

High-intensity interval training for knee osteoarthritis: a narrative review

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Abstract: Knee osteoarthritis (OA) is the most common joint disease worldwide. Exercise therapy has been identified as a first-line treatment option in patients suffering from knee OA. High-intensity interval training (HIIT) is an innovative exercise modality with potential in improving various disease-related outcomes. The purpose of this review is to explore the impact of HIIT on knee OA symptoms and physical functioning. A comprehensive search of scientific electronic databases was conducted to identify the articles on the effects of HIIT on knee OA. Thirteen studies were included in this review. Nine compared the effects of HIIT with those of low-intensity training, moderate-intensity continuous training, or a control group. Three evaluated the effects of HIIT alone. Eight reported a decrease in knee OA symptoms, and eight reported an increase in physical functioning. HIIT was shown to improve knee OA symptoms and physical functioning, but also aerobic capacity, muscle strength, and quality of life with minimal or no adverse events. However, compared to other exercise modalities, no clear superiority of HIIT was found. HIIT is a promising exercise strategy in patients with knee OA: anyway, the actual quality of evidence remains very low, and more high-quality studies are needed to confirm these promising outcomes.

Keywords: high intensity interval training; knee osteoarthritis; exercise therapy; rehabilitation; exercise rehabilitation

Introduction

Osteoarthritis (OA) is the most common joint disease worldwide, affecting approximately 15% of the worldwide population [1]. Moreover, the incidence of symptomatic OA is on the rise due to the aging of the population and the global obesity epidemic [2]. OA is a leading cause of disability and can affect people's physical and mental well-being. Symptoms are joint pain and stiffness with relevant consequences on functional status, significantly restricting daily activities, and often resulting in a reduction of quality of life (QoL) [3,4]. Knee OA is the most prevalent form of OA [5], and it is a leading cause of disability among older people, with recent data affirming that over 560 million people living with knee OA worldwide [6].

Physical activity is a safe, cost-effective, and recommended first-line knee OA treatment option for the management of pain and mobility for affected patients [7–14]. Exercise showed effect sizes comparable to those for simple analgesics and nonsteroidal anti-inflammatory drugs [15]. Unfortunately, few people with knee OA achieve recommended physical activity levels (i.e. 150 min/week of moderate intensity) [16–19], mainly demonstrating sedentary or inadequate physical activity behaviours [16,17]. Furthermore, people with knee OA have the added barriers of pain and functional limitations that make the recommended quantity of exercise intolerable [18,19].

Clinical guidelines recommend strength and aerobic training for patients with knee OA based on clinical trial evidence of effectiveness [9,15,20–22]. Aerobic training can promote the metabolism of adipose tissue, prevent muscle atrophy, accelerate the recovery of damaged cartilage, enhance the body's immunity, and reduce pain [23]. Strength training mediates pain relief [24], enhances psychological well-being [25], maintains cartilage integrity in animal models [26,27], and may increase the shock absorbing capability of lower extremity muscles during walking [28]. Even if exercise has been recognized as a core treatment for knee OA [29], it is still unclear which program is more effective [30]. One promising modality of therapeutic exercise in those with knee OA could be represented by high-intensity interval training (HIIT) [31].

HIIT involves short bursts of very intense activity alternated with short periods of rest or low-intensity exercises [32]. HIIT has been proposed as a time-efficient form of exercise that may overcome motivational barriers associated with traditional moderate intensity training [33]. Several studies have demonstrated the effectiveness of HIIT on both healthy and pathological subjects [34–36]. Prior research shows that performing HIIT two to three times per week is sufficient to promote adherence and important physiological changes, such as improvements in cardiorespiratory health, body composition, and insulin sensitivity [37,38]. HIIT has promising long-term adherence rates and offers similar physiological benefits as less intense long-duration exercise in a shorter period and with more pronounced effects on cardiorespiratory fitness [39,40]. Time efficiency and flexibility of exercise mode have supported the successful implementation of HIIT among individuals with obesity and older adults [41,42].

