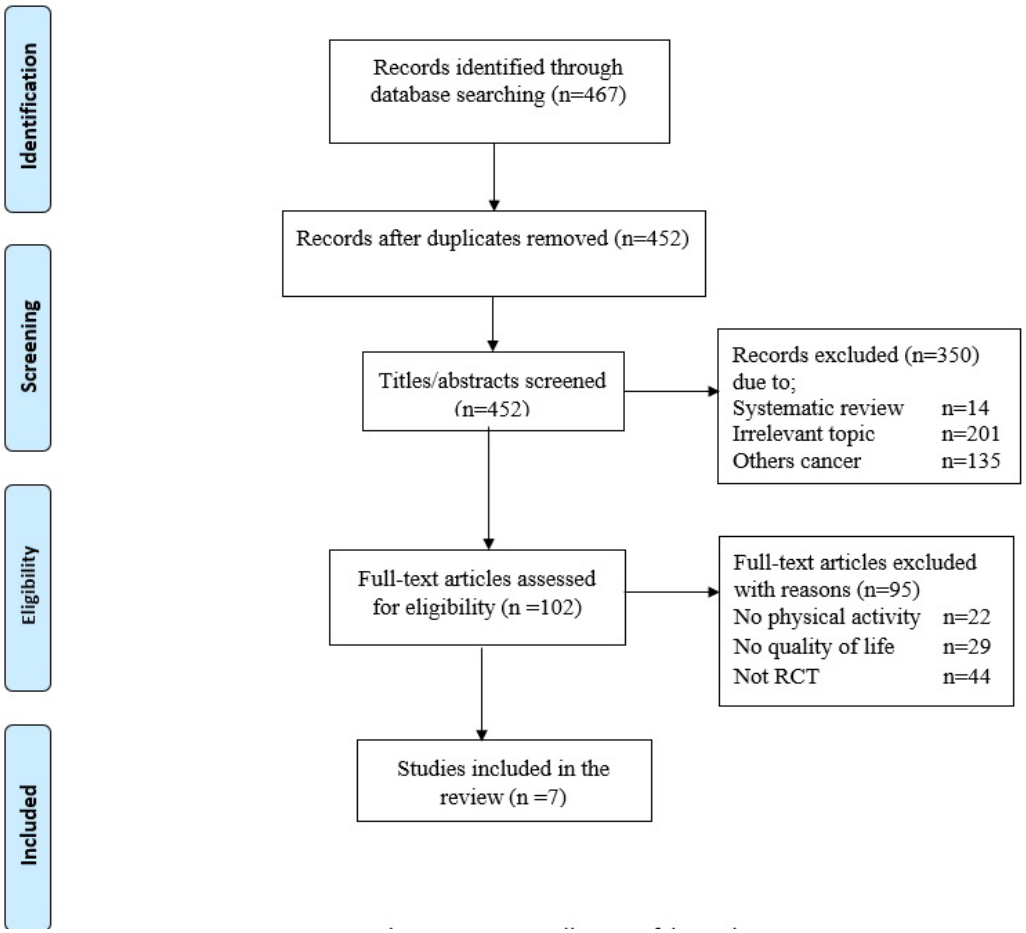

Figure 1. PRISMA Diagram of the Study

Table 3. Studies general characteristics

Study	Sample size and age (mean + SD)	Duration of diagnosis (mean + SD)	Stage of cancer	Tumor location
Courneya (2003)	Control n = 31 (M = 20, F = 11), Age = 61 + 13 years Intervention n = 62 (M = 34, F = 28), Age = 59 + 10 years	Control 71.65 (18.08) days Intervention 74.65 (34.02) days	Control I – II (n = 4) III (n = 27) Intervention I – II (n = 14) III (n = 44) IV (n = 4)	Control Colon (74.2%) Rectum (25.8%) Intervention Colon (77%) Rectum (23%)
Bourke (2011)	Control n = 9 (M = 7, F = 2), Age = 70.3 + 8.7 years Intervention n = 9 (M = 5, F = 4), Age = 67.9 + 5.7 years	Control 16.7 months Intervention 16.4 months	Dukes stages A to C	All colon cancers
Pinto (2013)	Control n = 26 (M = 12, F = 14), Age = 55.6 + 8.24 years Intervention n = 20 (M = 8, F = 12), Age = 59.5 + 11.2 years	Control 2.88 (1.67) years Intervention 3.14 (1.62) years	Completed treatment for stage I to III	Control Colon (58 %) Rectum (42 %) Intervention Colon (55 %) Rectum (45 %)
Brown (2018)	Control n = 13 (M = 4, F = 9), Age = < 60 years (69%), > 60 years (31%) Intervention Low dose n = 14 (M = 7, F = 7), Age = < 60 years (57%), > 60 years (43%) High dose n = 12 (M = 4, F = 8), Age = < 60 years (67%), > 60 years (33%)	Control < 12 months (62%), > 12 months (38%) Intervention Low dose < 12 months (71%), > 12 months (29%) High dose < 12 months (58%), > 12 months (42%)	Control I (n = 1), II (n = 5) III (n = 7) Intervention Low dose I (n = 2), II (n = 3), III (n = 7) High dose I (n = 2), II (n = 4), III (n = 6)	All colon cancers
Kim (2019)	Control n = 34 (M = 17, F = 17), Age = 56 + 10 years Intervention n = 37 (M = 18, F = 19), Age = 55 + 8 years	Control 10.6 (8.4) months Intervention 10.8 (5.8) months	Control II (n = 12) III (n = 22) Intervention II (n = 21) III (n = 16)	Control Colon (73%) Rectum (27%) Intervention Colon (55.9%) Rectum (44.1%)
Christensen (2019)	Control n = 20 (M = 11, F = 9), Age = 60 + 8 years Intervention n = 19 (M = 7, F = 12), Age = 57 + 10 years	Control 37 (256) days Intervention 40 (380) days	Control I (n = 4), II (n = 7) III (n = 9) Intervention I (n = 6), II (n = 4), III (n = 9)	Control Colon (85%) Rectum (15%) Intervention Colon (74%) Rectum (26%)
Ho (2020)	Control n = 56 (M = 30, F = 26), Age = 64.9 + 9.4 years Intervention Dietary+Physical activity n = 55 (M = 37, F = 18), Age = 63.2 + 11.4 years Dietary only n = 56 (M = 34, F = 22), Age = 65.9 + 9.8 years Physical activity only n = 56 (M = 40, F = 16), Age = 66.6 + 9.5 years	Not stated	Control I (n = 21), II (n = 43) III or IV (n = 36) Intervention Dietary+Physical activity I (n = 14), II (n = 24) III or IV (n = 16) Dietary only I (n = 9), II (n = 20) III or IV (n = 27) Physical activity only I (n = 8), II (n = 27) III or IV (n = 20)	Colon (60%) Rectum (40%)

