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REVIEW

High-intensity interval training in the therapy and aftercare of cancer patients: a systematic review with meta-analysis

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Abstract

Purpose This review and meta-analysis aimed to evaluate the effects of high-intensity interval training (HIIT) compared to usual care (UC) or moderate-intensity training (MIE) on physical fitness and health-related outcomes in cancer patients across all stages of therapy and aftercare.

Methods Databases were systematically searched in accordance with the PRISMA guidelines until October 4th, 2018. Eligibility criteria included adult patients of various cancer types, performing HIIT vs. UC or MIE. Outcomes of interest included physical fitness (cardiorespiratory fitness [VO_{2peak}] and functional capacity) and health-related outcomes (body composition, quality of life, cancer-related fatigue, and blood-borne biomarkers). Mean differences (MD) were calculated and pooled to generate effect sizes for VO_{2peak}.

Results The search identified 1453 studies, out of which 12 articles were included. The average duration of interventions was 6.7 ± 3.0 weeks, with 2.8 ± 0.5 sessions per week. The meta-analysis for VO_{2peak} showed superiority of HIIT compared to UC (MD 3.73; 95% CI 2.07, 5.39; $p < 0.001$) but not MIE (MD 1.36; 95% CI − 1.62, 4.35; $p = 0.370$). Similarly, no superior effects of HIIT compared to MIE were found for quality of life or changes in lean mass, while evidence was provided for a larger reduction in fat mass.

Conclusion This systematic review showed that short-term HIIT induces similar positive effects on physical fitness and health-related outcomes as MIE but seems to be superior compared to UC. Thus, HIIT might be a time-efficient intervention for cancer patients across all stages of therapy and aftercare.

Implications for Cancer Survivors High-intensity interval training (HIIT) is superior compared to usucal care in improving physical fitness and health-related outcomes in cancer patients across all stages of therapy and aftercare. Currently, there is no evidence for the benefits of HIIT compared to aerobic training of moderate intensity (MIE) for changes in cardiorespiratory fitness, lean mass and patient-reported outcomes. Reductions in fat mass may be more pronounced in HIIT compared to MIE when training is performed in aftercare.

Keywords Exercise medicine · Rehabilitation · HIIT · Exercise oncology

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Introduction

Oncological prehabilitation, rehabilitation, and palliative care are essential components for the treatment and/or secondary prevention of cancer- or treatment-related impairments [1, 2]. In addition, independent of the treatment phase, supervised exercise training is commonly performed to ameliorate quality of life (QoL) and to cope with activities of daily living by improving independency and psychosocial and cognitive health as well as physical fitness in cancer patients [1, 2]. Exercise as part of standard care to improve overall and progression-free survival of cancer patients was previously outlined by the Clinical Oncological Society of Australia position statement and the first clinical practice exercise guidelines [3, 4].

Previous research has provided evidence for a remarkable potential to reduce cancer-related and cancer-treatment–related effects through physical exercise [5, 6]. Furthermore, numerous types of physical training might reduce mortality and recurrence rates of various cancer entities [7–9]. It is likely that these beneficial effects are brought about in a dose–response manner, where exercise regimens which improve physical fitness and health-related outcomes to the greatest extent may have the largest impact in reducing cancer-related morbidity and mortality [10, 11].

High-intensity interval training (HIIT) has been proven to be a safe, feasible, and especially effective method to improve physical fitness, health-related outcomes, and patient-reported outcomes, e.g., improved QoL [10, 12–14] in various chronic diseases. However, research regarding HIIT in cancer patients remains scarce, with recent evidence suggesting that HIIT may also be an effective intervention for distinct cancer entities, such as breast [15], colorectal [16], and testicular cancer [17]. In addition to improvements in cardiorespiratory fitness and patient-reported outcomes, HIIT was found to be also more cost-effective in adult cancer patients compared to other types of endurance training, i.e., by lowering supervision time and overhead costs or by reducing medication use [18]. However, despite these preliminary benefits, concerns have been brought forward regarding possible detrimental effects of HIIT on inflammatory profiles, which may also affect tumor biology [19].

A recent systematic review on the impact of high-intensity exercise in cancer patients concluded that high-intensity exercise is feasible and safe in various cancer entities [20]. However, no clear distinction between intensive aerobic and strength training was made. Therefore, conclusions about the sole contribution of aerobic HIIT on the outcome parameters like body composition or cardiorespiratory fitness may not be reasonable. In addition, it was not distinguished between interventions carried out during or after treatment. Consequently, we performed a systematic literature review to investigate primarily the effects of sole HIIT on physical fitness (i.e., cardiorespiratory fitness [VO_{2peak}] and functional capacity [6-min walking test]) and health-related outcomes (i.e., body composition [BMI, lean and fat mass, waist and hip circumferences], blood-borne biomarkers [C-reactive protein, low-density lipoprotein, blood glucose concentration]) as well as patient-reported outcomes (i.e., QoL, cancer-related fatigue, anxiety, depression, treatment-related side effects) of cancer patients during all stages of therapy and aftercare. Special consideration was given to investigate whether HIIT is more effective than moderate-intensity training (MIE) in cancer patients and if this effect is dependent on the therapy phase (i.e., prehabilitation, during treatment, or aftercare).

Methods

A systematic literature search was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [21] and was registered with the international database of prospectively registered systematic reviews in health and social care (PROSPERO: CRD42018096817).

The electronic databases of PubMed, Web of Science, and EMBASE were systematically searched until October 4th, 2018, using identical search strings (Table 1). English and German language publications in human populations with no restrictions to the study design were included. Two authors (HM; NF) independently performed the literature search and disagreements were resolved by further consultation from a third author (MS). The search process included removing duplicates and screening titles, abstracts, and eligible full texts. Additionally, reference lists of all potentially eligible full texts and excluded cancer and exercise-related review articles were manually checked for further studies of relevance.

Eligibility criteria

Adult male and female cancer patients with malignant cancer types who were undergoing (in treatment) or completed (aftercare) common standalone or combinations of neo- or adjuvant therapies, including chemotherapy, radiation, hormonal therapy, immunotherapy, stem cell transplantation, and surgery, were eligible for this systematic review and meta-analysis. Studies comparing cancer patients participating in aerobic HIIT with either receiving aerobic MIE or usual care (UC) were considered. Studies involving high-intensity strength training, aerobic high-intensity continuous training, or a mixture of HIIT and continuous training or strength interventions were excluded. Furthermore, only training interventions with a duration of at least 3 weeks of HIIT were included to assure sufficient time for chronic adaptations to take place. High intensities were a priori defined as ≥ 75% of peak work rate (WR_{peak}), peak oxygen uptake (VO_{2peak}), peak heart rate (HR_{peak}), maximal heart rate (HR_{max}) [22], or equivalent

Table 1 Search terms used for PubMed, Web of Science, and EMBASE

Database	Category		
	Cancer	Therapy	HIIT
PubMed	neoplas*[Title/Abstract]) metastat*[Title/Abstract]) cancer*[Title/Abstract]) carcino*[Title/Abstract]) carcinoma*[Title/Abstract]) onco*[Title/Abstract]) tumor*[Title/Abstract]) tumour*[Title/Abstract]) malignan*[Title/Abstract])	medical oncology [Title/Abstract]) radiation[Title/Abstract]) immunotherp*[Title/Abstract]) chemotherp*[Title/Abstract]) hormonal therap*[Title/Abstract]) Aftercare[Title/Abstract]) After care[Title/Abstract]) After treatment[Title/Abstract]) usual care[Title/Abstract]) adjuvant*[Title/Abstract]) neoadjuvant*[Title/Abstract]) rehabilitation[Title/Abstract])	HIT[Title/Abstract]) HIIT[Title/Abstract]) High-intensit*[Title/Abstract]) High Intensity Interval Training*[Title/Abstract]) High intensity training*[Title/Abstract]) High intensity exercise program*[Title/Abstract]) High intensity aerobic exercise training*[Title/Abstract]) Interval training*[Title/Abstract]) High intensity exercise intervention*[Title/Abstract]) Intermittent Exercise*[Title/Abstract]) High intensity aerobic exercise progam*[Title/Abstract])
Web of Science	(TS = (neoplas* metastat* cancer* carcino* carcinoma* onco* tumor* tumour* malignan*)	(TS = (medical oncology radiation immunotherp* chemotherp* hormonal therap* Aftercare After care After treatment usual care adjuvant* neoadjuvant* rehabilitation)	(TS = (HIT HIIT High-intensit* High Intensity Interval Training* High intensity training* High intensity exercise program* High intensity aerobic exercise training* Interval training* High intensity exercise intervention* Intermittent Exercise* High intensity aerobic exercise progam*)
EMBASE	(neoplas* metastat* cancer* carcino* carcinoma* oncol* tumor* tumour* malignan*):ab,ti.	(medical oncology radiation immunotherp* chemotherp* hormonal therap* Aftercare After care After treatment usual care adjuvant* neoadjuvant* rehabilitation):ab,ti.	(HIT HIIT High-intensit* High Intensity Interval Training* High intensity training* High intensity exercise program* High intensity aerobic exercise training* Interval training* High intensity exercise intervention* Intermittent Exercise* High intensity aerobic exercise program*):ab,ti

The Boolean operator "OR" was used to nest search terms of each individual category and "AND" to combine the categories with one another. For each database, the Boolean operator "NOT" was used to filter for nonhuman, noncancerous, and nonexercise studies as follows: (animals; rat*; mice; mouse; murine; porcine; pig; piglet*; swine; rodent*; chicken*; rabbit*; canine; horse*; cattle*; turkey; sheep; rainbow trout; goat*; salmon*; zebrafish; heart failure; heart attack; coronary heart disease; stroke; Alzheimer disease; COPD; chronic obstructive pulmonary disease; asthma*; bronchitis; cystic fibrosis; adipositas; osteoporosis; diabet*; multiple sclerosis; Parkinson* disease; spinal cord injury; seizure*; hemophagocytic syndrom*; encephalopathy; epilepsy; neuropathy; arthroscopy; ACL; restless leg syndrom*; ankle instability*; ankle sprain*; lower back pain syndrom*; high-intensity forced ultrasound; high intensity forced ultrasound; HIFU)

rating of perceived exertion (RPE) ≥ 16 on the BORG's 6–20 scale [23]. Primary endpoints of interest were the effects of HIIT on physical fitness (i.e., VO_{2peak}, outcome parameters of functional assessments like the 6-minute walking test) and health-related outcomes (i.e., lean body mass, fat mass, and blood-borne biomarkers like C-reactive protein, blood lipids, and blood glucose) as well as patient-reported outcomes (i.e., QoL and cancer-related fatigue).