Previous studies have provided conflicting evidence regarding the impact of HIIT on knee OA symptoms. Some suggested that HIIT may be detrimental for knee OA symptoms due to the greater contact forces exerted on the joint [43], and that it might aggravate symptoms such as pain and swelling [44], although others did not support these findings [45,46]. In contrast, one study even suggested that short-term, high-intensity strength training is in fact safe and well tolerated by older adults with knee OA [47]. Additionally, preliminary evidence from a small-sample study has suggested that high-intensity resistance training may have beneficial effects on muscle strength compared to low-intensity resistance training in patients with knee OA [44].

Given these premises, the aim of this review was to understand what the benefits of HIIT in patients with knee OA are compared to other exercise modalities or no physical therapy regarding knee OA symptoms and physical functioning, and to what extent are these benefits superior to other exercise modalities.

Materials and Methods

To address the lack of available literature on the effects of HIIT on knee OA, the authors conducted a narrative review using a systematic approach. A comprehensive search of scientific databases, including PubMed, Scopus, and Web of Science, was performed by two independent authors (D.T. and J.V.) to collect relevant articles on the topic.

The included articles reported on the benefits of HIIT without a comparator group, or HIIT compared to other forms of training (such as low-intensity or moderate-continuous), or HIIT compared to control, on knee OA, and reported primary or secondary outcomes related to knee OA symptoms, muscle strength and physical or functional status. Reported improvements were defined as statistically significant for p-values <0.05.

Furthermore, to ensure the training protocols were considered as HIIT by the authors of the present review, only articles explicitly labelling their interventions as HIIT were included, and specific keywords “high-intensity interval training”, “high-intensity interval training AND osteoarthritis”, “high-intensity interval training AND osteoarthritis AND knee” were used during the search. Finally, the selected studies were evaluated using the CERT tool (Table 1), that is designed specifically for the reporting of exercise programs across all evaluative study designs for exercise research [48].

Table 1. Consensus on Exercise Reporting Template (CERT).

Study and year	WHAT (equipment)	WHO (experienced therapist?)	Individual/group (S/US)	HOW				Exercise program replicable/home components available?	Nonexercise components	WHE RE	WHEN, HOW MUCH	HOW TAILOR ING (of exercise based on...)	WELL (Delivered and performed as expected?)
				Adherence / adverse events (reported by...)	Motivation strategies	Progression							
Golightly, 2021	Cycle ergometer or treadmill; chest strap heart rate monitor	Yes	Individual (S)	Physiotherapist: number of sessions attended or completed/ participant + investigator	N.A.	N.A.	Yes, except exercise progression/ N.A.		In-centre	20 min (without warm-up/cooling-down); 10 reps of 1-min high-intensity bouts HI: 90% VO ₂ peak Rest: 1 min complete rest between reps; 24 h between training sessions	Exercise modality; exercise intensity	Yes	
Smith-Ryan, 2020	Electronically braked cycle ergometer	Yes	Individual (S)	Physiotherapist: number of sessions completed or total available/ participant	N.A.	N.A.	Yes, except exercise progression/ N.A.		In-centre	20 min (without warm-up/cooling-down); 10 reps of 1-min high-	Peak power output	Yes	

				+ investigator							intensity bouts HI: 90% peak power output Rest: 1 min between reps; 24 h between training sessions
											45 min (including warm-up) Part 1 -> 3 sets; 10 reps; concentric isokinetic knee extension and flexion at 60, 90 and 120°/sec angular velocity; 60% of baseline strength Part 2 -> 3 sets; 15 reps; concentric isokinetic knee extension and flexion at
King, 2008	Cycle ergometer ; dynamom eter (and accompa nying software)	Yes	N.A. (S)	Researcher/ participant	N.A.	New targets of 60% peak torques based on test protocols every 3 weeks	Yes/ N.A.	In- centre	Peak torques	Minimal modificat ion (due to increases in pain)	