*SD, standard deviation; M, male; F, female; n, sample size

Intervention characteristics

Randomised control trials studies that conducted exercise intervention for CRC survivors were reviewed, as shown in Table 4. The duration for the intervention ranged from 6 to 48 weeks, exclusive of the duration of follow-ups. Four studies [33, 36, 37, 39] reported the frequency of prescribed exercise intervention in days per week. Meanwhile, other studies applied the metabolic equivalent task (MET) per hour [38], the number of

Table 4. Intervention Characteristics and Outcomes Results

Study	Length of intervention (L) (weeks) Frequency (F) Exercise adherence (A) (%)	Exercise session duration (D) Intensity (I)	Type of exercises	Instrument for variables measurement (parameter) Quality of life (QoL) Fatigue (F) Depression (D) Anxiety (A) Sleep quality (SQ)	QoL results Significance
Courneya (2003]	L = 16 F= 3 – 5 times/week A = 75.8	D = 20 – 30 mins I = 65 to 75% HR_{max}	Home-based and personalised exercise programme; swimming, cycling or walking	QoL = FACT-C (score) F = FACT-F (score) D = CESD (score) A = STAI (score)	Control Pre = 107.0 (16.0) Pos = 109.8 (18.8) Intervention Pre = 106.0 (14.0) Pos = 107.4 (16.5) NS[a]S[b] Control Pre = 11.9 (10.8) Pos = 12.1 (10.8) Intervention Pre = 13.1 (10.1) Pos = 12.7 (10.9) NS[ab] Control Pre = 10.1 (12.0) Pos = 9.6 (10.9) Intervention Pre = 9.6 (8.1) Pos = 8.6 (8.7) NS[ab] Control Pre = 39.2 (14.5) Pos = 35.5 (12.6) Intervention Pre = 37.7 (11.3) Pos = 33.5 (12.6) NS[ab]
Bourke (2011)	L = 12 F = 2 times/week A = 90	D = 30 mis I = 55 to 85% HR_{max}	Supervised and home-based aerobic exercise (threadmills, rowing and cycling ergometers) and dietary advice	QoL = FACT-C (score) F = FACT-F (score)	Control Pre = 102 (15.0) Pos = 106 (13.0) Intervention Pre = 120 (10.0) Pos = 120 (11.0) NS[a] Control Pre = 42 (9) Pos = 43 (6) Intervention Pre = 43 (7) Pos = 48 (4) S[a]
Pinto (2013)	L = 12 F = 2 – 5 times/week A = 76	D = 20 – 30 mins I = 64 – 76% HR_{max}	Home-based exercise;brisk walking, biking or use of home exercise equipment	QoL = FACT-C (score) F = FACT-F (score)	Control Pre = 105.3 Pos = 110.8 Intervention Pre = 105.3 Pos = 111.3 NS[a]S[b] Control Pre = 39.1 Pos = 41.9 Intervention Pre = 39.1 Pos = 42.2 NS[a]S[b]

Table 4. Continued

Study	Length of intervention (L) (weeks) Frequency (F) Exercise adherence (A) (%)	Exercise session duration (D) Intensity (I)	Type of exercises	Instrument for variables measurement (parameter) Quality of life (QoL) Fatigue (F) Depression (D) Anxiety (A) Sleep quality (SQ)	QoL results Significance
Brown (2018)	L = 24 F = 150 min-wk-1 (Low dose group) , 300 min-wk-1 (High dose group) A = 93 (low dose group) and 89 (high dose group)	D = 30 – 60 mins I = 50 – 70% HR_{max}	Home-based aerobic exercise with threadmills	QoL = FACT-C (score) F = FSI (score) SQ = PSQI (score)	Control Pre = 115.2 (18.9) Δ -7.4 (4.6) Intervention Low dose Pre = 113.1 (13.7) Δ 2.8 (2.6) High dose 109.6 (14.0) Δ 2.0 (2.8) S[a] Control Pre = 6.9 (11.9) Δ 0.1 (2.5) Intervention Low dose Pre = 3.8 (7.2) Δ 0.9 (2.4) High dose 12.7 (17.2) Δ -5.9 (2.6) S[a] Control Pre = 6.75 (4.4) Δ 0.4 (0.7) Intervention Low dose Pre = 4.46 (3.0) Δ 0.1 (0.7) High dose 4.91 (2.9) Δ -0.7 (0.8) S[a]
Kim (2019)	L = 12 F = First 6 weeks; 18 MET-hours, after 6 weeks;27 MET-hours A = 81.1 (retention rate)	D = > 10, 000 steps + 30 mins of resistance exercises using the body weight I = 65% of the HR_{max}	Home-based exercises; brisk walking, hiking, stationary bike and resistance exercises with own body weight	QoL = FACT-C (score) F = FACT-F (score) D = PHQ (score)	Control Pre = 97.5 (19.9) Pos = 99.1 (19.1) Intervention Pre = 100.5 (18.1) Pos = 104.3 (17.5) NS[a]S[b] Control Pre = 41.0 (8.1) Pos = 42.3 (7.5) Intervention Pre = 39.7 (9.6) Pos = 42.6 (8.5) NS[a]S[b] Control Pre = 4.2 (4.3) Pos = 3.2 (4.8) Intervention Pre = 4.0 (4.5) Pos = 3.0 (4.5) NS[ab]
Christensen (2019)	L = 12 F = Prescribed interval walking for 150 min/week A = mean total adherence 90.5	D = not specified I = 150 min/wk	Walking	QoL = FACT-C (score)	Control Pre = 108 (19) Pos = 110 (18) Intervention Pre = 112 (17) Pos = 121 (11) NS[a]S[b]

