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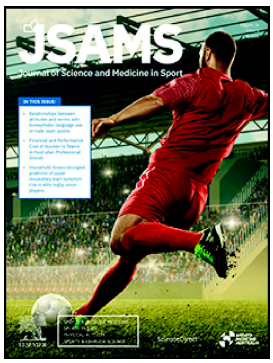

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Title:

Clinical updates on the effects of high intensity interval training (HIIT) exercise in people diagnosed with cancer. A systematic review and meta-analysis

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Key words: cancer, exercise, HIIT, oncology, quality of life, systematic review, meta-analysis

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Title:

Clinical updates on the effects of high intensity interval training (HIIT) exercise in people diagnosed with cancer. A systematic review and meta-analysis

Abstract:

Objective

To provide an updated critical evaluation on the effectiveness of high intensity interval training (HIIT) on health outcomes among cancer survivors.

Design

Systematic review and meta-analysis.

Method

A systematic search was conducted using databases CINAHL and Medline (via EBSCOhost platform), Scopus, Web of Science Core Collection, and the Cochrane Central Register of Controlled Trials. Randomised, controlled, exercise trials involving cancer survivors were eligible. Data on the effects of HIIT among individuals diagnosed with cancer at any stage were included. Risk of bias was assessed with the Mixed Methods Appraisal Tool (MMAT). Standardised mean differences (SMD) were calculated to compare differences between exercise and usual care. Meta-analyses (including subgroup analyses) were undertaken on the primary outcome of interest, which was aerobic fitness. Secondary outcomes were fatigue, quality of life, physical function, muscle strength, pain, anxiety, depression, upper-body strength, lower-body strength, systolic and diastolic blood pressure.

Results

Thirty-five trials from forty-seven publications were included, with intervention durations ranging between four to 18 weeks. Breast cancer participants were represented in the highest number of trials (n = 13, 37%). Significant effects in favour of HIIT exercise for improving aerobic fitness, quality of life, pain and diastolic blood pressure were observed (SMD range: 0.25-0.58, all $p<0.01$).

Conclusions

Participation in HIIT exercise was associated with higher retention and improvements in aerobic fitness, quality of life, pain and diastolic blood pressure. The present results provide updated contemporary evidence for clinicians (e.g., exercise physiologists and physiotherapists) to prescribe HIIT exercise for cancer survivors to improve health before, during and following treatment.

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Practical applications (non-scientific)

- Comprehensive meta-analysis of 35 trials (n=1893participants) using HIIT showed significant improvements across several physical outcomes in the cancer population.
- HIIT had a significant effect on improving aerobic fitness, fatigue, quality of life, pain and diastolic blood pressure compared to usual care.
- Non-significant effects were observed for physical function, muscle strength, anxiety, depression, fat mass, lean body mass, body fat (%) and systolic blood pressure using HIIT compared to the control groups.
- High retention rates were recorded at 95% (79% to 100%) for the HIIT groups and 92% (48% to 100%) for control groups, among different types of cancer populations.
- There was a total of 66 adverse events among participants allocated to HIIT exercise and 78 adverse events among participants allocated to comparator groups.
- Among the HIIT participants, 12 of the 66 adverse events were exercise-related and all were grade 1 (i.e., low severity; joint pain n=7; leg pain n=2; chest discomfort n=1; light-headedness n=1; muscle strain n=1).

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Introduction

There were approximately 19 million new cases of cancer globally in 2020, many will survive at least five years after their diagnosis (1), resulting in a population with unique long-term needs as a consequence of their cancer treatments. Cancer and its treatments can result in adverse side effects for individuals, including reductions in physical function, fatigue, psychological distress, and quality of life (2). Exercise is a widely accepted intervention to optimise physical, psychological and social aspects of holistic health and improve the wellbeing of those prior to, actively receiving, and recovering from cancer treatment (3-6). The Clinical Oncology Society of Australia (COSA) recommends that exercise should be implemented as adjunctive care for patients with cancer, as a method to counteract the adverse effects of cancer and the associated treatments (7).

Exercise can be beneficial throughout all stages of the cancer care continuum. Prior to treatment, exercise as a form of prehabilitation can lead to improved wellbeing and a reduction in the morbidity associated with cancer treatments (5, 8). Similarly, exercise throughout the cancer treatment experience has been demonstrated to preserve cardiovascular fitness, strength, and physical functioning, improve quality of life, and reduce fatigue (9). Following treatment, cancer survivors may benefit from participating in exercise, with physical activity improving a range of physical and psychosocial outcomes (10). Finally, participating in exercise can improve the quality of life, fitness, and fatigue for those receiving end of life palliative care (11).

High intensity interval training (HIIT) exercise is characterised by alternating intense bursts of activity followed by short recovery periods consisting of rest or light exercise (12). It focuses on exercising at, or near maximal oxygen uptake, and includes activities, such as, utilising treadmills and cycle ergometers. It has been demonstrated to result in benefits for cardiorespiratory fitness, skeletal muscle metabolism, vascular function, and other metabolic processes (12).