									180°/sec angular velocity; maximum effort Rest: minimal 24 h between sessions		
Keogh, 2018	Stationary bicycle	N.A.	Individual (US)	Participant (training diary)/ participant	N.A.	N.A.	Yes/ yes	Home- based	25 min HI: 7 min warm-up (progressi vely increasing intensity); 5 sets of high- intensity intervals at 110 rpm for 45 sec with 90 sec relative rest between sets at 70 rpm (low- intensity); 6-7 min cool-down (light- moderate intensity) Moderate- intensity: 3 min warm-up (light	Personal experie nce	Yes

									intensity); 20 min at 60-80rpm (moderate intensity); 2 min cooldown (light intensity)		
				Physiothera 2x/week pist/ in group participant (S) + investigator				2x/week in- centre	60 min; 3 sets; 10 reps HI: 70- 80% 1- RM, weighted vests during weight- bearing exercises		
De Zwart, 2022	Fitness devices; weighted vests; ankle weights; resistance band	Yes	1x/week individu al (US)	Log book/ participant + investigator	N.A.	↑ 5% 1- RM/ week, based on 1-RM measure ment from week 0, week 6 & week 10	Yes/ yes (paper hand- out)	1x/week home- based	LI: 40- 50% 1- RM, no additional weighted vests Rest: 90 sec between sets; 48h between training sessions	% 1-RM	Yes
Foroughi, 2011	Fitness devices	Yes	N.A. (S)	Researcher/ participant	N.A.	↑3% 1- RM	Yes/ N.A.	In- centre	3 sets; 8 reps (6-9 sec/rep); 80% 1RM	% 1-RM	Main protocol deviation: changing

							(equal to 15-18 on the Borg Rating of Perceived Exertion) Rest: 10-15 sec between reps; 1-2 min between sets C: minimal resistance; no progression	to an isometric form of training if the dynamic mode was causing pain, reducing the intensity of the intervention group and/or limiting the range of motion
Cycle Mangione ergometer, 1999 ; heart rate monitor	N.A.	N.A. (S)	Researcher/ N.A.	N.A.	N.A.	Yes, except exercise progression/ N.A.	In-centre HI: 60min (including warm-up and cool-down); 70% HR reserve LI: 60min (including warm-up and cool-down); 40% HR reserve Target HR zone is reached by an increase in speed of pedaling instead of	Maximum heart rate Yes

								an increase in resistance			
Bressel, 2014	Pool; water jet; aquatic treadmill	N.A.	N.A. (S)	Researcher/participant + investigator	Verbal motivation	Progression visualized in table in study article	Yes/N.A.	In-centre	18-30 min; 3-6 reps HI: 14-19 RPE; 30 sec – 2 min 30 sec Rest: 10 RPE; 1 min – 1 min 30 sec C: maintenance of typical activities of daily living; no new treatment	RPE	Yes
Thorstensson, 2005	Heart rate monitor (not obligatory); theraband	Yes	Group (S)	Researcher/N.A.	N.A.	Gradually increase in intensity by increased lever arm or range of motion	Yes/yes	In-centre + home-based	Weight-bearing exercises; 1 h; minimal 60% maximum HR	Maximum heart rate	Yes
Waller, 2017	Pool; heart rate monitors; therabands; Hydro-boots	Yes	Group (S)	Researcher/investigator	N.A.	Progression from barefoot to small resistance fins and large resistance boots	Yes/N.A.	In-centre	1 h (i.e. 15 min warm-up, 30 min intensive aquatic resistance training program, 10-15 min	RPE, heart rate, blood lactates	Yes

								group difference Rest: at least 48 h between sessions; 1 min between sets		
								60 min; 3 sets		
								HI: 4-8 reps; 75- 90% 1- RM		
								LI: 15 reps; 30- 40% 1- RM		
								C: 60 min educationa l workshops and seated stretching 2x/month for the first 6 months and the other months 1x/month		
Messier, 2021	Nautilus resistance training machine; Thera- Bands	Yes	Group (S)	Participant/ participant	Frequent contact; positive feedback; ↑ 5% 1- incentives RM/ 2 ; weeks, establishi ng personal commitm ent; promotin g a sense of communit y	1-RM measure ment (measure d each 9 weeks)	Yes/Yes	In- centre workshops and seated stretching 2x/month for the first 6 months and the other months 1x/month	% 1-RM	Yes
								Rest: 60- 90 sec between sets		