Table 4. Continued

Study	Length of intervention (L) (weeks) Frequency (F) Exercise adherence (A) (%)	Exercise session duration (D) Intensity (I)	Type of exercises	Instrument for variables measurement (parameter) Quality of life (QoL) Fatigue (F) Depression (D) Anxiety (A) Sleep quality (SQ)	QoL results Significance
Ho (2020)	L = 48 F = 5 days/week A = 62% (30 min of MVPA 5 days); 55% (60 min of MVPA 5 days)	D = 30 min for the first 6 months; 60 mins after 6 months I = 30 min of MVPA 5 days; 60 min of MVPA 5 days	Home-based exercise; walking	QoL = FACT-C (score) D = HADS-D (score) A = HADS-A (score)	Control Pre = 106.9 (16.6) Pos-6 mths = 120.6 (16.8) Pos-12 months = 120.3 (15.5) Intervention Dietary + Physical activity Pre = 110.4 (18.2) Pos-6 mths = 122.7 (14.2) Pos-12 months = 126.6 (9.6) Physical activity Pre = 110.8 (16.1) Pos-6 mths = 122.9 (15.7) Pos-12 months = 122.8 (14.8) Dietary Pre = 110.8 (16.1) Pos-6 mths = 122.7 (15.5) Pos-12 months = 124.3 (12.6) NS[ab] Control Pre = 11.8 (3.4) Pos-6 mths = 11.3 (3.2) Pos-12 months = 10.7 (2.8) Intervention Dietary + Physical activity Pre = 11.9 (3.7) Pos-6 mths = 10.8 (3.4) Pos-12 months = 9.3 (2.2) Physical activity Pre = 12.0 (3.2) Pos-6 mths = 10.7 (3.1) Pos-12 months = 10.9 (2.7) Dietary Pre = 11.4 (3.4) Pos-6 mths = 11.0 (3.1) Pos-12 months = 9.6 (2.8) NS[ab] Control Pre = 10.7 (3.8) Pos-6 mths = 9.0 (3.2) Pos-12 months = 9.1 (3.1) Intervention Dietary + Physical activity Pre = 10.6 (4.0) Pos-6 mths = 8.9 (2.4) Pos-12 months = 8.4 (1.6) Physical activity Pre = 10.1 (3.5) Pos-6 mths = 8.6 (3.0) Pos-12 months = 8.5 (2.4) Dietary Pre = 11.1 (3.9) Pos-6 mths = 8.7 (2.4) Pos-12 months = 8.3 (2.0) NS[ab]

FACT-C, Functional Assessment of Cancer Therapy-Colorectal questionnaire (FACT-C); FACT-F, Functional Assessment of Cancer Therapy Scale—Fatigue; CESD, Centre for Epidemiological Studies Depression scale; STAI, State-Trait Anxiety Inventory; FSI, Fatigue Scale Inventory; PSQI, Pittsburgh Sleep Quality Index; HADS, Hospital Anxiety and Depression Scale; NS, not significant; S, significant; a, time*group effect interaction; b, time effect

minutes per week [34, 35] to categorise the frequency of the intervention. The adherence rate obtained from the intervention studies ranged from 55% to 93%. All physical exercises performed by the CRC survivors in these studies were home-based exercise with prescribed intensity based on a percentage of a maximum heart rate (HRmax) ranging from 50% to 85% (HRmax).

Christensen et al. [35] placed their participants to perform exercises based on their preferences for 150 min/week. Similarly, Kim et al. [38] requested CRC survivors

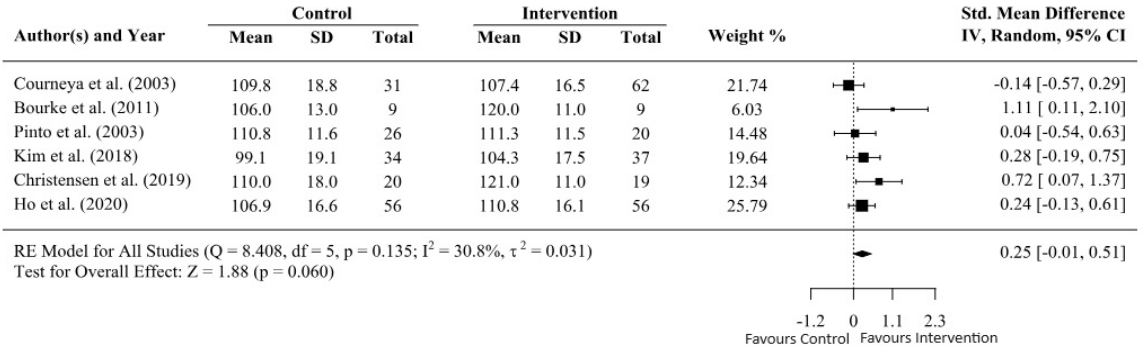

Figure 2(a). Meta-Analysis for the Effect Estimate of Exercise Intervention on the Health-Related Quality of Life Colorectal Cancer Survivors.