There is growing evidence to demonstrate the effectiveness of HIIT exercise throughout the cancer care continuum, however the evidence is yet to be pooled and critically synthesised. Existing evidence provides promising outcomes following HIIT exercise interventions in this population (13-16). The aim

of this review was to further explore the effectiveness of HIIT exercise on aerobic fitness and various health outcomes, including safety and feasibility to update the evidence for the potential use of HIIT exercise in the cancer population. To the best of the authors knowledge, to date this is the most comprehensive review and meta-analysis of HIIT across the cancer care continuum.

Methods

Search strategy and study selection

This review was registered on PROSPERO registry (ID: CRD42022377720) and was conducted and reported using the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement (17). Studies of quantitative design were included. Relevant systematic reviews were examined for potentially relevant studies. The Participants, Intervention, Comparator, and Outcome (PICO) framework (18) was used to develop the eligibility criteria as follows: Participants: All adults (>18 years) diagnosed with cancer, regardless of stage, treatment regime, stage in the cancer care continuum, who participated in a HIIT exercise intervention were considered for inclusion. Intervention: Randomised controlled trials, including pilot and feasibility trials that evaluate the effect of HIIT exercise on individuals diagnosed with cancer with any type and stage were included. Exercise was defined as any form of planned, structured, and repetitive bodily movement undertaken to improve or maintain fitness, performance or health (19), including aerobic, resistance, mixed-mode and other exercise. HIIT interventions that were between 80 and 100% VO2max or predicted maximum heart rate (HRmax), interspersed with recovery exercise or no exercise between intervals, were eligible. Typically, HIIT is referred to as an intense aerobic-based intervention, it can be further sub-categorised into low- and high-volume HIIT, as well as 'sprint interval training' (SIT). Comparators: Studies that compared HIIT exercise, including different intensities and frequencies to control or usual care groups were included. Studies were excluded if; (a) they were non-RCTs, (b) they were not related to the outcomes of the review, (c) had no control/comparison group, (d) were animals or in vitro experiments, (e) were commentaries, conference abstracts, editorials or abstracts only, (f) cohorts other than cancer survivors, (g) reviews studies (any type) or (h) were clinical trial registrations.

Searches were carried out on 29th November 2022 by two of the authors, including an expert librarian, using the databases CINAHL and Medline (via EBSCOhost platform), Scopus, Web of Science Core Collection, and the Cochrane Central Register of Controlled Trials. Searches were based on key words relating to the study and Medical Subject Headings (MeSH) for 'High Intensity Interval Training' and 'Cancer' were used. To increase the inclusivity of search results, no date or language limiters were applied. See Supplementary 1 for full record of database searches. Reference lists of eligible full text articles were reviewed to ensure no studies were overlooked. All records were managed using Endnote X20 and uploaded to the Covidence systematic review management software for the removal of duplicates and screening according to determined eligibility criteria.

Outcomes of interest

Meta-analyses (including subgroup analyses) were undertaken on the primary outcome of interest, which was aerobic fitness. Secondary outcomes of fatigue, quality of life, physical function, muscle strength, pain, anxiety, depression, upper-body strength, lower-body strength, systolic and diastolic blood pressure were also assessed.

Feasibility: participation and retention rates

Safety: frequency and severity of adverse events were assessed using the Common Terminology Criteria for Adverse Events (Version 6.0) to categorise and classify the events.

Data extraction and management

Two review authors independently screened all titles and abstracts of identified records against the inclusion criteria. A third reviewer resolved all conflicts. The full text of all potentially eligible records were retrieved and screened independently by two authors. Any conflicts were resolved by a third reviewer or via discussion.

Study characteristics were extracted by one author using a standardised extraction form. A second author checked the data extraction for accuracy. Data were extracted and included in a table of "overview of included studies" and included: author and year, purpose of study, setting, country, sample

size, participant demographic and clinical diagnosis, treatment types, study design, primary outcome measures, losses, retention and exclusion of participants.

The risk of bias was assessed for each included study using the Mixed Methods Appraisal Tool (MMAT) (20). Two authors independently assessed the studies and discussed any discrepancies with a third reviewer.

Statistical analysis

Meta-analyses were performed for aerobic fitness and health-related outcomes, which were analysed as continuous variables. Post-intervention means and standard deviations (SDs) were compared between the exercise and usual care groups. To facilitate comparisons across different measurement scales, standardized mean differences (SMDs) were used as the effect measures, calculated using RevMan software v5.3. Forest plots for each meta-analysis were generated using R statistical software v3.6.2. In cases where means and SDs were not reported in a paper (n=1 trial), the authors were contacted (n=0 responded), or formulas recommended by experts were utilized to estimate the means and/or SDs based on the available data (e.g., median, range, and sample size) (21). If a trial involved multiple instruments to assess an outcome, the instrument regarded as the gold standard or one with established validity and reliability was selected.