Data extraction

The following data were extracted from each eligible full text: (a) general study information (author's last name, publication year, study design, study aim, and outcome measures), (b) subject information (sample size, dropout rate, gender, age, current treatment/time point of therapy, type and stage of cancer), and (c) intervention data for HIIT and control groups (description, supervision, location, intensity, frequency, duration, start of intervention, follow-up period, compliance, and effects). Furthermore, objective measures of physical fitness (cardiorespiratory fitness [VO_{2peak}] and performance in the 6-minute walking test), as well as of body composition (BMI, lean body mass, body fat mass, waist and hip circumferences) and blood-borne markers (C-reactive protein, blood glucose concentration, and low-density lipoprotein levels) were assessed. Furthermore, patient-reported outcomes which are described at any health status or condition directly reported by the patient without interpretation by a clinician [24] were extracted. These included QoL, cancer-related fatigue, depression, anxiety, sleep quality, self-esteem, and treatment-related side effects. QoL included the assessment of the subscales physical functioning, emotional functioning, role functioning, cognitive functioning, and social functioning as well as reporting about the treatment-induced side effects, such as nausea, fatigue, insomnia, diarrhea, dyspnea, pain, or the loss of appetite. Cancer-related fatigue, on the other hand, was extracted through questionnaire-assessed measures of motivation, general, mental and physical fatigue, and reported reduced levels of physical activity. Additionally, any

reported adherence and completion rates as well as the number of adverse events were extracted.

Data synthesis and analysis

Intentionally, the meta-analysis was planned to be calculated for all outcomes of interest, but due to the overall low number of included studies, a reasonable calculation was possible for changes in VO_{2peak} only. The meta-analysis was performed using the statistical software R (www.r-project.org, General Package for Meta-Analysis). Considering the same outcome and unit of measure, the pooled mean differences (MD) were combined. The effect size of each study was then calculated by Cohen's *d* and was given weight by its inverse variance. A Cohen's *d* of 0.2, 0.5, and 0.8 represented small, moderate, and large effect sizes, respectively [25]. Based on the assumption of different true effect sizes, a random-effects model was used [26]. The heterogeneity was assessed with I^2 and *Q*-testing. The I^2 values were classified as a small (< 25%), medium (25–50%), and large (> 50%) heterogeneity, respectively [27]. A visual and statistical analysis for publication bias was conducted both using a funnel plot and the Egger's test [28]. Data are presented with 95% confidence intervals (CI).

Risk of bias assessment

The Cochrane Collaborations' risk of bias assessment tool [29] was used to evaluate the internal validity of the included randomized controlled trials (RCTs). Independently, two authors (HM; NF) examined the studies of interest for the following sources of bias: selection (sequence generation and allocation concealment), performance (blinding of participants/personnel), detection (blinding outcome assessors), attrition (incomplete outcome data), reporting (selective reporting), and other potential bias (e.g., recall bias). Additionally, included controlled trials (CTs) were assessed with the Cochrane risk of bias in nonrandomized studies (NOS)—of Interventions (ROBINS-I) assessment tool [30]. This tool assesses the risk within specific domains, such as bias due to confounders, selection, intervention, missing data, and measurement of outcomes. Despite the fact that blinding is nearly impossible in exercise interventions, this quality criterion was still assessed for integrity and in agreement with other systematic reviews in the field.

Results

A detailed overview of individual results across the included studies is provided in Tables 2 and 3. A total of 1453 studies were identified through the initial search strategy (Fig. 1). After screening of titles and abstracts, 1436 articles were found to be ineligible and were excluded. Seventeen full text articles remained for further eligibility assessment. Additionally, screening reference lists of related articles retrieved further five studies. Out of 22 full texts screened, ten papers were excluded based on reasons specified in Fig. 1. Consequently, 12 [16, 17, 31–40] articles were included for final evaluation.

Study and intervention characteristics

Ten RCTs and two CTs were identified in the systematic literature search, including one pilot RCT and one pilot CT, respectively. Among these studies, eight studies compared HIIT with UC [17, 31–37], while five studies compared HIIT with MIE [16, 33, 38–40]. One study included HIIT and both UC and MIE [33]. Out of the studies comparing HIIT with UC, two studies were carried out during a preoperative waiting period [34, 36] and one study performed HIIT during targeted therapy (i.e., in treatment) [31]. The remaining studies integrated HIIT after completion of different combinations of surgery, chemotherapy, radiation, and hormonal therapy (i.e., aftercare) [17, 32, 33, 35, 37]. All studies comparing HIIT with MIE were performed in aftercare, i.e., 1–24 months posttreatment.

A total number of $n = 448$ participants (mean age 58 ± 10 years) were included in the systematic review. More precisely, $n = 245$ (58 ± 10 years), $n = 69$ (58 ± 10 years), and $n = 134$ received HIIT, MIE, and UC, respectively. Recruited patients were diagnosed with various types of cancer, i.e., non-small cell lung cancer (38.5%) [31, 34, 36], colorectal (22.9%) [16, 40], rectal (7.7%) [32, 35], testicular (13.8%) [17, 37], and breast cancer (7.9%), as well as various cancer types (9.2%) [33, 38, 39]. Studies recruiting patients with various cancer entities included breast, cervical, colon, ovarian, and vaginal tumors, as well as melanoma, noninvasive urothelial carcinoma, and non-Hodgkin's lymphoma [38, 39]. Studies using the same study population (i.e., 37 and 38, 31 and 39, as well as 17 and 41) were included only once for pooled analysis.

The duration of the interventions ranged from a minimum of 21 days during a preoperative waiting period [34, 36] to a maximum of 8 weeks in treatment [31] and 12 weeks during aftercare [16, 17, 32, 33, 35, 37–40], respectively. The number of weekly HIIT sessions during the preoperative waiting period and treatment was on average 3.0 (0.0), while during aftercare 2.8 (0.4) weekly HIIT or MIE sessions were completed.

Training adherence and compliance was generally moderate to high in both HIIT and MIE groups. Training adherence for HIIT ranged from 87.2% (18.0%) during a preoperative waiting period [34] to 83.6% (12.4%) in treatment [31]. In aftercare, training adherence was 96.7% (1.7%) and 94.1% (3.7%) in HIIT and MIE, respectively [16, 32, 33, 35, 39, 40]. In the study by Schmitt and colleagues, 93% of all participants performed all HIIT or MIE sessions [38], while

Table 2 Characteristics of included studies (chronological order of publication date)

Study	Entity (timing)	Design	Sample	Training duration and frequency	Intervention characteristics	Conclusion
HIIT vs. UC						
Hwang et al. (2012) [31]	NSCL (T)	RCT	HIIT: $n = 5$ men and 8 women; age 61 ± 6 years; dropout: $n = 2$	8 weeks	HIIT: supervised cycling or treadmill; 2 to 5 min intervals at 80% of VO_{2peak} or RPE of 15–17; 2 to 5 min active recovery of moderate intensity at 60% of VO_{2peak} or RPE of 11–13; 10 min warm-up and 5 min cool-down; total of 30 to 40 min	HIIT showed no statistical significant improvements in cardiorespiratory fitness or measures of QoL compared to UC in non-small cell lung cancer patients.
			UC: $n = 7$ men and 4 women; age 59 ± 8 years; dropout: $n = 4$	3× week	UC: general patient education and social calls every 2 to 3 weeks	
West et al. (2015) [32]	Rectal (AC)	CT (pilot)	HIIT: $n = 14$ men and 8 women; age 64 (45–82) years UC: $n = 9$ men and 4 women; age 72 (62–84) years; dropout total: $n = 4$	6 weeks 3× week	HIIT: supervised cycling; 3 min moderate with work rate of 80% of oxygen uptake at lactate threshold; 2 min vigorous with work rate of 50% of difference in work rate between VO_{2peak} and oxygen uptake at lactate threshold; 5 min warm-up/cool-down; session length: total of 20 min progressed to 40 min; 6 × 3 min moderate and 6 × 2 min severe intensity UC: no exercise intervention	HIIT performed immediately postneoadjuvant chemo–radiotherapy induced superior improvements in cardiorespiratory fitness compared to UC in patients with rectal cancer.
Dolan et al. (2016)[Ŧ] [33]	Breast (AC)	RCT (pilot)	HIIT: $n = 12$ women; age 56 ± 9 years; dropout: $n = 0$ UC: $n = 10$ women; age 59.4 ± 9 years; dropout: $n = 2$	6 weeks 3× week	HIIT: supervised treadmill walking/running; 2 weeks of 3 to 4 min at 80% of VO_{2peak}; 1 to 3 min active recovery at 50–55% of VO_{2peak}; remaining 4 weeks progression with 2 to 3 min at 80–95% of VO_{2peak}; 2 min active recovery at 55–60% of VO_{2peak}; total 4–6 bouts; average total of 36 min UC: maintain normal activity and dietary habits	HIIT significantly improved cardiorespiratory fitness and body composition parameters compared to UC in breast cancer survivors.
Licker et al. (2016) [34]	NSLC (T)	RCT	HIIT: $n = 41$ men and 33 women; age 64 ± 13 years; dropouts: $n = 7$	21 to 33 days 3× week	HIIT: supervised cycling; 2 × 10 min of 15 s sprint intervals at 80–100% of peak power output and 15 s passive recovery; 4 min rest between sets; 5 min warm-up at 50% of peak power output and 5 min cool-down at 30% of peak power output; total of 34 min	HIIT resulted in significantly larger improvements in cardiorespiratory fitness and walking distance in the 6-min walking test compared to UC.
			UC: $n = 50$ men and 22 women; age 64 ± 10 years; dropouts: $n = 6$		UC: 4 × 30 min walks per week; patient education	
	Rectal (AC)	CT (pilot)		6 weeks		