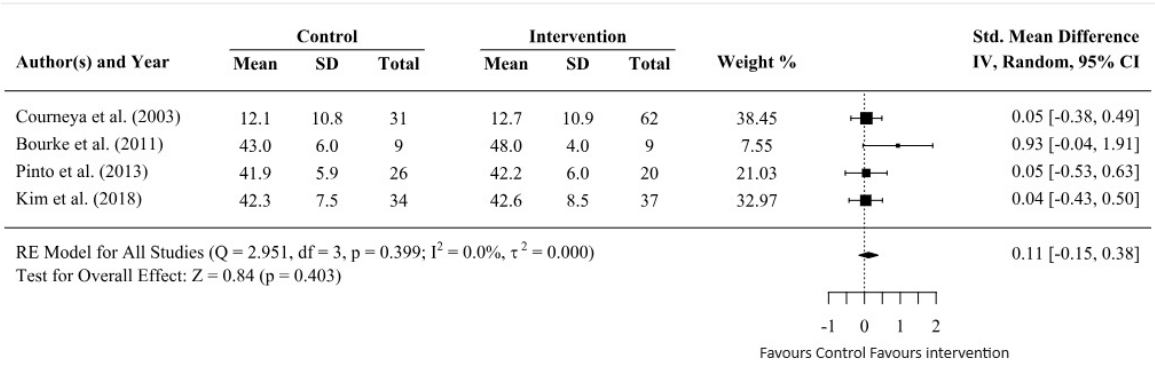

Figure 2(b). Meta-Analysis for the Effect Estimate of Exercise Intervention on the Fatigue Symptom Colorectal Cancer Survivors.

in their study to do home-based exercises of more than 18 METs hours per week for the first 6 weeks later increasing to 27 MET-hours for the remaining 6 weeks consisting of more than 10,000 steps with 30 min of resistance exercise using the body weight. Brown et al. [34] had two groups of intervention frequency namely the low dose group with 150 min-wk-1 and the high dose group with 300 min-wk-1.

Bourke et al. [33] initiated the participants in his study to exercise in supervised groups twice a week and home-based exercise once a week for the first six weeks.

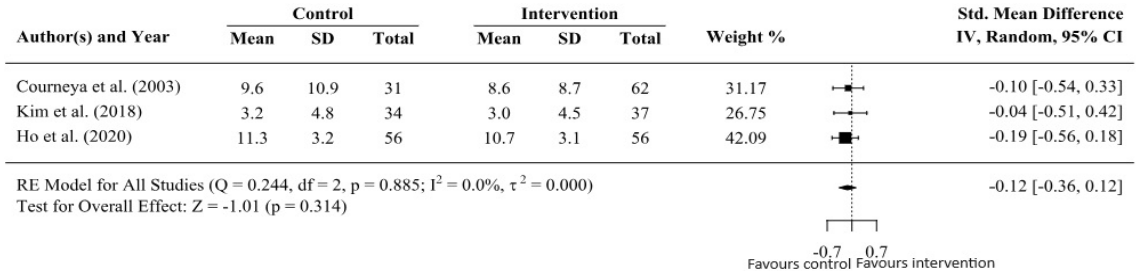

Figure 2(c). Meta-Analysis for the Effect Estimate of Exercise Intervention on the Depression Symptom Colorectal Cancer Survivors.

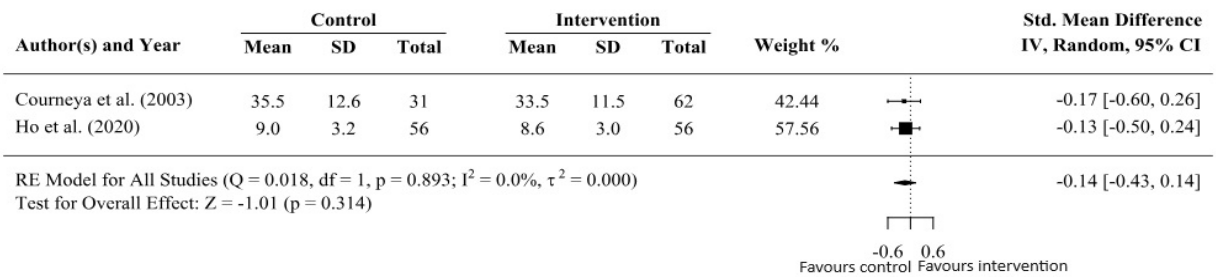

Figure 2(d). Meta-Analysis for the Effect Estimate of Exercise Intervention on the Anxiety Symptom Colorectal Cancer Survivors.

Later, during the remaining six weeks, it changed into twice a week of home-based exercise and supervised exercise once a week. Other studies prescribed the duration of exercise ranged from 20–30 and 60 minutes daily consisting of home-based aerobic exercises with treadmills [34] or walking, cycling, and swimming [35-39]. In addition to physical exercise, two studies [34, 37] included dietary advice in their intervention. Ho et al. [37] grouped the intervention group combined with dietary and physical activity intervention group, physical activity only and dietary intervention only.