At the trial level, data from each meta-analysis were combined. Funnel plots were employed to assess publication bias, plotting SMDs against standard errors and examining for asymmetries or missing sections (22) . The following thresholds were used to describe effect sizes: less than 0.20 denoted a small effect, 0.20–0.50 indicated a medium effect, and greater than 0.50 represented a large effect (23). Statistical significance was set at a P value less than .05. Cochran's Q test was utilized to evaluate statistical heterogeneity, and the proportion of overall outcome variability was examined using the I^2 statistic (23, 24) . The I^2 values were interpreted as follows: I^2=0%–29%, no heterogeneity; I^2=30%−49%, moderate heterogeneity; I^2=50%−74%, substantial heterogeneity; and I^2=75%−100%, considerable heterogeneity (24) ref. Planned subgroup analyses were conducted to assess the effects of cancer type (prostate or testicular, lung, breast, colorectal, urological or bladder, leukemia or

haematological and mixed) and treatment status (pre-treatment or pre-surgery, post-treatment, during treatment and mixed [studies involved participants during and post-treatment]).

Results

Literature search

A total of 35 trials (comprising of 47 published papers) were included (see Figure 1; Table 1). Quality appraisal results can be found in Supplementary 2. Most of the issues were related to blinding of outcome assessors to the intervention, which is common in exercise studies.

Figure 1. Article selection process according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Guidelines (25).

Study and participant characteristics

Participants with difference types of cancers were included and a total of (n = 1893) were represented in this review. Specifically, the studies were inclusive of participants diagnosed with breast (n = 13), testicular (n = 1), prostate (n = 5), bladder (n = 1), lung (n = 5), mixed (n = 4), colorectal (n = 4), and haematological (n = 2). An overview of the study characteristics is shown in Table 1, and individual study characteristics are provided in more detail in the data extraction table, supplementary 3. Supplementary 4 shows the HIIT prescription used in each study and supplementary 5shows the outcome collection measures for each study.

Table 1. Overview of study characteristics (n=36 trials).

Intervention characteristics

Intervention durations ranged between 4-18 weeks (average 10 weeks). A total of 35 intervention arms and 36 control arms were evaluated. Interventions were carried out during: i) prehabilitation (n = 7)(26-32); ii) treatment naïve, including active surveillance (n = 5) (33-37); iii) treatment (n = 15) (38-60); iv) survivorship (n = 10) (14, 16, 61-69); and v) a combination of active and completed treatment (n =

1) (70) stages. HIIT exercise training protocols varied across the interventions; a breakdown can be found in supplementary table 4.

Meta-analysis results

Aerobic fitness and other health outcomes of interest: Meta-analysis of 27 trials (n=1282 participants) showed that HIIT had significant effects for improving aerobic fitness (SMD=0.58 [95% CI=0.44, 0.72], I^2=29%, p<0.01) compared to control groups (Figure 2). Significant effects of HIIT were also observed for fatigue (n=13 trials, n=766 participants, SMD=0.36 [95% CI=0.21, 0.51], I^2=0, p<0.01), quality of life (n=13 trials, n=699 participants, SMD=0.25 [95% CI=0.06, 0.44], I^2=24, p=0.01), pain (n=7 trials, n=454 participants, SMD=0.27 [95% CI=0.08, 0.45], I^2=0, p<0.01) and diastolic blood pressure (n=7 trials, n=213 participants, SMD=0.55 [95% CI=0.18, 0.92], I^2=39, p<0.01) compared to usual care (Figures 2 and 3). No significant effects were observed for physical function, muscle strength, anxiety, depression, fat mass, lean body mass, body fat (%) and systolic blood pressure (SMD range= 0.00 to 0.35, all p>0.05)

Subgroup analyses: Results for subgroup analyses for aerobic fitness are shown in supplementary

6. Subgroup analyses showed no significant difference between cancer types (prostate or testicular, lung, breast, colorectal, urological or bladder, leukemia or haematological and mixed) and treatment status (pre-treatment or pre-surgery, post-treatment, during treatment and mixed [studies involved participants during and post treatment]) on changes in aerobic fitness (test for subgroup differences p>0.05). For cancer type, significant improvements (all p<0.05) in aerobic fitness were observed for prostate or testicular (SMD=0.67 [95% CI=0.32, 1.02]), lung (SMD=0.52 [95% CI=0.30, 0.74]), breast (SMD=0.70 [95% CI=0.43, 0.96]), colorectal (SMD=0.83 [95% CI=0.35, 1.31]) and mixed (SMD=0.59 [95% CI=0.01, 1.17]). For treatment, improvements in aerobic fitness (all p<0.05) were observed pre- (SMD=0.47 [95% CI=0.29, 0.65]), post- (SMD=0.84 [95% CI=0.54, 1.14]) and during treatment (SMD=0.59 [95% CI=0.34, 0.84]).