Table 2 (continued)

Study	Entity (timing)	Design	Sample	Training duration and frequency	Intervention characteristics	Conclusion
Brunet et al. (2017) [35]ŦŦ			HIIT: $n = 14$ men and 8 women; age 64 (45–82) years		HIIT: supervised cycling; 3 min moderate with work rate of 80% of oxygen uptake at lactate threshold; 2 min vigorous with work rate of 50% of difference in work rate between VO_{2peak} and oxygen uptake at lactate threshold; 5 min warm-up/cool-down; session length: total of 20 min progressed to 40 min; 6 × 3 min moderate and 6 × 2 min severe intensity	HIIT did not show larger effects on self-reported QoL as compared to UC in patients with rectal cancer.
			UC: $n = 9$ men and 4 women; age 72 (62–84) years; dropout total: $n = 4$	3× week	UC: no exercise intervention	
Karenovics et al. (2017)ŦŦŦ [36]	NSCL (T)	RCT	HIIT: $n = 41$ men and 33 women; age 64 ± 13 years; dropouts: $n = 7$	21 to 33 days 3× week	HIIT: supervised cycling; 2 × 10 min of 15 s sprint intervals at 80–100% of peak power output and 15 s passive recovery; 4 min rest between sets; 5 min warm-up at 50% of peak power output and 5 min cool-down at 30% of peak power output; total of 34 min	HIIT-induced improvements in cardiorespiratory fitness were limited to the preoperative period. No statistical significant differences for functional and clinical outcomes were observed 1 year after lung cancer surgery between HIIT and UC.
			UC: $n = 50$ men and 22 women; age 64 ± 10 years; dropouts: $n = 6$		UC: 4 × 30 min walks per week; patient education	
Adams et al. (2017) [17]	Testicular (AC)	RCT	HIIT: $n = 35$ men; age 44 ± 11 years; dropouts: $n = 0$	12 weeks 3× week	HIIT: supervised uphill treadmill walking/running; 4 × 4 min progressing from 75 to 95% VO_{2peak}; 3 min active recovery at 5 to 10% below ventilatory threshold; 5 min warm-up/cool-down ± 5% of ventilatory threshold; total of 35 min	HIIT showed superior improvements in cardiorespiratory fitness compared to UC in testicular cancer survivors.
			UC: $n = 28$ men; age 43 ± 10 years; dropouts: $n = 2$		UC: maintained habitual exercise	
Adams et al. (2018)ŦŦŦŦ [37]	Testicular (AC)	RCT	HIIT: $n = 35$ men; age 44 ± 11 years; dropouts: $n = 0$; lost in follow-up: $n = 4$	12 weeks	HIIT: supervised uphill treadmill walking/running; 4 × 4 min progressing from 75 to 95% VO_{2peak}; 3 min active recovery at 5 to 10% below ventilatory threshold; 5 min warm-up/cool-down ± 5% of ventilatory threshold; total of 35 min	HIIT led to significantly improved values of self-esteem, cancer-related fatigue, and health-related QoL compared to UC.
			UC: $n = 28$ men; age 43 ± 10 years; dropouts: $n = 2$; lost in follow-up: $n = 6$	3× week	UC: maintained habitual exercise	

Table 2 (continued)

Study	Entity (timing)	Design	Sample	Training duration and frequency	Intervention characteristics	Conclusion
HIIT vs. MIE						
Schmitt et al. (2016) [38]	Various (AC)	RCT	HIIT: $n = 13$ women; age 53 ± 8 years; dropout: N/R	3 weeks HIIT: 3× week	HIIT: supervised uphill walking; 8 × 1 min walking with workload at approx. 95% of peak heart rate; 2 min of slow walking as active recovery; 5 min warm-up with workload at 70% peak heart rate; total of 29 min	HIIT and MIE were similarly effective in improving QoL, cancer-related fatigue, and body composition in cancer survivors of various entities.
			MIE: $n = 13$ women; age 54 ± 9 years; dropout: N/R	MIE: 2× week	MIE: supervised continuous walking or cycling; 75 min moderate intensity, i.e., 60 min outdoor walking and 15 min indoor cycling with workload at 60% peak heart rate	
Dolan et al. (2016) [33]	Breast (AC)	Pilot RCT	HIIT: $n = 12$ women; age 56 ± 9 years; dropout: $n = 0$ MIE: $n = 12$ women; age 56 ± 9 years; dropout: $n = 1$	6 weeks HIIT: 3× week MIE: 3× week	HIIT: supervised treadmill walking/running; 2 weeks of 3 to 4 min at 80% of VO_{2peak}; 1 to 3 min active recovery at 50–55% of VO_{2peak}; remaining 4 weeks progression with 2 to 3 min at 80–95% of VO_{2peak}; 2 min active recovery at 55–60% of VO_{2peak}; total 4–6 bouts; average total of 36 min MIE: supervised continuous treadmill walking/running; weeks 1 to 4 with 3.22 km at 55–60% of VO_{2peak}; progressed to 4.02 km at 70% of VO_{2peak}; average time of 40 min	HIIT was similarly effective as MIE in improving cardiorespiratory fitness and body composition in breast cancer survivors.
Devin et al. (2016) [16]	Colorectal (AC)	RCT	HIIT: $n = 18$ men and 12 women; age 61 ± 11 years; dropouts: $n = 1$	4 weeks HIIT: 3× week	HIIT: supervised cycling; 4 × 4 min with workload at 85–95% at peak heart rate; 3 min active recovery with workload at 50–70% of peak heart rate; 10 min warm-up with workload at 50–70% of peak heart rate; total of 38 min	HIIT led to superior adaptations in cardiorespiratory fitness and body composition compared to MIE in colorectal cancer survivors.
			MIE: $n = 8$ men and 9 women; age 62 ± 11 years; dropouts: $n = 1$	MIE: 3× week	MIE: supervised continuously cycling of 50 min with workload at 50–70% of peak heart rate	
Toohey et al. (2016) [39]	Various (AC)	RCT	HIIT: $n = 8$ women	12 weeks HIIT: 3× week	HIIT: supervised cycling or treadmill running; progressively increasing from 3 to 7 × 30 s workload at ≥ 85% peak heart rate; 1 min rest; 5 min warm-up/cool-down; total of 14.5 to 20.5 min	HIIT and MIE led to similar improvements in functional capacity and QoL. Absolute fat mass significantly decreased in HIIT but not MIE in cancer survivors of various entities.
				MIE: 3× week	MIE: supervised continuous cycling or treadmill running; 20 min with workload	

Table 2 (continued)

Study	Entity (timing)	Design	Sample	Training duration and frequency	Intervention characteristics	Conclusion
			MIE: $n = 8$ women, age all patients 52 ± 13 years; dropout: $n = 0$		at ≤ 55% peak heart rate; 5 min warm-up/cool-down	
Devin et al. (2018) [40]	Colorectal (AC)	RCT	HIIT: $n = 13$ men and 5 women; age 61 ± 12 years; dropout: $n = 1$	8 weeks HIIT: 3× week	HIIT: supervised cycling; 4 × 4 min with workload at 85–95% of peak heart rate; 3 min active recovery with workload at 50–70% of peak heart rate; 10 min warm-up with workload at 50–70% of peak heart rate; total of 38 min	HIIT led to superior improvements in cardiorespiratory fitness and decreases in fat mass. No differences were observed between HIIT and HIIT-tapered. Beneficial adaptations were maintained during a 4-week follow-up in HIIT and HIIT-tapered but not in MIE for colorectal cancer survivors.
			$HIIT_t$: $n = 10$ men and 10 women; age 62 ± 10 years; dropout: $n = 1$	$HIIT_t$: 3× for weeks 1 to 4 and 1× week till end	$HIIT_t$: supervised cycling; 4 × 4 min with workload at 85–95% of peak heart rate; 3 min active recovery with workload at 50–70% of peak heart rate; 10 min warm-up with workload at 50–70% of peak heart rate; total of 38 min; tapered frequency	
			MIE: $n = 9$ men and 10 women; age 60 ± 11 years; dropout: $n = 2$	MIE: 3× week	MIE: supervised continuous cycling of 50 min with workload at 70% of peak heart rate	

All results are presented as mean ± SD

[Ŧ] included an HIIT, a MIE, and an UC group

[ŦŦ] Same sample as West et al. [32]

[ŦŦŦ] Same sample as Licker et al. [34] + 1 year follow-up

[ŦŦŦŦ] Same sample as Adams et al. [17] + 3 month follow-up with survey

AC, aftercare; *CT*, nonrandomized controlled trial; *HIIT*, high-intensity interval training; $HIIT_t$, tapered high-intensity interval training; *MIE*, moderate-intensity exercise; *N/R*, not reported; *NSCL*, non-small cell lung cancer; *RCT*, randomized controlled trail; *RPE*, rate of perceived exertion; *T*, in treatment; *UC*, usual care; VO_{2peak}, peak oxygen uptake