Jan, 2008	Leg press machine; bicycle (warm-up); cold pack (after exercise)	Yes	Individual (S)	Researcher/ N.A.	N.A.	↑5% 1-RM/ 2 weeks	Yes/N.A	In-centre intervention	C: no %1-RM	Yes
									HI: 30 min; 60% 1-RM; 3 sets; 8 reps LI: 50 min; 10% 1-RM; 10 sets; 15 reps Rest: 1 min between sets; 5 min between left and right knee sessions	

Abbreviations. S: supervised; US: unsupervised; HI: High-Intensity; LI: Low-Intensity; reps: repetitions; 1-RM: One Repetition Maximum; HR: heart rate; rpm: revolutions per minute; I: intervention group; C: control group; 1-RM: One Repetition Maximum; N.A.: Not Available; RPE: Rate of Perceived Exertion.

Results

The results of the research lead to the selection of 13 articles. A summary of the characteristics of the included studies is provided in Table 2. To facilitate understanding of the results, we categorized the studies into the following sections: HIIT (alone), HIIT vs low-intensity training (LIT), HIIT vs moderate-intensity continuous training (MICT), HIIT vs control (CT), and HIIT vs LIT vs CT. We recommend that readers refer to the individual articles for additional details regarding the training protocols.

Table 2. Characteristics of included studies.

Study and year	Exercise modality	NOS; Age (mean, years); Sex (female, n)	Groups	Exercise duration & sessions	Outcomes	Results	Drop-out rate
Golightly, 2021	CIT: cycling or walking	29; 63 ± 7; 19	I: High-intensity (n = 29)	12 weeks; 24 sessions; 2x/week	Adverse events; feasibility; physical function; knee OA symptoms; balance; muscle strength; cardiorespiratory fitness; body composition	70% adherence No adverse events related to the program ↑ Physical function* ↓ Knee OA symptoms* ↑ Balance* ↑ Muscle strength* ↑ Cardiorespiratory fitness* Body composition: no significant changes	27.59%
Smith-Ryan, 2020	CIT: cycling	16; 59.9 ± 8.3; 12	I: High-intensity (n = 16)	6 weeks; 12 exercise sessions + 2 testing sessions at baseline + 2 post-test sessions; 2x/week exercise sessions	Primary: feasibility Secondary: cardiorespiratory fitness (i.e. VO ₂ peak); knee OA symptoms; circulating biomarkers of metabolism	Moderate feasibility: no adverse events related to the program, >96% adherence ↑ Cardiorespiratory fitness* ↓ Knee OA symptoms* ↓ Amino acids (i.e. methionine*, phenylalanine*, tyrosine*, serine) ↑ Aspartate/ asparagine ↓ Acylcarnitine	18.75%
King, 2008	RT: lower extremity	14; 48.35 ± 6.51; 2	I: High-intensity (n = 14)	12 weeks; 36 sessions; 3x/week	Primary: knee extensor and flexor strength; pain; adherence Secondary: dynamic knee joint loading; patient-reported outcomes; self-efficacy after training	No adverse events ↑ Knee extensor and flexor strength* No increases in pain during or after training High adherence	N.A.

						Dynamic knee joint loading & patient-reported outcomes: no significant changes ↑ Self-efficacy after training (i.e. function subscale)*	
Keogh, 2018	CIT: cycling	27; 62.4 ± 8.3; 13	I1: High-intensity interval training (n = 9) I2: Moderate-intensity continuous training (n = 8)	8 weeks; 32 sessions; 4x/week	Primary: feasibility (i.e. enrolment rate, withdrawal rate, exercise adherence, number of adverse events) Secondary: efficacy (i.e. health-related quality of life, physical function, body composition)	54% enrolment rate 37% rate of withdrawal Very high exercise adherence 28 adverse events (24 related to one HIIT participant) ↑ Health-related quality of life* ↑ Physical function* Body composition: no significant changes	37%
De Zwart, 2002	RT: lowerextremity	177; 67.7 ± 5.8; 107	I1: High-intensity (n = 89) I2: Low-intensity (n = 88)	12 weeks; 36 sessions; 3x/week	Primary: isokinetic muscle strength; estimated 1-RM Secondary: knee pain; physical functioning; knee OA symptoms	No adverse events related to the program ↑ Isokinetic muscle strength ↑ estimated 1-RM** ↓ Knee pain ↑ Physical functioning ↓ Knee OA symptoms	6%

Table 2. Continued.