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Feasibility and safety: Median (range) recruitment rate was 52% (6% to 90%) and median (range) retention rates were 95% (79% to 100%) for HIIT and 92% (48% to 100%) for the control conditions. There were a total of 66 exercise and non-exercise-related adverse events among participants allocated to HIIT (n=12 grade 1 events; n=1 grade 2 events; n=32 grade 3 events; n=15 grade 4 events; n=6 grade 5 events) and 78 adverse events among participants allocated to control (n=0 grade 1 events; n=0 grade 2 events; n=57 grade 3 events; n=15 grade 4 events; n=6 grade 5 events). Among the HIIT participants, 12 of the 66 adverse events were exercise-related and all were grade 1 (joint pain n=7; leg pain n=2; chest discomfort n=1; light-headedness n=1; muscle strain n=1).

Figure 2. Meta-analysis results for aerobic fitness, fatigue, quality of life, physical function, muscle strength, pain, anxiety and depression, comparing HIIT to control.

Figure 3. Meta-analysis results for fat mass, lean body mass, body fat (%), systolic blood pressure and diastolic blood pressure, comparing HIIT to control.

Discussion

This systematic review and meta-analysis set out to provide an updated evaluation on the effectiveness of high intensity interval training (HIIT) on health outcomes among cancer survivors across the cancer care continuum. To date, this is the largest meta-analysis on HIIT in cancer, inclusive of thirty-five trials from forty-seven publications, representing 1893 participants with cancer. Broadly, existing HIIT intervention duration ranged between four to 18 weeks (average 10 weeks) and biased in favour of breast cancer participants. Significant effects in favour of HIIT exercise for improving aerobic fitness, quality of life, pain and diastolic blood pressure were observed which have important clinical translation implications.

These findings have several implications that could be considered in clinical practice when supporting people with cancer. Prehabilitation is an underutilised area of potential use of HIIT, and a critical time where people are preparing for major cancer surgeries and extensive treatment regimes. HIIT provided significant health benefits identified in this systematic review and could provide an efficient intervention to improve or maintain fitness prior to cancer treatments. It is useful to note that no significant effects were observed for lean mass, fat mass, muscle strength or physical function, which are often targeted outcomes for patients across the cancer continuum. The interval nature of HIIT, which is interspersed with rest periods, could mean that it would potentially be more tolerable for individuals who have less time or who are deconditioned. It could also be used in a lower more tolerable volume for people with more serious health challenges.

It is recommended that individual health assessments and preferences be taken into consideration when using HIIT prescription and session monitoring should occur, at least in the first instance (Figure 4), this is in line with current cancer specific exercise recommendations (71). Although HIIT may not be for everyone, as one size do not fit all, it should not be ruled out as something that cannot be offered. It has been reported to be more potent than moderate intensity training and even more enjoyable in some other populations such as overweight women and young adults (72, 73). Figure 4 has therefore been developed based on the findings of this review, to assist clinicians practically, in implementing a HIIT program for people with cancer.

Figure 4: Exercise recommendations, considerations and HIIT session guidelines for people with cancer.

Future recommendations

An important area for future research lies in the evaluation of different exercise intensities in the context of HIIT exercise for people diagnosed with cancer. A notable limitation of the current systematic review and meta-analysis was the inadequate reporting of exercise intensity in the included studies. Without

detailed information on exercise intensity, it becomes challenging to ascertain the specific impact of varying intensities of HIIT on cancer-related outcomes. Understanding the optimal intensity of HIIT exercise for people diagnosed with cancer could help tailor exercise interventions to individual needs and potentially maximize the benefits derived from such interventions. Future studies should prioritize accurate and standardized reporting of exercise intensity to enable a more comprehensive evaluation of the effects of different intensities of HIIT exercise in the cancer population, across the entire cancer care continuum.

Conclusion

Exercise intensity and dose should be carefully considered when prescribing exercise for the cancer population because different personal effects can be achieved by adjusting these factors. This review and meta-analysis demonstrated that HIIT exercise significantly improved aerobic fitness, fatigue, quality of life, pain and diastolic blood pressure compared to the comparator groups and therefore should be considered when prescribing exercise for people diagnosed with cancer. HIIT's potent effect could be key to promptly improving the health of people undergoing significant anti-cancer treatments. HIIT is currently underutilised in prehabilitation, during treatment and at end-of-life care for many diverse cancer populations. A low volume HIIT prescription could be tolerated well in people with health challenges, however, more research in this area is needed.