Table 3 Summary of changes in physical fitness, patient-reported outcomes, and health-related parameters (chronological order of publication date)

Author (year)	Outcomes	Results			Attendance HIIT [%]
		Within-group changes		Between-group changes	
HIIT vs. UC					
Hwang et al. (2012) [31]	VO_{2peak} [mL·kg^{-1}·min^{-1}]	HIIT↑: + 1.6; 95% CI + 0.9, + 2.3; $p < 0.005$	UC↓: − 0.4; 95% CI − 1.2, + 0.4; $p = 0.27$	HIIT↑: $p < 0.005$	71.2
	QoL				
	Dyspnea	HIIT↓: − 5.8; $p = 0.01$	UC↓: − 1.6; $p = 0.06$	HIIT↓: $p = 0.06$	
	Fatigue	HIIT↓: − 5.1; $p = 0.05$	UC↓: − 9.1; $p = 0.01$	HIIT↔ UC: $p = 0.30$	
	Biomarker				
	CRP [mg·L^{-1}]	HIIT↓: − 0.91	UC↑: − 5.04	HIIT↔ UC: $p = 0.20$	
West et al. (2015) [32]	VO_{2peak} [mL·kg^{-1}·min^{-1}]				92
	Weeks 0–6	HIIT↑: + 2.65; 95% CI 1.19, + 4.10; $p < 0.00$	UC↓: − 1.25; 95% CI, 23.14, + 0.64; $p = 0.19$	HIIT↑: + 3.90; 95% CI 1.52, + 6.28; $p = 0.002$	
	Weeks 6–15	HIIT↓: − 0.6	UC↓: − 2.0	HIIT↑: − 1.4	
Dolan et al. (2016)[Ŧ] [33]	VO_{2peak} [Δ%]	HIIT↑: + 11.48 ± 10.5	UC↓: − 5.97 ± 7.2	HIIT↑: $p < 0.0001$	98.7
	Body composition				
	Circumference hip [Δ%]	HIIT↓: − 1.81 ± 2.2	UC↑: + 0.77 ± 1.24	HIIT↓: $p = 0.002$	
	Circumference waist [Δ%]	HIIT↓: − 2.16 ± 2.9	UC↑: + 1.95 ± 2.98	HIIT↓: $p = 0.004$	
	BW [Δ%]	HIIT↓: − 0.67 ± 1.9; $p = 0.04$	UC↑: + 1.44 ± 1.62	HIIT↑: $p = 0.031$	
	Biomarker				
	CRP [Δ%]	HIIT↓: − 5.54 ± 12.4	UC↑: + 228.9 ± 192.6	HIIT↔ UC: H = 0.232	
	Glucose [Δ%]	HIIT↑: + 2.68 ± 3.8	UC↓: − 1.18 ± 2.2	HIIT↔ UC: H = 0.509	
Licker et al. (2016) [34]	VO_{2peak} [mL·kg^{-1}·min^{-1}]	HIIT↑: + 2.9; IQR − 1.1 to + 4.2[1] ES: + 0.46; 95% CI + 0.26, + 0.66[1]	UC↓: − 1.5; IQR − 3.2 to + 0.5[1]	HIIT↑: $p = 0.004$	87
	Presurgery				
	Functional capacity				
	6MWT [m]	HIIT↑: + 66; IQR + 8 to + 125[1] ES: + 0.49; 95% CI + 0.24, + 0.74	UC ↓: − 2; IQR − 9 to + 5[1]	HIIT↑: $p = 0.001$	
Brunet et al. (2017)[ŦŦ] [35]	QoL				96
	Pain	HIIT↓: − 24.5[1]; $p > 0.14$	UC↓: − 24.5[1]; $p > 0.14$	HIIT↔ UC: $p = 0.67$	
	Fatigue	HIIT↓: − 11[1]; $p < 0.01$	UC↓: − 11[1]; $p < 0.01$	HIIT↔ UC: $p = 0.10$	
	Insomnia	HIIT↔ : 0[1]; $p > 0.26$	UC↓: − 33[1]; $p_c = 0.04$	HIIT↔ UC: $p = 0.89$	
Karenovics et al. (2017)[ŦŦŦ] [36]	VO_{2peak} [mL·kg^{-1}·min^{-1}]	HIIT↑: + 2.9; 95% CI + 1.1, + 4.2 ES: + 0.46; 95% CI 0.26, + 0.66	UC↓: − 1.5; 95% CI − 3.2, + 0.5	HIIT↑: $p < 0.01$	87
	Presurgery				
	Δpre-/postsurgery	HIIT↓: − 11.5; 95% CI − 4.8, − 18.2; $p = 0.02$	UC↓: − 12.8; 95% CI − 9.7, − 15.9; $p = 0.02$	HIIT↔ UC: $p = 0.80$	
	QoL				
	Dyspnea	HIIT↔ 0[1]; $p = 0.91$	UC↔ : 0[1]; $p = 0.78$		
Adams et al. (2017) [17]	VO_{2peak} [mL·kg^{-1}·min^{-1}]	HIIT↑: + 4.2	UC↑: + 0.6	HIIT↑: + 3.7; 95% CI + 2.4, + 5.1; $p < 0.001$	99
	Biomarker				
	CRP [mg·L^{-1}]	HIIT↓: − 0.64	UC↓: − 0.05	HIIT↓: − 0.6; 95% CI − 1.24, − 0.03; $p = 0.045$	
	LDL [mmol·L^{-1}]	HIIT↓: − 0.29	UC↑: + 0.01	HIIT↓: − 0.26; 95% CI − 0.46, − 0.05; $p = 0.014$	
	Glucose [mmol·L^{-1}]	HIIT↓: − 0.08	UC↑: + 0.11	HIIT↓: − 0.09; 95% CI − 0.31, − 0.13; $p = 0.39$	
	QoL				99

Table 3 (continued)

Author (year)	Outcomes	Results			Attendance HIIT [%]
		Within-group changes		Between-group changes	
Adams et al. (2018) [37]	Mental component score	HIIT↑: + 2.4	UC↓: − 2.7	HIIT vs. UC↑: + 3.9; 95% CI 0.3, + 7.5; $p = 0.03$	
	Physical component score	HIIT↑: + 2.6	UC↑: + 0.7	HIIT↔UC: + 1.1; 95% CI 1.2, + 3.5; $p = 0.34$	
	Physical functioning	HIIT↑: + 1.7	UC↑: + 0.7	HIIT↔UC: + 0.3; 95% CI − 1.5, + 2.1; $p = 0.77$	
	Role-physical	HIIT↑: + 3.4	UC↓: − 0.2	HIIT vs. UC↑: + 2.2; 95% CI 0.02, + 4.3; $p = 0.048$	
	Bodily pain	HIIT↑: + 1.8	UC↓: − 0.7	HIIT↔UC: + 1.3; 95% CI − 1.8, + 4.3; $p = 0.41$	
	General health	HIIT↑: + 3.7	UC↓: − 0.1	HIIT vs. UC↑: + 3.2; 95% CI 0.6, + 5.8; $p = 0.016$	
	Vitality	HIIT↑: + 3.8	UC↓: − 2.1	HIIT vs. UC↑: + 5.4; 95% CI 2.2, + 8.5; $p = 0.001$	
	Social functioning	HIIT↑: + 2.0	UC↓: − 1.8	HIIT vs. UC↑: + 3.3; 95% CI 0.8, + 5.8; $p = 0.011$	
	Role-emotional	HIIT↑: + 1.9	UC↓: − 0.9	HIIT↔UC: + 1.5; 95% CI − 1.7, + 4.7; $p = 0.36$	
	Mental health	HIIT↑: + 2.5	UC↓: − 2.7	HIIT vs. UC↑: + 3.2; 95% CI − 0.1, + 6.5; $p = 0.054$	
	Cancer-related fatigue	HIIT↑: + 4.2	UC↓: − 1.1	HIIT vs. UC↑: + 4.4; 95% CI 1.5, + 7.3; $p = 0.003$	
	Depression	HIIT↓: − 1.1	UC↓: − 0.5	HIIT↔UC: − 0.2; 95% CI − 1.6, + 1.3; $p = 0.81$	
	Anxiety	HIIT↓: − 1.7	UC↑: + 1.2	HIIT↔UC: − 1.6; 95% CI − 3.9, + 0.8; $p = 0.19$	
	Stress	HIIT↓: − 2.4	UC↑: + 0.7	HIIT↔UC: − 1.7; 95% CI − 4.4, + 1.0; $p = 0.22$	
	Self-esteem	HIIT↑: + 2.0	UC↓: − 1.0	HIIT vs. UC↑: + 1.8; 95% CI 0.2, + 3.4; $p = 0.029$	
	Sleep quality	HIIT↓: − 0.6	UC↔: + 0.0	HIIT↔UC: − 0.6; 95% CI − 1.4, + 0.2; $p = 0.15$	
HIIT vs. MIE					
Schmitt et al. (2016) [38]	VO_{2peak} [mL·kg^{-1}·min^{-1}]	HIIT↓: − 0.1; $p = 0.42$; ES: − 0.02	MIE↑: + 2.5; $p < 0.01$; ES: + 0.46	HIIT vs. MIE↑: $p = 0.01$; ES: + 1.27	93
	Body composition				
	BM [kg]	HIIT↓: − 0.4; $p = 0.06$; ES: − 0.03	MIE↔: 0; $p = 0.48$; ES: + 0.00	HIIT↔MIE: $p = 0.22$; ES: − 0.18	
	FFM [kg]	HIIT↑: + 0.1; $p = 0.38$; ES: + 0.01	MIE↑: + 0.5; $p = 0.03$; ES: + 0.10	HIIT↔MIE: $p = 0.24$; ES: − 0.17	
	MM [kg]	HIIT↔: 0; $p = 0.40$; ES: + 0.01	MIE↑: + 0.5; $p = 0.04$; ES: + 0.10	HIIT↔MIE: $p = 0.24$; ES: − 0.17	
	BF [kg]	HIIT↓: − 0.5; $p = 0.02$; ES: − 0.05	MIE↓: − 1.4; $p = 0.06$; ES: − 0.13	HIIT↔MIE: $p = 0.31$; ES: + 0.15	
	Cancer-related fatigue				
	Reduced motivation	HIIT↓: − 2.6; $p < 0.00$; ES: − 0.85	MIE↓: − 1.7; $p = 0.01$; ES: − 0.72	HIIT↔MIE: $p = 0.34$; ES: − 0.13	
	Reduced activity	HIIT↓: − 1.7; $p = 0.01$; ES: − 0.55	MIE↓: − 1.9; $p = 0.01$; ES: − 0.80	HIIT↔MIE: $p = 0.80$; ES: + 0.04	
	Fatigue				
	General	HIIT↓: − 1.3; $p = 0.02$; ES: − 0.45	MIE↓: − 3.2; $p < 0.00$; ES: − 0.90		