Study and year	Exercise modality	NOS; Age (mean, years); Sex (female, n)	Groups	Exercise duration & sessions	Outcomes	Results	Drop-out rate
Foroughi, 2011	RT: lower extremity	54; 64 ± 7; 54	I1: High-intensity (n = 26) I2: Low-intensity (n = 28)	6 months; 78 sessions; 3x/week	Primary: dynamic shank angles; knee adduction angles; knee adduction moment of the most symptomatic knee Secondary: muscle strength; gait speed; osteoarthritis symptoms	Two minor adverse events in the control group Dynamic shank angles: knee adduction angles, knee adduction moment: no change over time ↑ Muscle strength** ↑ Gait speed* ↓ Osteoarthritis symptoms*	9%
Mangione, 1999	Cardio-respiratory continuous training: cycling	39; 71 ± 6.9; 26	I1: High-intensity (n = 19) I2: Low-intensity (n = 20)	10 weeks; 30 sessions; 3x/week	Functional status; gait; overall and acute pain; aerobic capacity	↑ Functional status* ↑ Gait* ↓ Overall pain* No increase in acute pain ↑ Aerobic capacity*	7.8%
Bressel, 2014	CIT + balance training: aquatic treadmill	18; 64.5 ± 10.2; 16	I: High-intensity (n = 18) C: Control group (n = 18)	High-intensity: 6 weeks; 2-3x/week Control: 4 weeks	Pain; balance; physical function; mobility	No adverse events related to the program ↓ Pain** ↑ Balance** ↑ Physical function** ↑ Mobility**	0%
Thorstensson, 2005	RT: lower extremity	61; 56 ± 6; 31	I: High-intensity (n = 30) C: Control (n = 31)	6 weeks; 12 sessions; 2x/week	Primary: self-reported pain; function; knee-related quality of life Secondary: health status; functional performance	Self-reported pain & function: no significant differences between groups ↑ Quality of life** (at 6 weeks & 6 months) ↑ Health status** (at 6 weeks) ↑ Functional performance*	8%
Waller, 2017	RT: aquatic	87; 63.8 ± 2.4; 87	I: High-intensity (n = 43)	16 weeks; 48 sessions; 3x/week	Primary: body composition; walking speed	High adherence ↓ Fat mass** (after 4 months intervention)	2% (after 16 weeks)

	C: Control (n = 44)	Secondary: leisure time physical activity	Lean mass: no significant changes ↑ Walking speed** (after 4 months intervention and 12 months follow-up) Leisure time physical activity: significant effect on fat mass loss	13% (after 12-month follow-up)
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Table 2. Continued.

Study and year	Exercise modality	NOS; Age (mean, years); Sex (female, n)	Groups	Exercise duration & sessions	Outcomes	Results	Drop-out rate
Calatayud, 2017	RT: lower extremity	50; I: 66.8 ± 4.8, C: 66.7 ± 3.1; 37	I: High-intensity (n = 25) C: Control (n = 25)	8 weeks; 24 sessions; 3x/week	WOMAC; SF-36; VAS; isometric knee flexion; isometric knee extension; isometric hip abduction; active knee range of motion; functional tasks	↓ WOMAC** ↑ SF-36** ↓ VAS** ↑ Isometric knee flexion** ↑ Isometric knee extension** ↑ Isometric hip abduction** ↑ Active knee range of motion (i.e. flexion and extension)** ↑ Functional tasks**	12%
Messier, 2021	RT: lower & upper extremity, core	65; 151	I1: High-intensity (n = 127) I2: Low-intensity (n = 126) C: Control (n = 124)	18 months; 3x/week	Primary: knee pain; knee joint compressive force Secondary: physical function; mobility; disease progression; thigh skeletal muscle volume; thigh fat	29 nonserious adverse events related to the program No statistically significant difference between high-intensity and	25%

				volume; IL-6 serum levels; knee extensor strength; hip abductor strength	control group or high-intensity and low-intensity group
Jan, 2008	RT	102; 63.3 ± 6.6 (high-intensity), 61.8 ± 7.1 (low-intensity), 62.8 ± 7.1 (control); 79	I1: High-intensity (n = 34) I2: Low-intensity (n = 34) C: Control (n = 34)	8 weeks; 24 sessions; 3x/week Pain; function; walking time; muscle torque	↓ Pain* ↑ Function* ↓ Walking time* ↑ Muscle torque* No statistically significant differences between the high-intensity and low-intensity groups