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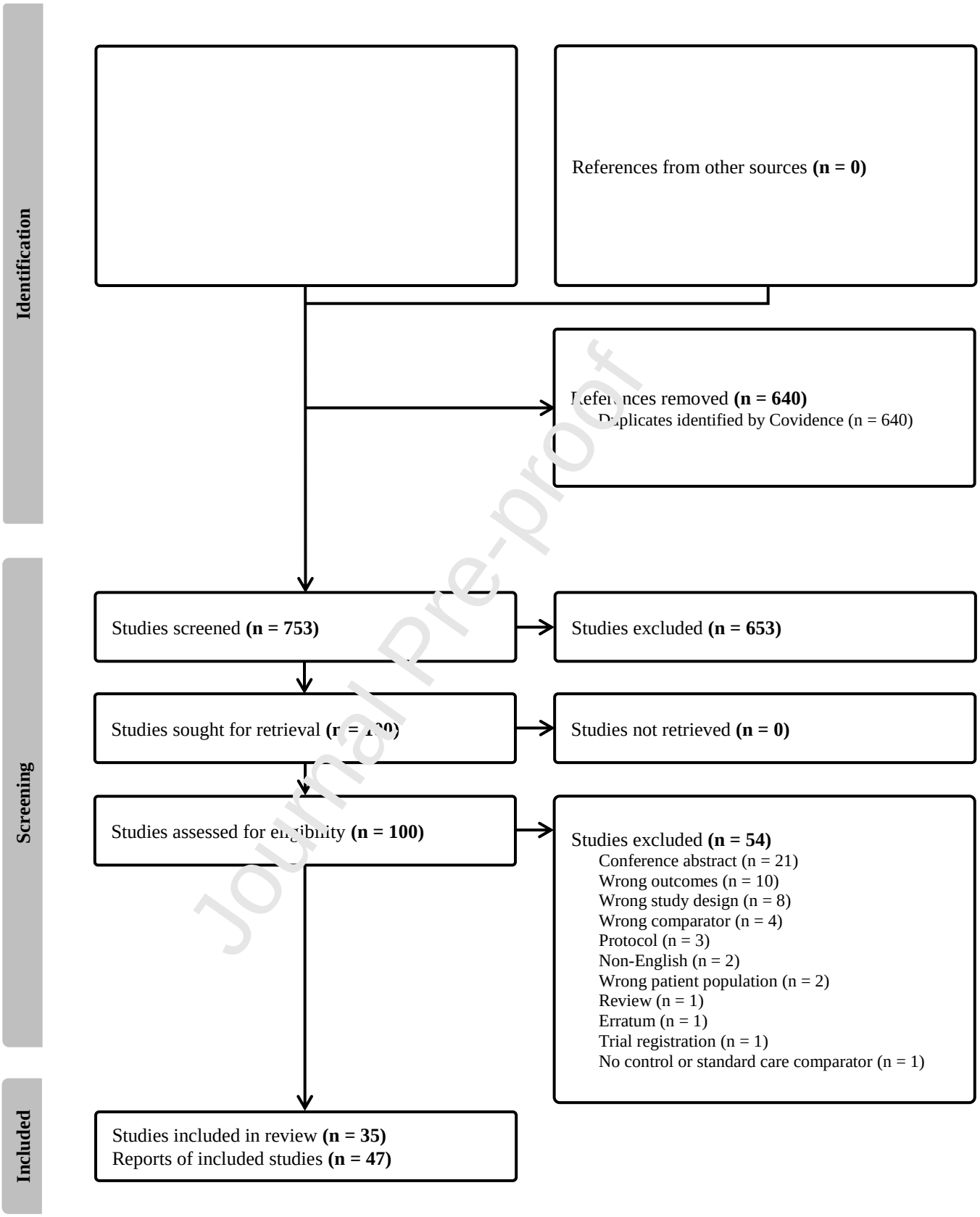

Figure 1. Search strategy and article selection process according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Guidelines (25).

Table 1. Overview of study characteristics (n=35 trials).