Table 3 (continued)

Author (year)	Outcomes	Results			Attendance HIIT [%]
		Within-group changes		Between-group changes	
				HIIT vs. MIE↓: $p = 0.04$; ES: + 0.30	
	Physical	HIIT↓: − 1.6; $p = 0.01$; ES: − 0.52	MIE↓: − 1.6; $p = 0.06$; ES: + 0.44	HIIT↔MIE: $p = 0.95$; ES: + 0.01	
	Mental	HIIT↓: − 2.1; $p = 0.01$; ES: − 0.46	MIE↓: − 1.3; $p = 0.07$; ES: − 0.37	HIIT↔MIE: $p = 0.50$; ES: − 0.09	
	QoL	HIIT↑: + 9.5; $p < 0.00$; ES: + 0.79	MIE↑: + 17.4; $p < 0.00$; ES: + 1.14	HIIT↔MIE: $p = 0.09$; ES: − 0.24	
	Functioning				
	Physical	HIIT↑: + 4.1; $p = 0.04$; ES: + 0.35	MIE↑: + 12.7; $p < 0.00$; ES: + 0.89	HIIT↔MIE: $p = 0.07$; ES: − 0.28	
	Social	HIIT↓: − 2.4; $p = 0.33$; ES: − 0.08	MIE↑: + 17.6; $p = 0.01$; ES: + 0.64	HIIT vs. MIE↑: $p = 0.02$; ES: − 0.34	
	Emotional	HIIT↑: + 11; $p = 0.03$; ES: + 0.46	MIE↑: + 31.5; $p < 0.00$; ES: + 1.25	HIIT vs. MIE↑: $p = 0.03$; ES: − 0.32	
	Cognitive	HIIT↑: + 8.9; $p = 0.07$; ES: + 0.31	MIE↑: + 13.2; $p = 0.04$; ES: + 0.48	HIIT↔MIE: $p = 0.66$; ES: − 0.06	
	Role	HIIT↑: + 23; $p = 0.01$; ES: + 1.04	MIE↑: + 30.9; $p < 0.00$; ES: + 1.23	HIIT↔MIE: $p = 0.45$; ES: − 0.10	
	Fatigue	HIIT↓: − 12.1; $p = 0.02$; ES: − 0.67	MIE↓: − 30.2; $p < 0.00$; ES: − 1.46	HIIT vs. MIE↓: $p = 0.02$; ES: + 0.35	
	Pain	HIIT↓: − 1.3; $p = 0.42$; ES: − 0.07	MIE↓: − 23.1; $p < 0.00$; ES: − 0.91	HIIT vs. MIE↓: $p = 0.02$; ES: + 0.34	
	Dyspnea	HIIT↓: − 5.4; $p = 0.21$; ES: − 0.22	MIE↓: − 20.7; $p = 0.03$; ES: − 0.66	HIIT↔MIE: $p = 0.20$; ES: + 0.18	
	Insomnia	HIIT↓: − 10.3; $p = 0.02$; ES: − 0.35	MIE↓: − 18; $p = 0.01$; ES: − 0.35	HIIT↔MIE: $p = 0.32$; ES: + 0.14	
Dolan et al. (2016)[T] [33]	VO_{2peak} [Δ%]	HIIT↑: + 11.48 ± 10.5	MIE↑: + 12.95 ± 10.4	HIIT↔MIE	HIIT: 98.7 MIE: 98.6
	Body composition				
	Circumference hip [Δ%]	HIIT↓: − 1.81 ± 2.2	MIE: − 2.17 ± 2.26	HIIT↔MIE	
	Circumference waist [Δ%]	HIIT↓: − 2.16 ± 2.9	MIE↓: − 2.51 ± 2.5	HIIT↔MIE	
	BW [Δ%]	HIIT↓: − 0.67 ± 1.9; $p = 0.04$	MIE↓: − 0.41 ± 2.08		
	Biomarker				
	CRP [Δ%]	HIIT↓: − 5.54 ± 12.4	MIE↓: − 11.02 ± 19.4	HIIT↔MIE: H = 0.232	
	Glucose [Δ%]	HIIT↑: + 2.68 ± 3.8	MIE↑: + 0.89 ± 2.7	HIIT↔MIE: H = 0.509	
Devin et al. (2016) [16]	VO_{2peak} [$mL \cdot kg^{-1} \cdot min^{-1}$]	HIIT↑: + 3.5 ± 3.5; $p < 0.001$	MIE↑: + 0.9 ± 2.8; $p = 0.245$	HIIT↑: $p = 0.021$	HIIT: 97.0 MIE: 97.1
	Body composition				
	BM [kg]	HIIT↓: − 0.3 ± 1.2[1]; $p = 0.005$	MIE↑: + 0.3 ± 1.2[1]; $p = 0.142$	HIIT↑: $p = 0.005$	
	LM [kg]	HIIT↑: + 0.72 ± 0.80; $p = 0.002$	MIE↑: + 0.43 ± 1.06; $p = 0.299$	HIIT↔MIE: $p = 0.363$	
	FM [kg]	HIIT↓: − 0.74 ± 0.65; $p < 0.001$	MIE↓: − 0.21 ± 0.99; $p = 0.448$	HIIT↔MIE: $p = 0.060$	
	BF [%]	HIIT↓: − 1.0 ± 1.0; $p < 0.001$	MIE↓: − 0.38 ± 1.34; $p = 0.308$	HIIT↔MIE: $p = 0.123$	
Toohey et al. (2016) [39]	QoL [Δ%]	HIIT↑: 17.44; 95% CI 6.65–28.23	MIE↑: 6.14; 95% CI 1.84–10.45	HIIT↔MIE: $p = 0.20$ (time effect)	93.75
	Functional well-being	HIIT↑: $p < 0.05$			
	Emotional well-being	HIIT↑: $p < 0.05$			
	Functional capacity				
	SST [Δ%]	HIIT↓: − 23.46; 95% CI − 32.31, + 14.61	MIE↓: − 6.39; 95% CI − 13.18, + 0.40	HIIT↔MIE: $p = 0.06$ (time effect)	
	6MWT [Δ%]	HIIT↑: + 18.53; 95% CI 7.01, + 30.06	MIE↑: + 1.16; 95% CI − 3.85, 6.17	HIIT↔MIE: $p = 0.50$ (interaction effect)	
	Body composition				
	BF [Δ%]	HIIT↓: − 0.88; 95% CI − 6.97, 8.73	MIE↓: − 2.20; 95% CI − 7.61, + 3.22	HIIT↓ vs. MIE: $p = 0.03$	
	FM [Δ%]	HIIT↓: − 5.50; 95% CI − 9.61, 1.39	MIE↑: + 0.29; 95% CI − 3.71, + 4.29	HIIT↓ vs. MIE: $p = 0.004$	
	BW [Δ%]	HIIT↓: − 2.43; 95% CI − 4.08, 0.78	MIE↓: − 0.06; 95% CI − 1.03, + 0.91	HIIT↓ vs. MIE: $p = 0.01$	
	LM [Δ%]	HIIT↑: + 0.09; 95% CI − 2.30, 2.49	MIE↓: − 0.09; 95% CI − 1.96, + 2.49	HIIT↔MIE: $p = 0.22$ (time effect)	

Table 3 (continued)