Meta-analysis of HRQoL and other outcomes

One study was excluded from meta-analysis because it did not present mean and standard deviation at post-intervention study [34]. Meanwhile, for study by Ho et al. [37], the mean and standard deviation of HRQoL, fatigue, depression, and anxiety scores were taken from the control group and physical activity intervention group only. The assessment of publication bias was unreliable because insufficient studies were included in the meta-analysis.

Effects of exercise intervention on health-related quality of life

Seven studies included in this review evaluated the quality of life after exercise intervention [33-39]. However, one study was excluded in meta-analysis because absence of mean and standard deviation reported after the intervention [34].

The results of the meta-analysis of pooled data on HRQoL from six studies [33, 35-39] involving 379 participants (exercise intervention group, n = 203; control group, n = 176) showed no significant effect of exercise intervention on HRQoL in the intervention group compared to control group [SMD = 0.25; 95% CI; –0.0, 0.51; Z = 1.88; p = 0.06; I^2 = 30.8%] (Figure 2(a)). Albeit the p-value was slightly above the conventional significance threshold of 0.05, the results hint at a borderline level of significance for the overall effect size across the studies and shows the effect favours the intervention group. In addition, according to a study by Brown et al., 300 minutes a week of aerobic exercise was associated with a higher quality of life compared to 150 minutes a week of aerobic exercise and control group without exercise.

Furthermore, two studies [35, 38] demonstrated an increase of HRQoL scores significantly in the intervention group at post-baseline assessment compared to no changes in the control group after home-based exercise. Nevertheless, the intention-to-treat analysis carried out by Courneya et al. [36] found no significant difference in HRQoL score between the groups. Later, exploratory ancillary analysis performed on the increased and decreased cardiovascular fitness revealed significant differences in the increased group for change in the HRQoL score.

Effects of exercise intervention on fatigue, anxiety, and depression

Four studies reported the effects of exercise on fatigue [33, 36, 39, 38] involving 228 participants (exercise intervention group, n = 128; control group, n = 100). A meta-analysis of pooled fatigue scores after exercise intervention compared to control group showed no significant difference [SMD = 0.11; 95% CI; –0.15, 0.38; Z = 0.84; p = 0.403; I^2 = 0.0%] (Figure 2(b)).

In contrast, the remaining study showed that fatigue score was improved in a dose-response fashion whereby high dose group 300 min-wk-1 contribute to the largest improvements followed by low dose group 150 min-wk-1 compared to the control group after 6 months of home-based aerobic exercise intervention [34]. This result correlates with the study by Bourke et al. [33] revealed there was a significant difference in improvement in the fatigue score of the intervention group compared with the control group.

Three studies reported the effects of exercise on depression [36, 38, 37] involving 276 participants (exercise intervention group, n = 155; control group, n = 121). A meta-analysis of pooled depression scores after exercise intervention compared to control group showed no significant difference [SMD = –0.12; 95% CI; –0.36, 0.12; Z = –1.01; p = 0.314; I^2 = 0.0%] (Figure 2(c)). However, exploratory ancillary analysis performed in a study [36] reported a borderline significant decreased of depression scores in the increased fitness level group from baseline to post-intervention.

Two studies reported the effects of exercise on anxiety [36, 37] involving 205 participants (exercise intervention group, n = 118; control group, n = 87). Further meta-analysis of pooled anxiety scores after exercise intervention compared to control group showed no significant difference [SMD = –0.14; 95% CI; –0.43, 0.14; Z = –1.01; p = 0.314; I^2 = 0.0%] (Figure 2(d)). Nevertheless, the ancillary analysis done by Courneya et al. [36] revealed a significant decrease in anxiety score between increased and decreased fitness after home-based exercise intervention.

Discussion

Several cancer survivors endure the side effects of the illness and therapy after being diagnosed and treated. Exercise intensities vary depending on the kind of cancer, and it is an essential component of non-pharmaceutical therapy. Therefore, the effect of exercise on HRQoL in colorectal cancer survivors following treatment has been the focus of inconclusive research. Thus, the purpose of this meta-analysis was to assess the effect of exercise on HRQoL in CRC survivors after treatment.

The findings in this meta-analysis demonstrated that there was a borderline significant improvement of HRQoL level after exercise intervention compared to usual care group among CRC survivors. Meanwhile, other outcomes for fatigue, depression, and anxiety scores showed no significant effects observed after exercise intervention. These findings are consistent with the results of previous meta-analysis reported that no association was observed between HRQoL and exercise intervention in their RCTs' meta-analysis [24, 40].

Despite the borderline significant evidence of exercise improve HRQoL, an improvement of roughly one-half of

a standard deviation (d = 0.5) is considered a minimally clinically important difference for patient-reported HRQoL measures when compared to the control group [41]. Hence, the level of HRQoL improvement in these studies [33, 35, 38] is, therefore, compatible, with a clinically significant benefit.

However, this meta-analysis findings was contradicted with a meta-analysis study done on RCTs by Kraemer e.t al. [23], which reported an adherence rate of more than 80% of home-based physical exercise programs were significant to improve the HRQoL but not fatigue, depression, and anxiety among CRC patients undergoing treatment. There is also evidence from other meta-analysis study on RCTs is effective in improving QoL, fatigue and among CRC patients either preparing, undergoing, or having completed treatment [42]. Meanwhile, other meta-analysis on RCTS verified improvement of disease-specific QoL among CRC survivors after physical intervention. It reported more intense physical activity gives better QoL [13].