Note. NOS: Number of subjects; RT: Resistance Training; CIT: Cardiorespiratory Interval Training; 1-RM: One Repetition Maximum; OA: osteoarthritis; IL-6: interleukin 6; VO₂peak: peak oxygen consumption; N.A.: Not Available; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index; SF-36: Physical Functioning Scale of the Short Form-36; VAS: Visual Analogue Scale.

*p < 0.05. **significant difference between groups.

HIIT (without a comparator group)

Three studies reported the outcomes of HIIT alone for knee OA.

A pilot study by Golightly et al. [49] assessed the feasibility and changes in outcomes of a HIIT program in patients with symptomatic knee OA. Twenty-nine participants were enrolled to a 12-week (2x/week) supervised HIIT program. The authors stated that their HIIT program improved the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores (32.4 ± 14.0 , 28.8 ± 19.2 , and 20.0 ± 13.7 at baseline, six and 12 weeks, respectively), 20-meters fast-paced walk test measured in seconds (12.5 ± 5.4 , 11.5 ± 5.0 , 10.0 ± 2.8 at baseline, six and 12 weeks, respectively), 30-second chair-stand test measured in repetitions (12.6 ± 5.4 , 14.5 ± 6.1 , 16.4 ± 6.4 at baseline, six and 12 weeks, respectively), stair-climb test measured in seconds (13.8 ± 7.3 , 11.5 ± 6.4 , 10.6 ± 6.2 at baseline, six and 12 weeks, respectively), timed up and go test measured in seconds (7.9 ± 4.8 , 7.3 ± 4.4 , 6.0 ± 1.4 at baseline, six and 12 weeks, respectively), balance measured as single leg stance in seconds (15.1 ± 11.0 , 19.2 ± 11.6 , 21.0 ± 11.9 at baseline, six and 12 weeks, respectively), isometric knee extensor strength measured in Newton meter (Nm) (average right knee 71.1 ± 33.4 , 72.5 ± 36.5 , 77.8 ± 37.9 at baseline, six and 12 weeks, respectively, average left knee 68.3 ± 35.0 , 72.2 ± 37.3 , 72.1 ± 33.5 at baseline, six and 12 weeks, respectively), and cardiorespiratory fitness, with most changes occurring as early as six weeks.

Another pilot and feasibility study by Smith-Ryan et al. [31] examined the feasibility of a 6-week HIIT program in patients with symptomatic OA. Sixteen participants were enrolled to a 6-week (12 exercise sessions + two testing sessions at baseline + two post-test sessions) HIIT program (2x/week). The authors stated that their HIIT program improved cardiorespiratory fitness and OA symptoms measured with WOMAC (pre-testing total score 36.15 ± 8.60 , post-testing at six weeks 25.46 ± 16.09) in concert with metabolic alterations indicative of improved skeletal muscle energetics.

The last study on HIIT alone for knee OA was performed by King et al. [45] to evaluate the effects of a HIIT knee extensor and flexor resistance training program on strength, pain, and adherence in patients with advanced knee OA and varus malalignment. Fourteen patients with medial compartment knee OA and malalignment were enrolled to a 12-week (3x/week) HIIT program. The authors concluded that their supervised HIIT training can produce substantial increases in knee extensor and flexor strength (strength increased from 28% to 46%, relative to baseline values) in middle-aged patients with advanced knee OA and varus malalignment, without concomitant increases in pain, adverse events, or decreases in adherence. Adherence was generally good throughout the studies (the drop-out rate was 27.59%, 18.75% and not defined in the last article, respectively), and no adverse events related to the training programs were reported.