Author (year)	Outcomes	Results			Attendance HIIT [%]
		Within-group changes		Between-group changes	
	Circumference hip [Δ%]	HIIT↓: − 5.22; 95% CI − 9.01, 1.44	MIE↓: − 2.75; 95% CI − 6.30, + 0.80	HIIT↔MIE: $p = 0.11$ (time effect)	
	Circumference waist [Δ%]	HIIT↓: − 6.64; 95% CI − 9.92, 3.36	MIE↓: − 2.62; 95% CI − 4.82, + 0.42	HIIT↔MIE: $p = 0.32$ (time effect)	
	Biomarker				
	CRP [Δ%]	HIIT↓: − 5.95; 95% CI − 43.18, + 31.28	MIE↑: + 19.44; 95% CI − 1.75, + 40.64	HIIT↔MIE: $p = 0.51$ (interaction effect)	
	Glucose [Δ%]	HIIT↓: − 2.40; 95% CI − 10.18, + 5.39	MIE↓: − 1.41; 95% CI − 8.12, + 5.29	HIIT↓ vs. MIE: $p = 0.01$	
Devin et al. (2018) [40]	VO_{2peak} [$mL \cdot kg^{-1} \cdot min^{-1}$]			HIIT↑ vs. MIE: + 2.3; 95% CI + 0.0, + 4.7; $p = 0.049$	HIIT: 99.3
	Weeks 0–8	HIIT↑: + 5.2; $p < 0.001$	MIE↑: + 2.7; $p < 0.001$	$HIIT_t$↔MIE: + 1.5; 95% CI − 0.6, + 3.7; $p = 0.210$	$HIIT_t$: 99.9
		$HIIT_t$↑: + 4.1; $p < 0.001$		HIIT↔$HIIT_t$: + 0.8; 95% CI − 1.1, + 2.7; $p = 0.422$	
	Weeks 8–12 (follow-up)	HIIT↓: − 1.0; $p = 0.349$ $HIIT_t$↓: − 0.7; $p = 0.534$	MIE↓: − 2.0; $p = 0.032$		MIE: 100
	Weeks 0–12	HIIT↑: + 4.2; $p < 0.001$	MIE↑: + 0.7; $p = 0.689$	HIIT↑ vs. MIE: + 3.3; 95% CI + 0.8, + 5.8; $p = 0.006$	
		$HIIT_t$↑: + 3.4; $p < 0.001$		$HIIT_t$↑ vs. MIE: + 2.8; 95% CI + 0.5, + 5.1; $p = 0.013$ HIIT↔$HIIT_t$: + 0.5; 95% CI − 1.5, + 2.5; $p = 0.637$	
	Body composition			HIIT↔MIE: + 0.1; 95% CI − 0.7, + 0.8; $p = 1.000$	
	LM [kg]	HIIT↑: + 0.5; $p = 0.141$	MIE↑: + 0.6; $p = 0.689$; $p = 0.157$	$HIIT_t$↔MIE: − 0.1; 95% CI − 0.9, + 0.6; $p = 1.000$	
	Weeks 0–8	$HIIT_t$↑: + 0.4; $p = 0.682$		HIIT↔$HIIT_t$: + 0.2; 95% CI − 0.7, + 1.1; $p = 1.000$	
	Weeks 8–12 (follow-up)	HIIT↔: 0; $p = 1.000$ $HIIT_t$↓: − 0.1; $p = 1.000$	MIE↑: + 0.2; $p = 0.841$		
	Weeks 0–12	HIIT↑: + 0.5; $p = 0.269$	MIE↑: + 0.8; $p = 0.027$	HIIT↔MIE: − 0.2; 95% CI − 1.1, + 0.6; $p = 1.000$	
		$HIIT_t$↑: + 0.3; $p = 0.730$		$HIIT_t$↔MIE: − 0.4; 95% CI − 1.3, + 0.5; $p = 0.910$ HIIT↔$HIIT_t$: + 0.2; 95% CI − 0.7, + 0.1; $p = 0.938$	
	FM [kg]			HIIT↑ vs. MIE: − 0.7; 95% CI − 1.4, + 0.0; $p = 0.038$	
	Weeks 0–8	HIIT↓: − 1.1; $p < 0.001$	MIE↓: − 0.3; $p = 0.994$	$HIIT_t$↔MIE: − 0.4; 95% CI − 1.0, + 0.2; $p = 0.324$	
		$HIIT_t$↓: − 0.7; $p = 0.004$		HIIT↔$HIIT_t$: − 0.3; 95% CI − 0.9, + 0.2; $p = 0.324$	
	Weeks 8–12 (follow-up)	HIIT↑: + 0.1; $p = 0.554$ $HIIT_t$↓: − 0.1; $p = 1.000$	MIE↑: + 0.1; $p = 1.000$		
	Weeks 0–12	HIIT↓: − 1.0; $p < 0.001$	MIE↓: − 0.2; $p = 1.000$	HIIT↑ vs. MIE: − 0.7; 95% CI − 1.4, + 0.0; $p = 0.045$	

Table 3 (continued)

Author (year)	Outcomes	Results		Attendance HIIT [%]
		Within-group changes	Between-group changes	
		$HIIT_{t}$↓: − 0.7; $p = 0.004$	$HIIT_{t}$↔MIE: − 0.6; 95% CI − 1.3, + 0.1; $p = 0.082$ HIIT↔$HIIT_{t}$: − 0.1; 95% CI − 0.7, + 0.5; $p = 0.725$	

All results are presented as mean ± SD. Change within and between groups are presented as ↑ (increase), ↓ (decrease), and ↔ (no change). Level of statistical significance is $p < 0.05$. p_c: corrected critical p value (correction for multiple testing via Simes procedure $p < 0.017$)

[1] Results are presented as median and IQR

[F] Included an HIIT, a MIE, and an UC group

[FF] Same sample as West et al. [32]

[FFF] Same sample as Licker et al. [34] + 1-year follow-up

[FFFF] Same sample as Adams et al. [17] + 3-month follow-up with survey

Δ, change; *6MWT*, 6-minute walking test; *95% CI*, 95% confidence intervals; *BF*, body fat; *BM*, body mass; *BW*, body weight, ; *CRP*, C-reactive protein; *ES*, effect size; *FFM*, fat-free mass; *FM*, fat mass; *HIIT*, high-intensity interval training; *HIIT*$_t$, tapered high-intensity interval training; *IQR*, interquartile range; *LDL*, low-density lipoprotein; *LM*, lean mass; *MIE*, moderate-intensity exercise; *MM*, muscle mass; *QoL*, quality of life; *SST*, sit-to-stand test; *UC*, usual care; VO_{2peak}, peak oxygen uptake

Toohey and colleagues reported only an overall adherence of 93.8% [39], irrespective of HIIT or MIE training. Overall reported dropout rates ranged from 4.9 to 9.9% (HIIT: $n = 12$ (4.9%); MIE: $n = 4$ (5.8%); and UC: $n = 14$ (9.9%)). If itemized by timing of the intervention, $n = 13$ (2.9%) terminated training during a preoperative waiting period and $n = 6$ (1.3%) in treatment, while $n = 15$ (3.3%) dropped out in aftercare.

Risk of bias assessment

The results of the methodological quality assessment of all included studies are summarized in Fig. 2. An appropriate procedure for a randomly generated sequence was fully described in six studies [16, 17, 31, 37, 38, 40], out of which three concealed the allocation [16, 31, 40]. Performance bias was found in all included trials. However, due to the characteristics of exercise interventions and the fact that blinding of participants is nearly impossible, this poses no threat to internal validity. Only three studies [17, 31, 37] blinded outcome assessors. A high risk of incomplete outcome data was found in one trial [31]. One study displayed moderate [32] and another serious risk [35] in the confounding domain. All other domains were rated as low risk.

Intervention effects and pooled analysis

Physical fitness

An overview of the effects of individual studies is presented in Fig. 3. The meta-analysis for changes in VO_{2peak} revealed a large effect for HIIT compared to UC (MD 3.73, 95% CI 2.07, 5.39; $p < 0.001$). However, no additional benefit of HIIT was found compared to MIE (MD 1.36; 95% CI − 1.62, 4.35; $p = 0.370$). When combining evidence of all studies, which compared HIIT to a control condition (i.e., UC and MIE), the MD was 3.00 (95% CI 1.65, 4.36; $p < 0.001$).

Functional capacity was assessed only in two studies. During a preoperative waiting period, HIIT induced statistically significant improvements in the 6-minute walking test as compared to UC (median + 66 vs. − 2 m, $p = 0.001$) [34], while this was not observed when compared to MIE in aftercare [39].

Body composition

Body composition was assessed exclusively in studies comparing HIIT and MIE with the exception that one study included an UC group as well [16, 33, 38–40]. Body composition parameters were measured by dual-energy X-ray absorptiometry (DXA) [16, 38–40] and anthropometric measures [33]. No significant between-group differences were observed for changes in lean mass in either of the studies. However, in two studies [39, 40], changes in fat mass were statistically larger