Study	Sample Size	Cancer Type	Exercise Duration and Attendance
Adams et al., 2017 (61); Adams et al., 2018 (62)	n=63; >50	Type: testicular; treatment: single orchidectomy, radiotherapy & chemotherapy; stage: not specified	12 weeks; 99% exercise session attendance
Alizadeh et al., 2019 (38)	n=52; >50	Type: breast; treatment: surgery, chemotherapy, radiotherapy & hormone; stage: non-metastatic & hormone-responsive	12 weeks; exercise adherence not reported
Ansund et al., 2021 (39)	n=88; >50	Type: breast; treatment: chemotherapy consisting of anthracyclines, taxanes, or a combination of the two	16 weeks; exercise adherence not reported
Baguley et al., 2022 (40)	n=23; <50	Type: prostate; treatment: radiation, chemotherapy, and ADT; stage: Gleason score 8.4 (1.1)	Weeks 12-20 of a 20-week intervention; 93.4% exercise session attendance
Banerjee et al., 2018 (26)	n=60; >50	Type: bladder; treatment: surgery and chemotherapy; stage: not specified	Two exercise sessions per week prior to surgery; 83% exercise session attendance
Bhatia et al., 2019 (27)	n=151; >50	Type: lung; treatment: prehabilitation for surgery; stage: early-stage (IIIA or less) non-small cell	Median of 8 sessions prior to surgery; 87% exercise session attendance
Blackwell et al., 2020 (28)	n=40; <50	Type: urological; treatment; prehabilitation for treatment; stage: not specified	4 weeks; 84% exercise session attendance
Devin et al., 2018 (63)	n=57; >50	Type: colorectal; treatment: surgery, chemotherapy, and radiotherapy; stage: I-IV	12 weeks; 99% exercise session attendance
Dimeo et al., 1997 (41)	n=70; >50	Type: various; treatment: chemotherapy; stage: not specified	Hospitalisation duration of high-dose chemotherapy; exercise adherence not reported
Djurhuus et al., 2022 (29)	n=30; <50	Type: prostate; treatment: prehabilitation for radical prostatectomy	8 weeks; 100% exercise session attendance
Dolan et al., 2016 (64)	n=33; <50	Type: breast; treatment: combinations of surgery, chemotherapy, radiation, and hormonal therapy; stage: early (I-IIIA)	6 weeks; exercise adherence not reported
Dunne et al., 2016 (30)	n=38; <50	Type: colorectal liver metastasis; treatment: prehabilitation for surgical resection; stage: IV	4 weeks; 18 of 19 patients completed 100% of sessions
Egegaard et al., 2019 (42)	n=15; >50	Type: non-small cell lung cancer (NSCLC); treatment: concomitant chemoradiotherapy; stage: IIIa, IIIb, IV	7 weeks; 90% exercise session attendance
Gonzalo-Encabo et al., 2022 (43)	n=30; <50	Type: breast; treatment: neoadjuvant and adjuvant anthracycline chemotherapy; stage: II and III	8 weeks; 82.3% exercise session attendance
Hooshmand Moghadam et al., 2021 (65)	n=45; <50	Type: breast; treatment: surgery and concomitant chemotherapy or radiotherapy, hormonal therapy including tamoxifen and aromatase inhibitors	12 weeks; 86% exercise session attendance
Hwang et al., 2012 (44)	n=24; <50	Type: non-small cell lung; treatment: targeted therapy including Iressa, Tarceva , and Afatinib; stage: IIIA, IIIB, and IV	8 weeks; 71.2% exercise session attendance
Kang et al., 2021 (35); Kang et al., 2022a, (33); Kang et al., 2022b (34)	n=52; >50	Type: prostate, treatment: active surveillance; stage: T1c and T2a	12 weeks; 96% exercise session attendance
Karenovics et al., 2017 (31); Licker et al., 2017 (32)	n=151: >50	Type: lung; treatment: surgery; stage: ASA classes 3 and 4	Prehabilitation before surgery; 69% exercise session attendance
Lee et al., 2019a (46); Lee et al., 2019b (45); Lee et al., 2020 (47) ,	n=30; <50	Type: breast, treatment: anthracycline-based chemotherapy; stage: II & III	8 weeks; 82.3% exercise session attendance

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MacDonald et al., 2021 (36)	n=18; <50	Type: chronic lymphocytic leukemia (CLL); treatment: no treatment; stage: Rai stage 0 or 1	12 weeks; 99% exercise session attendance
MacVicar et al., 1989 (48)	n=45; <50	Type: breast; treatment: chemotherapy; stage: II	10 weeks; exercise adherence not reported
Mijwel et al., 2018a (49); Mijwel et al., 2018b (50); Mijwel et al., 2018c (51); Mijwel et al., 2019 (52); Wiggenraad et al., 2020 (53); Hiensch et al., 2021 (54); Bolam et al., 2019 (55)	n=240; >50	Type: breast; treatment: chemotherapy; stage: I-IIIa	16 weeks; 83% (RT–HIIT group) and 75% (AT–HIIT group) exercise session attendance
Morielli et al., 2021 (56)	n=36; <50	Type: rectal; treatment: scheduled to receive standard long-course neoadjuvant chemoradiation (NACRT) consisting of radiation with concurrent chemotherapy, followed by total mesorectal excision; stage: III (64% of participants)	Throughout NACRT (approximately 5-6 weeks); 82% exercise session attendance
Northey et al., 2019 (66)	n=17; <50	Type: breast; treatment: post-treatment; stage: I-III	12 weeks; 78.7% (HIIT group), 79.4% (MOD group) exercise session attendance
Ochi et al., 2022 (67)	n=50	Type: breast; treatment: completed initial treatment except for hormone therapy; stage: I-IIa	12 weeks; 86% exercise session attendance
Papadopoulos et al., 2021 (37)	n=18; <50	Type: prostate; treatment: active surveillance; stage: early stage	8 weeks; 96% exercise session attendance
Persoon et al., 2017 (68)	n=109; >50	Type: hematologic malignancy; treatment: post autologous stem cell transplantation; stage: not reported	18 weeks; 86% exercise session attendance
Piraux et al., 2021 (57)	n=78; >50	Type: prostate; treatment: radiotherapy; stage: not reported	5 or 8 weeks (depending on radiotherapy regime); 93.5% exercise session attendance
Piraux et al., 2022 (58)	n=18; <50	Type: rectal; treatment: chemoradiotherapy; stage: II-IIA	5 weeks; 92% exercise session attendance
Reljic et al., 2022 (59)	n=27; <50	Type: advanced; treatment: ongoing anticancer therapy; stage: III-IV	12 weeks; 92.5% exercise session attendance
Samhan et al., 2021 (69)	n=60; >50	Type: breast; treatment: post-treatment; stage: I-III	8 weeks; adherence not reported
Schulz et al., 2018 (70)	n=26; <50	Type: breast; treatment: post and during treatment (chemotherapy, radiotherapy, hormone therapy)	6 weeks; 73% completed 12 sessions, 20% completed 11 sessions and 7% completed 10 sessions
Sommer et al., 2016 (60)	n=40; <50	Type: non-small cell lung; treatment: surgical resection; stage: 1, 2, 3A	Duration – not reported; 67% preoperative and 73% postoperative exercise session attendance
Toohey et al., 2018 (14)	n=75; >50	Type: breast (47), Ovarian (2), appendix (1), anal (1), cervical (1), liver (1), oesophageal (1), Melanoma (1), leiomyosarcoma (1), unknown primary (1); treatment: surgery, radiation therapy, hormone therapy, chemotherapy, no chemotherapy; stage: I-II (45), II-IV (12)	12 weeks; 76% exercise session attendance
Toohey et al., 2020 (16)	n=17; <50	Type: breast; treatment: surgery, radiation, surgery plus chemotherapy, surgery plus radiation, surgery plus chemotherapy plus radiation	12 weeks; 78.7% (HIIT group) and 79.4% (moderate group) exercise session attendance