HIIT vs MICT

Only one study by Keogh et al. [50] evaluated the feasibility and potential benefits of HIIT cycling as an alternative exercise option to MICT cycling for patients with knee OA. Twenty-seven participants were enrolled to an 8-week (4x/week) HIIT or MICT program. Significant benefits in health-related QoL measured with WOMAC (pre- and post-test scores for the HIIT group 36.1 ± 15.0 and 34.8 ± 15.5 , respectively, pre- and post-test scores for the MICT group 21.2 ± 14.6 and 22.9 ± 14.4 , respectively) were found for both groups, with the HIIT group also reporting significant increases in functional performance as assessed using the Timed Up and Go measured in seconds (pre- and post-test 8.9 ± 2.0 and 7.8 ± 1.1 , respectively) and Sit to Stand measured in seconds (pre- and post-test 11.1 ± 2.2 and 13.1 ± 2.7 , respectively) functional tests. The enrolment rate and adherence rate for both the HIIT and MICT groups was comparable to other cycling studies involving similar populations [51–53] with a withdrawal rate of 37%. Nonetheless, the number of adverse events (HIIT: two of nine participants, 26 adverse events; MICT: one of eight participants, two adverse events) appeared very high, although 24 of these adverse events were reported by one HIIT patient with a Bakers cyst on their knee, who still completed 25 of the requested 32 exercise sessions.

HIIT vs LIT

Three studies evaluated the outcomes of HIIT vs LIT for knee OA.

One recent study by de Zwart et al. [54] assessed whether resistance HIIT led to increased muscle strength compared to resistance LIT in patients with knee OA. One-hundred and seventy-seven participants were enrolled to a 12-week (3x/week) HIIT or LIT program. In both HIIT and LIT groups, muscle strength measured in Nm per kilogram (Nm/kg) (0.98 ± 0.40 and 1.11 ± 0.40 at baseline and 12 weeks, respectively, for the HIIT group, 1.02 ± 0.41 and 1.15 ± 0.42 at baseline and 12 weeks, respectively, for the LIT group), knee pain measured with the Numeric Rating Scale (4.8 ± 2.3 and 2.9 ± 2.0 at baseline and 12 weeks, respectively, for the HIIT group, 5.1 ± 2.4 and 2.7 ± 2.4 at baseline and 12 weeks, respectively, for the LIT group) and WOMAC-Physical Functioning (21.3 ± 13.0 and 16.8 ± 12.2 at baseline and 12 weeks, respectively, for the HIIT group, 20.4 ± 13.3 and 16.4 ± 12.6 at baseline and 12 weeks, respectively, for the LIT group) were significantly increased after 12 weeks of training and at follow-up compared to the start of the training. Interestingly, it was found a higher estimated 1 RM strength values favouring HIIT. Interestingly, significant differences were found in the Hospital Anxiety and Depression scale between the HIIT and LIT groups in favour of the HIIT group. The authors concluded that HIIT did not result in greater improvements in isokinetic muscle strength, pain and physical functioning compared to LIT in patients with knee OA but was well-tolerated so they suggested that either intensity of resistance training could be utilised in exercise programs for patients with knee OA.

In a study by Foroughi et al. [55], the authors hypothesized that HIIT progressive resistance training would improve lower limb dynamic alignment and function (lower knee adduction moment, increased muscle strength, and fewer knee OA symptoms). Fifty-four women with knee OA were enrolled in into a 6-month (3x/week) HIIT or LIT exercise program. Dynamic alignment and knee adduction moment did not change over time or between groups. Muscle strength improved in both groups over time, but significantly more in the HIIT group (overall relative change in strength was 52.5% in the HIIT and 33.0% in the LIT group). By contrast, gait speed measured in meters per second (m/s) (1.1 ± 0.17 and 1.2 ± 0.17 at baseline and six months, respectively, for the HIIT group, 1.1 ± 0.19 and 1.2 ± 0.17 at baseline and six months, respectively, for the LIT group) and pain measured with WOMAC (5.7 ± 3.3 and 3.83 ± 2.7 at baseline and six months, respectively, for the HIIT group, 6.7 ± 3.5 and 5.5 ± 3.6 at baseline and six months, respectively, for the LIT group) improved over time in both groups. Improvements in shank adduction angle were related to improvements in self-reported disability, but not to changes in muscle strength, gait velocity, or pain. Although muscle strength improved significantly more in the HIIT group, the hypothesized reduction in knee adduction moment, shank and knee adduction angles were not evident after either exercise modality.