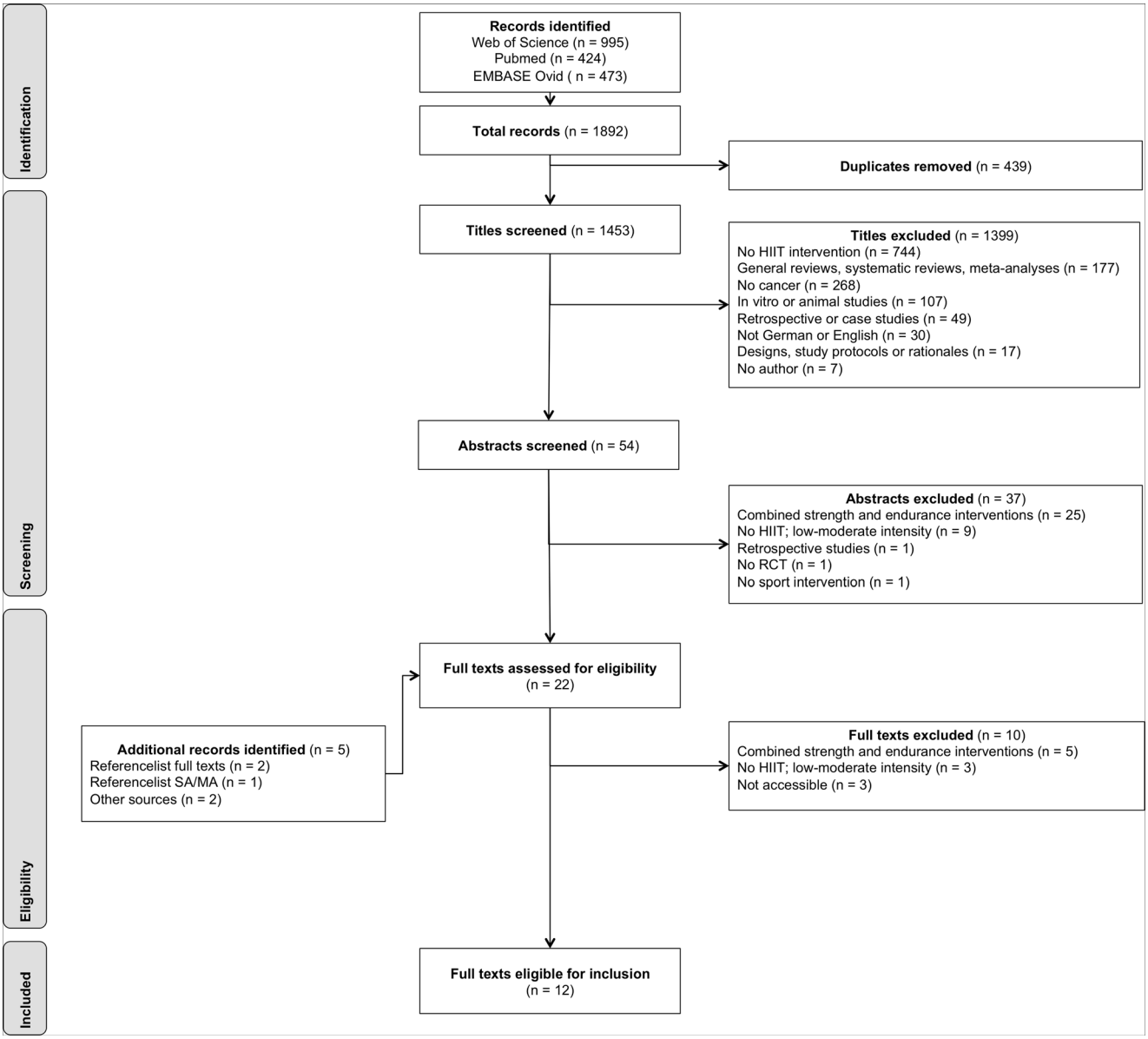

Fig. 1 PRISMA flowchart of the systematic review process. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses

during HIIT compared to MIE in aftercare (− 5.5 vs. + 0.29%, $p = 004$ and − 4.0 vs. − 1.1%, $p = 0.038$, respectively). No between-group differences for changes in waist and hip circumferences were observed in the study by Dolan and colleagues [33].

Blood-borne biomarkers

HIIT compared to UC in aftercare resulted in significant reductions in C-reactive protein (CRP) (no Δ% provided, $p = 0.045$) and low-density lipoprotein levels (no Δ% provided, $p = 0.014$) [17]. In contrast, no significant interaction was observed for HIIT and UC during targeted therapy [31]. When comparing HIIT and MIE, no differences in the changes of CRP were observed, while a significant interaction in favor for HIIT but not MIE was found in fasting blood glucose levels (− 2.40 vs. + 1.41%, $p = 0.01$) [39].

Patient-reported outcomes

Very few studies have used similar tools for the evaluation of patient-reported outcomes, hindering direct comparisons between different studies. Comparing HIIT and UC, two studies [31, 35] incorporated measures of QoL, assessed by the European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire (EORTC QLQ-C 30), while one more study used the Health Survey (SF-36). No between-group differences were observed for the global health status and QoL in treatment [31] and the multi-item symptom scales "pain", "fatigue," and "insomnia" in aftercare [35]. In

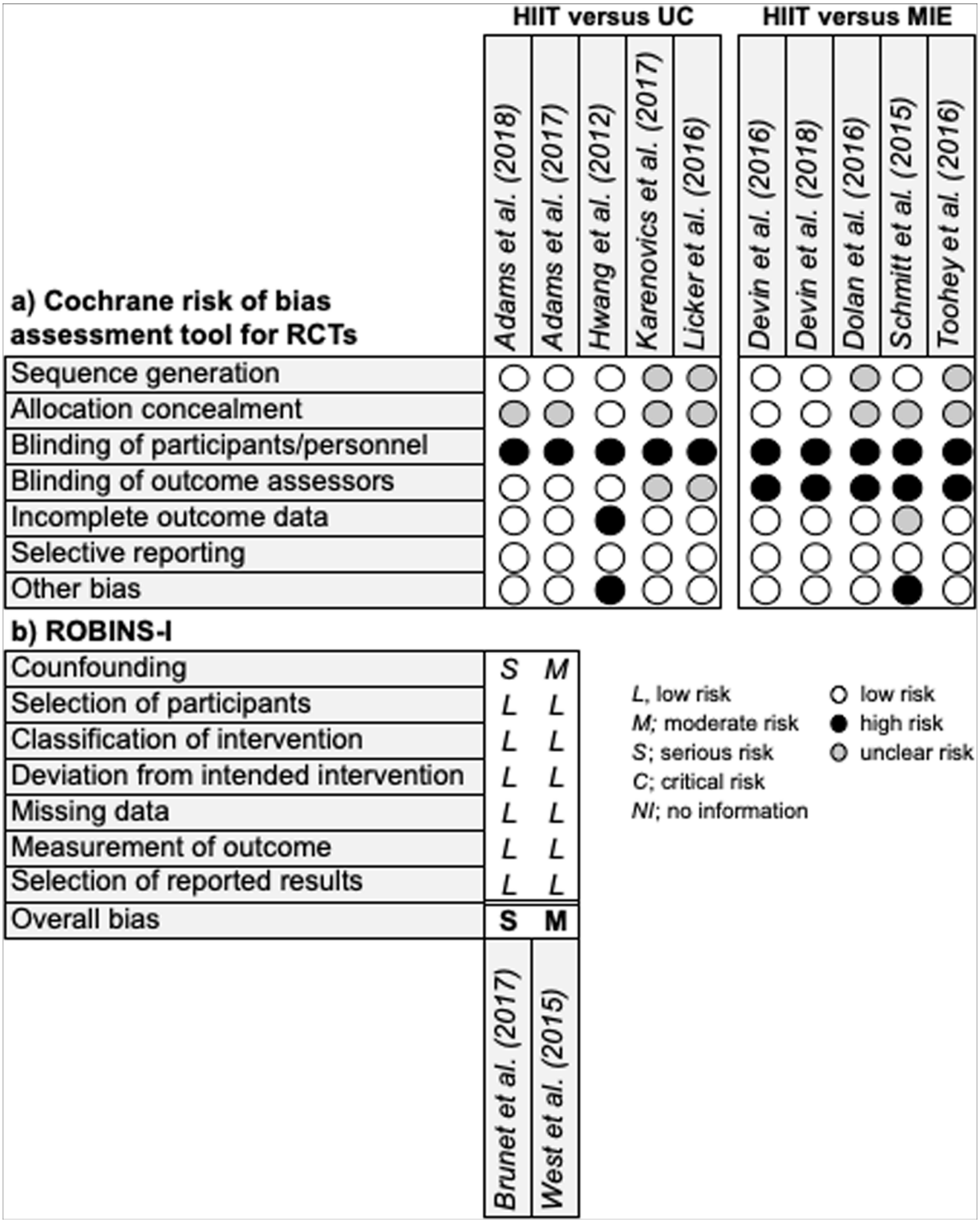

Fig. 2 Risk of bias assessment for the included study

contrast, HIIT showed statistically significant improvements compared to UC for some item scales of the SF-36 [37]. Compared to UC, HIIT led to significantly improved cancer-related fatigue assessed by the Functional Assessment of Cancer Therapy Fatigue scale (FACT-F) as well as improved values for self-esteem but not for depression, anxiety, stress, or sleep quality [37] (Table 3).

Similarly, changes in QoL induced by HIIT and MIE were assessed only in two studies carried out in aftercare [38, 39], using different tools (i.e., Functional Assessment of Cancer Therapy-General [FACT-G] and EORTC-QLQ-C30 as well as the Multidimensional Fatigue Inventory [MFI-20]). While Toohey and colleagues did not report statistical between-group differences [39], Schmitt and colleagues reported MIE