The lack of significant results in the exercise intervention impact on HRQoL CRC survivors compared to usual care group may be partially explained by several factors. Firstly, the contamination of the control group may explain the non-modification of HRQoL scores in the study by Courneya et al. [36] which is similar to Lin et al. [43]. In both studies, the control groups were not restricted from doing exercise during the intervention. Secondly, the insignificant difference in HRQoL in the studies by Pinto et al. [39] and Ho et al.[37] is most likely the result of a potential ceiling effect on the quality of life and exercise interventions. Therefore, CRC survivors with lower baseline levels of exercise should be included in future investigations.

Thirdly, the significant improvements in QoL between groups in Brown et al. [34] showed that exercise had a dose-response effect on HRQoL results. Previous studies looked at exercise volumes ranging from 60 to 150 minutes per week, which may not have been enough to encourage improvements in HRQoL.

Besides that, exercise type recommended also influenced the effectiveness of exercise intervention performed. It is because according to clinical guidelines in oncology, exercise programs combining resistance and aerobic training improve HRQoL more than those that exclusively include aerobic or resistance training only. Next, the majority of the individuals that were recruited for this study were under 60 years old, which suggests that this age group may be more vulnerable to HRQoL deficits and frequently motivated to engage in beneficial risk-reducing behaviours.

Implications for Further Research

Even though research findings provided a body of solid evidence for being physically active for the quality of life enhancement, many perspectives, barriers, and preferences need to be acknowledged and addressed to increase physical activity participation rates among CRC survivors [44]. Thus, specific aspects such as the best time to initiate the exercise and presence of medical comorbidities may complicate the physical activity engagement. Meanwhile, motivational readiness should also be considered when attempting to increase physical activity in CRC survivors [39].

A greater understanding of essential intervention-related factors, such as the timing and mode of intervention delivery, intervention length, and exercise characteristics in terms of frequency, intensity, type, time (FITT factors) are also required to maximise the effects of exercise [45]. Besides that, individuals with poor quality of life, fatigue, and physical function improved significantly following the exercise intervention, implying that the most significant benefit of treatments may focus on those most in need [45, 39]. Therefore, healthcare providers are recommended to encourage sedentary cancer survivors to engage in physical activity, even at modest levels [46]. Besides that, more experimental studies should be carried out with rigorous methodology to evaluate the safety of exercise interventions before it is recommended as a routine activity in post-treatment management for CRC survivors.

Limitations

The limitation of this systematic review is that variations of patient populations, outcome definitions, type, and frequency of physical exercises are not the same across studies. Few eligible studies in this review are home-based exercise interventions; therefore, other structured and supervised exercise programs are not available for comparison. A future systematic review should include other types of physical activity interventions utilised to identify an effective physical activity intervention to help CRC survivors maintain their health and quality of life for long periods of time.

In conclusion, the result of the meta-analysis in this work provides key insights into the effect of exercise on HRQoL CRC survivors. This review provides additional evidence to support implementing physical activity as part of standard care regime to improve quality of life. However, future studies should optimise exercise participation and adherence and determine the type of exercise, length of the program or exercise session, and intensity of exercise required for CRC survivors to further confirm the effects of exercise intervention on HRQoL CRC survivors.

Author Contribution Statement

Research concept and study design: NJ and ZIA; Literature review and data collection: NJ, NH, and ZIA; Data analysis and interpretation: NJ, IHB and ZIA; Writing of manuscript: NJ, IHB and ZIA; Reviewing/ editing manuscript: All authors. All authors have read and agreed to the published version of the manuscript.

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Approval

The data was synthesised from the published research (secondary data analysis). Thus, this study did not require ethical approval and was not part of the approved student thesis.

Conflict of Interest

The authors declare no conflict of interest.

Data Availability

There was no available data in this study.

Study Registration

This study was registered at The International Prospective Register of Systematic Reviews (PROSPERO-CRD42022332393).