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Figure 2. Meta-analysis results for aerobic fitness, fatigue, quality of life, physical function, muscle strength, pain, anxiety and depression, comparing HIIT to control.

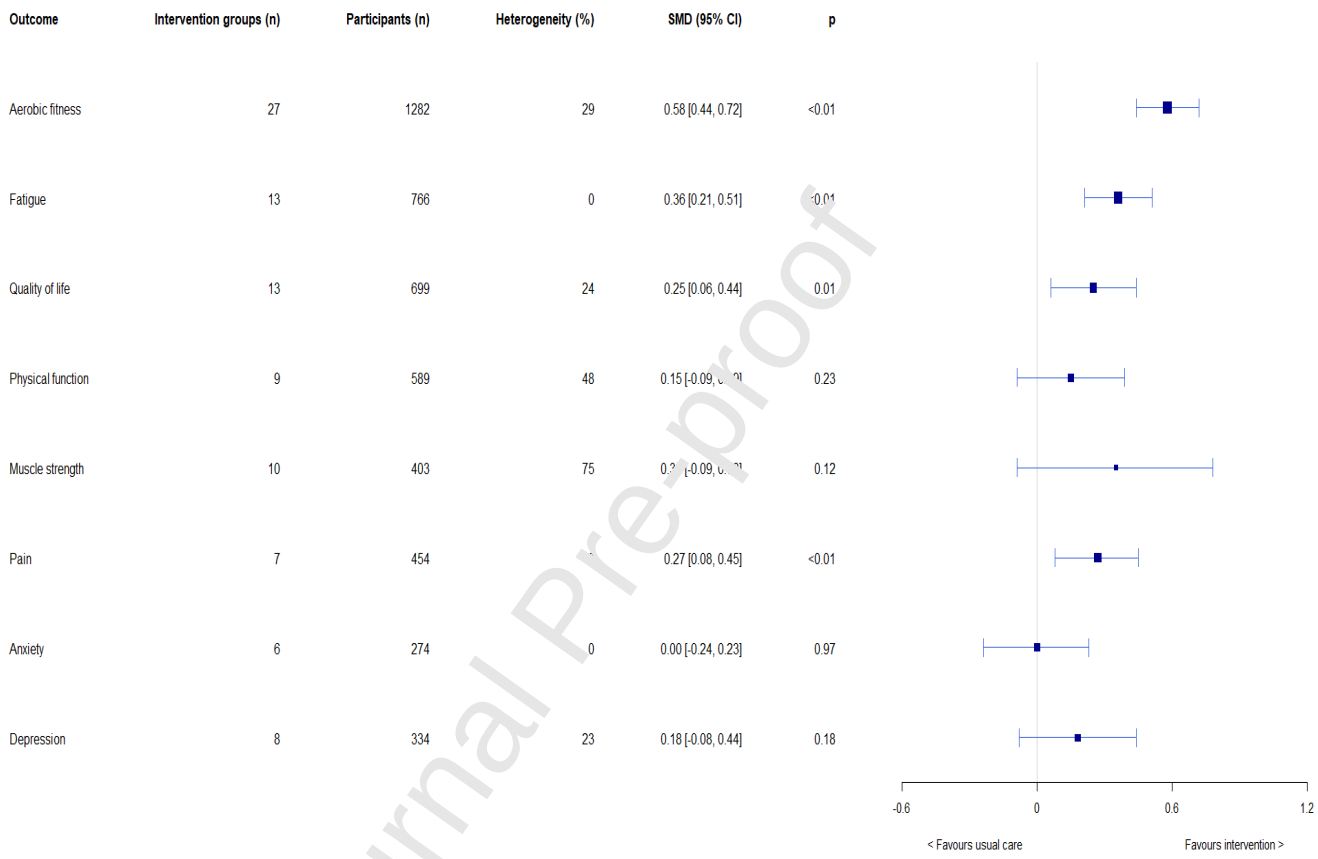

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Figure 3. Meta-analysis results for fat mass, lean body mass, body fat (%), systolic blood pressure and diastolic blood pressure, comparing HIIT to control.

Outcome	Intervention groups (n)	Participants (n)	Heterogeneity (%)	SMD (95% CI)	p
Fat mass	8	255	61	0.21 [-0.21, 0.62]	0.33
Lean body mass	10	282	10	0.16 [-0.10, 0.42]	0.22
Body fat (%)	7	281	99	0.00 [-0.46, 0.46]	0.99
Systolic blood pressure	7	213	23	0.22 [-0.1 , 0.5]	0.18
Diastolic blood pressure	7	213	39	0.5 [0.18, 0.92]	<0.01

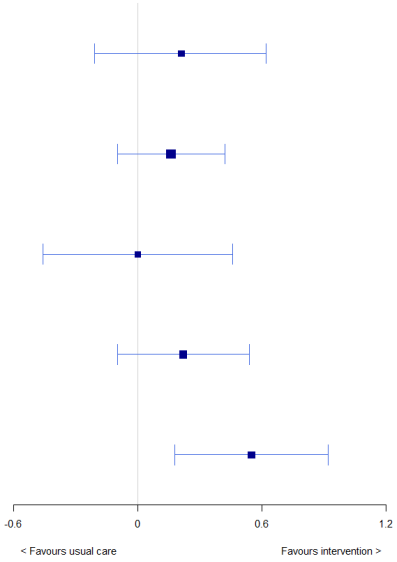

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Figure 4: Exercise recommendations, considerations and HIIT session guidelines for people with cancer.

General recommendations (74)	Follow ACSM's relative and absolute contraindications for exercise**.**
Cancer specific exercise considerations (75)	**<u>Absolute contraindications:</u>** Bone pain During IV treatment: · febrile illness: 38°C/100.4°F– even if feeling well; · Resting SBP < 85 mmhg; · haemoglobin (hb): < 8.0g/dl or < 80 g/l (without CVD), < 9.0g/dl or 90g/l (with CVD) Platelets: < 20,000 µl Absolute neutrophils: < 0.5 × 109/l **<u>Relative contraindications:</u>** During IV treatment: · Vomiting or diarrhea within 24–36 hours; · Platelets: 20,000 – 50,000 µl (low impact, light intensity) *Relative contraindications can be suspended if exercise benefits outweigh risk. Proceed with caution.*
HIIT session guidelines	Intervention period - average 10 weeks (4-18 weeks)
	Sessions - 3 times per week – bike or treadmill – aim for regular exercise patterns