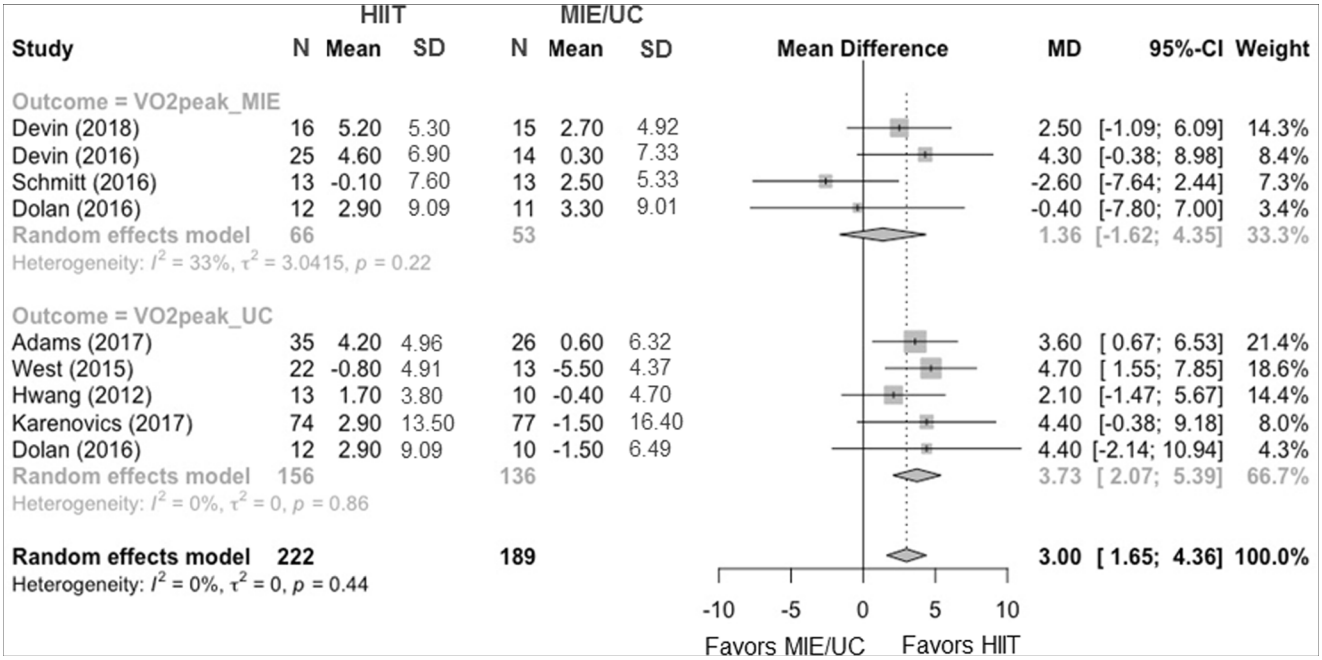

Fig. 3 Forest plot illustrating changes in cardiorespiratory fitness (VO_{2peak}) as a result of HIIT vs. UC or HIIT vs. MIE. HIIT, high-intensity interval training; UC, usual care; MIE, moderate-intensity training

to be superior to HIIT for subscales of "general fatigue" (− 22.1 vs. − 11.2%, $p = 0.04$), "social functioning" (+ 35.5 vs. − 3.5%, $p = 0.02$), "emotional functioning" (+ 79.3 vs. + 18.1%, $p = 0.03$), and "pain" (− 41.9 vs. + 18.1%, $p = 0.02$) [38].

Discussion

The purpose of this systematic review and meta-analysis was to determine if HIIT positively affects physical fitness and health-related outcomes in cancer patients during any stage of treatment and aftercare. The effect sizes of our meta-analysis indicate larger improvements in VO_{2peak} when HIIT was compared to UC. However, this effect declined when compared to MIE both in treatment and aftercare, indicating that HIIT may not be necessary to achieve favorable cardiorespiratory adaptations in cancer patients. Furthermore, our systematic literature review revealed no superior effects of HIIT on QoL and changes in lean mass as compared to MIE, while some evidence was provided for a larger reduction in fat mass following HIIT in aftercare.

For several years, HIIT has been utilized in clinical populations other than cancer with positive effects being reported on vascular function, cardiorespiratory fitness, cardiovascular risk factors, blood-borne biomarkers, and body composition [41]. However, only recently, the scientific interest has arisen to implement HIIT in the supportive therapy of cancer patients. These studies predominantly used multimodal intervention strategies including aerobic and resistance training as well as other modalities or therapies, such as relaxation and psychosocial support [20]. This is making it difficult to attribute the observed beneficial effects to aerobic HIIT.

Our review with meta-analysis expands to previous studies by exclusively investigating the effectiveness of aerobic HIIT for cancer patients. In fact, our meta-analysis revealed significantly larger improvements in VO_{2peak} in HIIT compared to UC, while this difference was negligible when HIIT was compared to MIE. Thus, a clear advantage of HIIT over other aerobic training modes may not be confirmed at this time, based on adaptations in VO_{2peak}. However, it should be noted that this conclusion was based on four studies only. Although our risk of bias assessment revealed a high quality for the majority of the included studies, the overall low number of investigations should be considered, especially in light of the multiple facets of this disease (i.e., various cancer types and numerous treatment options). Moreover, a rather short duration of interventions (3 to 6 weeks) across a number of included studies might have not been sufficient enough to distinguish between the induced physiological responses of HIIT or MIE [16, 33, 38].

A possible practical explanation for our findings may be related to the exercise intensity and HIIT modality. While current guidelines for cancer patients [42] recommend a weekly volume of 150 min of moderate or 75 min of vigorous aerobic exercise, it remains unknown whether intensity zones used in healthy individuals or in the therapy of chronic diseases can be ultimately applied to cancer patients in different phases of therapy. In a study by Scharhag-Rosenberger and colleagues [43], it was shown that standardized intensities typically used for exercise prescription in healthy individuals

may easily under- or overestimate the actual intensity perceived by breast cancer survivors. According to the authors, maximal heart rate appeared to be the most valid measure to prescribe exercise intensities, whereas a slight under- and overestimation of intensity zones was observed when intensities were prescribed based on VO_{2peak} or heart rate reserve. While it remains unknown whether these findings may be applied to patients diagnosed with other cancer entities, the included studies of this review used both peak/maximal measures of VO_2 and maximal heart rate for intensity control.

In line with the findings for cardiorespiratory fitness, our systematic review also revealed that the aerobic training mode does not seem to affect changes in lean mass, while reductions in fat mass may be larger in HIIT compared to MIE [16, 38–40]. This finding is of importance as increased visceral body fat is associated with negative health outcomes and increased mortality in cancer patients [44, 45]. Furthermore, body composition may impact chemotherapy tolerance and severity of treatment side effects [46, 47]. Interestingly, in contrast to our findings, in a recent review on the effects of high-intensity exercise in cancer patients, both reductions in fat mass and concomitant increases in lean mass following high-intensity exercise training were observed [20]. However, since this review included combined interventions (i.e., HIIT and resistance training), it is likely that these effects were induced by strength training rather than the HIIT modality.

Only very few studies have assessed the effects of HIIT on QoL or cancer-related fatigue in treatment [31] or aftercare [35, 38, 39]. Results of these studies indicated no beneficial effect of HIIT for cancer-related fatigue or QoL when compared to MIE. However, one study showed superior effects of HIIT compared to UC in terms of improving cancer-related fatigue and vitality, even during a 3-month follow-up [37]. Furthermore, it was shown that improvements in cardiorespiratory fitness mediated cancer-related fatigue and QoL parameters [37]. This finding is in line with a meta-analysis of exercise interventions for cancer patients, showing that intense aerobic exercise was more successful in improving QoL [48]. Furthermore, these findings advocate a dose–response hypothesis, where exercise-induced improvements in QoL might be dependent on exercise intensity. Recently, Mijwel and colleagues [15] showed significantly improved QoL in breast cancer compared to UC by adding HIIT to other exercise therapy modalities during chemotherapy. However, the largest improvements were shown within the concurrent training group combining resistance exercise and HIIT. Therefore, the contribution of either of the training modalities cannot be teased out. In addition, the heterogeneity of the instruments used to assess patient-reported outcomes in the studies included in this review could have at least partially contributed to the controversial results.

Blood-borne biomarkers were assessed in three studies only. Interestingly, these studies showed positive effects of HIIT when carried out in an aftercare setting [17, 39] but not during targeted therapy [31]. These positive effects were reflected by the reduced concentrations of inflammatory markers and increased insulin sensitivity [17]. The anti-inflammatory mechanisms of HIIT may be crucial for cancer patients, not only because inflammation is directly linked to tumor growth but also as a protection in patients at high risk of chemotoxicity or treatment-related cardiotoxicity [49].

When interpreting the findings of this review, one should bear in mind a few limitations. Firstly, there has been a language bias, which could have resulted in missing potential studies of interest. Furthermore, the overall number of included studies was low and the included patients varied considerably in cancer diagnoses and statuses as well as treatments (i.e., in treatment vs. aftercare). Despite a low risk of bias in all included studies, this limits the comparison between studies and makes it difficult to draw definite conclusions for all cancer entities. Furthermore, HIIT protocols also differed considerably in modality, frequency, intensity, and duration across included studies. Therefore, the performance of further randomized controlled trials with the following focus is highly encouraged: (a) direct comparisons between HIIT and MIE; (b) effects of different HIIT protocols on cancer-related outcomes, such as treatment completion and tumor biology; and (c) the feasibility and motivational impact of HIIT across major cancer entities, disease stage, and different treatments.

Conclusion

Our systematic review with meta-analysis revealed that short-term HIIT appeared to be more beneficial than UC for improvements of physical fitness and health-related outcomes, while a clear advantage compared to continuous training with moderate intensities remains questionable. As such, the implementation of HIIT for cancer patients both during treatment and aftercare may be encouraged, especially in patients where time is of concern. However, due to the overall low number of available studies focusing on body composition, patient-reported outcomes, and blood-borne biomarkers, there is an urgent need for further studies investigating the effectiveness of HIIT in this population and during all stages of treatment and aftercare.

Submission declaration and verification The authors declare that this manuscript is not under consideration for publication elsewhere, that its publication is approved by all authors and tacitly or explicitly by the responsible authorities where the work was carried out, and that, if accepted, it will not be published elsewhere in the same form, in English or in any other language, including electronically without the written consent of the copyright holder.

Author contribution HM contributed to the design of the study, the literature search, data screening and extraction, statistical analyses, manuscript preparation and editing, and submission. NF contributed to the design of the study, the literature search, data screening and extraction, statistical analyses, manuscript preparation and editing, and submission.

JW contributed to the design of the study as well as data screening and extraction. YY contributed to the data extraction, statistical analyses, and manuscript preparation. SC contributed to the data extraction and statistical analyses and contributed theoretical expertise and writing and editing of the manuscript. WB contributed to the data extraction and statistical analyses and contributed theoretical expertise and writing and editing of the manuscript. MS contributed to the design of the study, the literature search, data screening and extraction, and statistical analyses; provided methodological input and theoretical expertise; and contributed to writing and editing of the manuscript and submission.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This manuscript does not contain any studies with human participants or animal subjects performed by any of the authors.

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