References

1. Lyon F. International Agency for Research on Cancer [Internet] France [Cited 2022 Dec 12] Available from: https://gco.iarc.who.int/today/en?
2. Fitzmaurice C, Akinyemiju TF, Al Lami FH, Alam T, Alizadeh-Navaei R, Allen C, et al. Global, regional, and national cancer incidence, mortality, years of life lost, years lived with disability, and disability-adjusted life-years for 29 cancer groups, 1990 to 2016: A systematic analysis for the global burden of disease study. JAMA Oncol. 2018;4(11):1553-68. https://doi.org/10.1001/jamaoncol.2018.2706.
3. Arnold M, Sierra MS, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global patterns and trends in colorectal cancer incidence and mortality. Gut. 2017;66(4):683-91. https://doi.org/10.1136/gutjnl-2015-310912.
4. Miller KD, Nogueira L, Mariotto AB, Rowland JH, Yabroff KR, Alfano CM, et al. Cancer treatment and survivorship statistics, 2019. CA Cancer J Clin. 2019;69(5):363-85. https://doi.org/10.3322/caac.21565.
5. Balhareth A, Aldossary MY, McNamara D. Impact of physical activity and diet on colorectal cancer survivors' quality of life: A systematic review. World J Surg Oncol. 2019;17(1):153. https://doi.org/10.1186/s12957-019-1697-2.
6. Cramer H, Lauche R, Klose P, Dobos G, Langhorst J. A systematic review and meta-analysis of exercise interventions for colorectal cancer patients. Eur J Cancer Care (Engl). 2014;23(1):3-14. https://doi.org/10.1111/ecc.12093.
7. Soares-Miranda L, Abreu S, Silva M, Peixoto A, Ramalho R, da Silva PC, et al. Cancer survivor study (casus) on colorectal patients: Longitudinal study on physical activity, fitness, nutrition, and its influences on quality of life, disease recurrence, and survival. Rationale and design. Int J Colorectal Dis. 2017;32(1):75-81. https://doi.org/10.1007/s00384-016-2671-x.
8. Sánchez-Jiménez A, Cantarero-Villanueva I, Delgado-García G, Molina-Barea R, Fernández-Lao C, Galiano-Castillo N, et al. Physical impairments and quality of life of colorectal cancer survivors: A case-control study. Eur J Cancer Care (Engl). 2015;24(5):642-9. https://doi.org/10.1111/ecc.12218.
9. Wan Puteh SE, Saad NM, Aljunid SM, Abdul Manaf MR, Sulong S, Sagap I, et al. Quality of life in malaysian colorectal cancer patients. Asia Pac Psychiatry. 2013;5 Suppl 1:110-7. https://doi.org/10.1111/appy.12055.
10. Peng YN, Huang ML, Kao CH. Prevalence of depression and anxiety in colorectal cancer patients: A literature review. Int J Environ Res Public Health. 2019;16(3). https://doi.org/10.3390/ijerph16030411.
11. Jansen L, Herrmann A, Stegmaier C, Singer S, Brenner H, Arndt V. Health-related quality of life during the 10 years after diagnosis of colorectal cancer: A population-based study. J Clin Oncol. 2011;29(24):3263-9. https://doi.org/10.1200/jco.2010.31.4013.
12. Jacobsen PB, Donovan KA, Vadaparampil ST, Small BJ. Systematic review and meta-analysis of psychological and activity-based interventions for cancer-related fatigue. Health Psychol. 2007;26(6):660-7. https://doi.org/10.1037/0278-6133.26.6.660.
13. Jung Y, Chung J, Son H. Physical activity interventions for colorectal cancer survivors: A systematic review and meta-analysis of randomized controlled trials. Cancer Nurs. 2021;44(6):E414-e28. https://doi.org/10.1097/ncc.0000000000000888.
14. Buffart LM, Thong MS, Schep G, Chinapaw MJ, Brug J, van de Poll-Franse LV. Self-reported physical activity: Its correlates and relationship with health-related quality of life in a large cohort of colorectal cancer survivors. PLoS One. 2012;7(5):e36164. https://doi.org/10.1371/journal.pone.0036164.
15. Grimmett C, Bridgewater J, Steptoe A, Wardle J. Lifestyle and quality of life in colorectal cancer survivors. Qual Life Res. 2011;20(8):1237-45. https://doi.org/10.1007/s11136-011-9855-1.
16. Krouse RS, Wendel CS, Garcia DO, Grant M, Temple LKF, Going SB, et al. Physical activity, bowel function, and quality of life among rectal cancer survivors. Qual Life Res. 2017;26(11):3131-42. https://doi.org/10.1007/s11136-017-1641-2.
17. Lewis C, Xun P, He K. Physical activity in relation to quality of life in newly diagnosed colon cancer patients: A 24-month follow-up. Qual Life Res. 2014;23(8):2235-46. https://doi.org/10.1007/s11136-014-0679-7.
18. Rodriguez JL, Hawkins NA, Berkowitz Z, Li C. Factors associated with health-related quality of life among colorectal cancer survivors. Am J Prev Med. 2015;49(6 Suppl 5):S518-27. https://doi.org/10.1016/j.amepre.2015.08.007.
19. Vallance JK, Boyle T, Courneya KS, Lynch BM. Associations of objectively assessed physical activity and sedentary time with health-related quality of life among colon cancer survivors. Cancer. 2014;120(18):2919-26. https://doi.org/10.1002/cncr.28779.
20. van Roekel EH, Winkler EA, Bours MJ, Lynch BM, Willems PJ, Meijer K, et al. Associations of sedentary time and patterns of sedentary time accumulation with health-related quality of life in colorectal cancer survivors. Prev Med Rep. 2016;4:262-9. https://doi.org/10.1016/j.pmedr.2016.06.022.
21. Eyl RE, Xie K, Koch-Gallenkamp L, Brenner H, Arndt V. Quality of life and physical activity in long-term (≥5 years post-diagnosis) colorectal cancer survivors - systematic review. Health Qual Life Outcomes. 2018;16(1):112. https://doi.org/10.1186/s12955-018-0934-7.
22. Grimmett C, Simon A, Lawson V, Wardle J. Diet and physical activity intervention in colorectal cancer survivors: A feasibility study. Eur J Oncol Nurs. 2015;19(1):1-6. https://doi.org/10.1016/j.ejon.2014.08.006.
23. Kraemer MB, Priolli DG, Reis IGM, Pelosi AC, Garbuio ALP, Messias LHD. Home-based, supervised, and mixed exercise intervention on functional capacity and quality of life of colorectal cancer patients: A meta-analysis. Sci Rep. 2022;12(1):2471. https://doi.org/10.1038/s41598-022-06165-z.
24. Gao R, Yu T, Liu L, Bi J, Zhao H, Tao Y, et al. Exercise intervention for post-treatment colorectal cancer survivors: A systematic review and meta-analysis. J Cancer Surviv. 2020;14(6):878-93. https://doi.org/10.1007/s11764-020-