	Initial supervision by a qualified, experienced professional until confident and normal exercise responses. Supervision also recommended with lack of exercise exposure, complex health conditions and new symptom presentations
	<u>Pre-exercise monitoring</u> – HR, BP, BGL's (during treatment), blood counts, unusual symptoms – proceed if in normal ranges
	<u>During exercise monitoring</u> – HR, BP for the first session (minimum) to understand individuals' response
	Warm up - 5-10 minutes - 50% HRpeak
	HIIT's - 1 – 4 min at 75 – 90% HRpeak, 13-15 RPE with 1-4 minutes rest in between Start with shorter HIITs initially and longer rests in between, work with what is tolerated by the individual, progress as tolerated, and regress as needed
	Cool down - 10 minutes – 50% HRpeak
	<u>Post exercise monitoring</u> – HR and BP, until back to normal ranges

ACSM – American college of sports medicine; IV – intravenous; C – Celsius; F – Fahrenheit; SBP – systolic blood pressure; mmgH – millimetres of mercury; hb – haemoglobin; g – grams; dl – decilitre; gl – gigalitre; µl – microlitre; CVD – cardiovascular disease; L – litre; HR – heart rate; BP – blood pressure; BGL's – blood glucose levels; HIIT – high intensity interval training, RPE – rate of perceived exertion.

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Declarations of interest

None.

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Confirmation of Ethical Compliance

NIL – review.

Credit Author Statement

Contribution of authors

Concept/design: K. Toohey; systematic data search: M. Turner and M. Hunter; data screening and extraction: all listed authors; data analysis: K. Toohey and B. Singh; data interpretation: K. Toohey, M. Hunter and B. Singh; draft: K. Toohey; critical revision, writing contribution and approval: all listed authors.

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