00900-z.
25. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, et al. The prisma statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: Explanation and elaboration. BMJ. 2009;339:b2700. https://doi.org/10.1136/bmj.b2700.
26. Centre for Reviews and Dissemination. Systematic Reviews: CRD's Guidance for Undertaking Reviews in Health Care. Centre for Reviews and Dissemination, University of York; 2009.
27. Maher CG, Sherrington C, Herbert RD, Moseley AM, Elkins M. Reliability of the pedro scale for rating quality of randomized controlled trials. Phys Ther. 2003;83(8):713-21.
28. van Leeuwen M, Husson O, Alberti P, Arraras JI, Chinot OL, Costantini A, et al. Understanding the quality of life (qol) issues in survivors of cancer: Towards the development of an eortc qol cancer survivorship questionnaire. Health Qual Life Outcomes. 2018;16(1):114. https://doi.org/10.1186/s12955-018-0920-0.
29. Cochran WG. The combination of estimates from different experiments. Biometrics. 1954;10(1):101-29. https://doi.org/10.2307/3001666.
30. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med. 2002;21(11):1539-58. https://doi.org/10.1002/sim.1186.
31. R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing; 2020. Available from: https://www.r-project.org/
32. Viechtbauer W. Conducting meta-analyses in r with the metafor package. J Stat Softw. 2010;36(3):1 - 48. https://doi.org/10.18637/jss.v036.i03.
33. Bourke L, Thompson G, Gibson DJ, Daley A, Crank H, Adam I, et al. Pragmatic lifestyle intervention in patients recovering from colon cancer: A randomized controlled pilot study. Arch Phys Med Rehabil. 2011;92(5):749-55. https://doi.org/10.1016/j.apmr.2010.12.020.
34. Brown JC, Damjanov N, Courneya KS, Troxel AB, Zemel BS, Rickels MR, et al. A randomized dose-response trial of aerobic exercise and health-related quality of life in colon cancer survivors. Psychooncology. 2018;27(4):1221-8. https://doi.org/10.1002/pon.4655.
35. Christensen JF, Sundberg A, Osterkamp J, Thorsen-Streit S, Nielsen AB, Olsen CK, et al. Interval walking improves glycemic control and body composition after cancer treatment: A randomized controlled trial. J Clin Endocrinol Metab. 2019;104(9):3701-12. https://doi.org/10.1210/jc.2019-00590.
36. Courneya KS, Friedenreich CM, Quinney HA, Fields AL, Jones LW, Fairey AS. A randomized trial of exercise and quality of life in colorectal cancer survivors. Eur J Cancer Care (Engl). 2003;12(4):347-57. https://doi.org/10.1046/j.1365-2354.2003.00437.x.
37. Ho M, Ho JWC, Fong DYT, Lee CF, Macfarlane DJ, Cerin E, et al. Effects of dietary and physical activity interventions on generic and cancer-specific health-related quality of life, anxiety, and depression in colorectal cancer survivors: A randomized controlled trial. J Cancer Surviv. 2020;14(4):424-33. https://doi.org/10.1007/s11764-020-00864-0.
38. Kim JY, Lee MK, Lee DH, Kang DW, Min JH, Lee JW, et al. Effects of a 12-week home-based exercise program on quality of life, psychological health, and the level of physical activity in colorectal cancer survivors: A randomized controlled trial. Support Care Cancer. 2019;27(8):2933-40. https://doi.org/10.1007/s00520-018-4588-0.
39. Pinto BM, Papandonatos GD, Goldstein MG, Marcus BH, Farrell N. Home-based physical activity intervention for colorectal cancer survivors. Psychooncology. 2013;22(1):54-64. https://doi.org/10.1002/pon.2047.
40. Machado P, Pimenta S, Oliveiros B, Ferreira JP, Martins RA, Cruz J. Effect of exercise training on quality of life after colorectal and lung cancer surgery: A meta-analysis. Cancers (Basel). 2021;13(19). https://doi.org/10.3390/cancers13194975.
41. Norman GR, Sloan JA, Wyrwich KW. Interpretation of changes in health-related quality of life: The remarkable universality of half a standard deviation. Med Care. 2003;41(5):582-92. https://doi.org/10.1097/01.Mlr.0000062554.74615.4c.
42. Singh B, Hayes SC, Spence RR, Steele ML, Millet GY, Gergele L. Exercise and colorectal cancer: A systematic review and meta-analysis of exercise safety, feasibility and effectiveness. Int J Behav Nutr Phys Act. 2020;17(1):122. https://doi.org/10.1186/s12966-020-01021-7.
43. Lin KY, Shun SC, Lai YH, Liang JT, Tsauo JY. Comparison of the effects of a supervised exercise program and usual care in patients with colorectal cancer undergoing chemotherapy. Cancer Nurs. 2014;37(2):E21-9. https://doi.org/10.1097/NCC.0b013e3182791097.
44. Ray AD, Twarozek AM, Williams BT, Erwin DO, Underwood W, 3rd, Mahoney MC. Exercise in african american and white colorectal cancer survivors: A mixed methods approach. Rehabil Oncol. 2018;36(4):188-97. https://doi.org/10.1097/01.Reo.0000000000000125.
45. Buffart LM, Kalter J, Sweegers MG, Courneya KS, Newton RU, Aaronson NK, et al. Effects and moderators of exercise on quality of life and physical function in patients with cancer: An individual patient data meta-analysis of 34 rcts. Cancer Treat Rev. 2017;52:91-104. https://doi.org/10.1016/j.ctrv.2016.11.010.
46. McGettigan M, Cardwell CR, Cantwell MM, Tully MA. Physical activity interventions for disease-related physical and mental health during and following treatment in people with non-advanced colorectal cancer. Cochrane Database Syst Rev. 2020;5(5):Cd012864. https://doi.org/10.1002/14651858.CD012864.pub2.