Mangione et al. [56] evaluated the effects of HIIT and LIT stationary cycling on functional status, gait, overall and acute pain, and aerobic capacity were examined. Thirty-nine adults with knee OA were randomized to either HIIT or LIT exercise group for 10 weeks (3x/week) of stationary cycling. The authors concluded that participants with knee OA in both groups improved in timed chair rise measured in seconds (23.31 ± 9.10 and 19.11 ± 6.62 at baseline and after 10 weeks, respectively), in the distance walked in six minutes measured in meters (489.59 ± 109.16 and 533.78 ± 104.99 at baseline and after 10 weeks, respectively), in the range of walking speeds measured in m/s (1.04 ± 21 and 1.05 ± 20 at baseline and after 10 weeks, respectively, for slow walking, 1.59 ± 33 and 1.67 ± 33 at baseline and after 10 weeks, respectively, for fast walking), in the amount of overall pain relief (in the 70% of training sessions subjects reported that pain decreased immediately after cycling), and in aerobic capacity measured at the treadmill GXT test in minutes (10.98 ± 3.95 and 13.17 ± 4.21 at baseline and after 10 weeks, respectively) with no differences between HIIT and LIT groups. Anyway, the authors stated that the intensity of exercise did not have a differential effect on these outcomes. The authors finally highlighted that the improvements in function and aerobic capacity demonstrated in their study

suggested that training was more than a "practice effect," because testing was carried out using a variety of walking-based measures, and training was performed by stationary cycling. Adherence was generally very good throughout the studies (the drop-out rate was of 6%, 9%, and 7.8%, respectively). Interestingly, two minor adverse events during testing occurred in the LIT group in the study by Foroughi et al. [55], and two minor adverse events occurred during the testing and training in the study by Mangione et al. [56], but it was not specified in which group.

HIIT vs CT

Four studies evaluated the effects of HIIT vs CT for knee OA.

Bressel et al. [14] quantified the efficacy of a HIIT aquatic treadmill exercise program on measures of pain, balance, function, and mobility in patients with knee OA. Eighteen participants were enrolled into a 6-week HIIT protocol (2-3x/week). The participants involved in the study first completed a 4-week non-exercise control period followed by a 6-week aquatic treadmill exercise program that incorporated a balance and HIIT training component. The authors observed that patients with OA display reduced joint pain measured with the Knee Injury and Osteoarthritis Outcome Score' (KOOS) subscale, with scores being 30–49% greater at six weeks than at pre-test evaluation, reduced usual pain values (at six weeks being 213% lower than the pre-test), improved balance measured with the sensory organization test equilibrium and strategy scores (values after the 6-week intervention being 10 and 2.5% greater than baseline, respectively), improved also function measured with the sit-to-stand test (rising index scores improved from $0.49 \pm 0.19\%$ at baseline to $0.33 \pm 0.11\%$ after six weeks), and mobility measured with walking speeds in seconds (8.6 ± 1.4 at baseline to 7.8 ± 1.1 after six weeks, 10% lower). The same benefits were not observed after a non-exercise control period. The authors suggested that aquatic treadmill exercise that incorporates high-intensity intervals is well tolerated by patients with OA and seems to be effective at managing symptoms of OA.

Thorstensson et al. [57] tested the effects of a short-term, HIIT on self-reported pain, function, and QoL. Sixty-one middle-aged participants were randomly randomized to HIIT or CT groups. Thirty participants were enrolled to a 6-week (2x/week) HIIT program. The authors stated that a 6-week high-intensive exercise program had no effect on pain or function in middle-aged patients with moderate to severe radiographic knee OA. Anyway, in the HIIT group, an improvement was seen at six weeks in KOOS subscale QoL after six weeks compared to the CT group (40 ± 15 and 46 ± 21 , respectively), and the difference between groups was still persistent at six months.

A RCT study by Waller et al. [58] investigated the effects of a 4-month (3x/week) HIIT aquatic resistance training on body composition and walking speed in post-menopausal women with mild knee OA, immediately after intervention and after 12-months follow-up. Additionally, influence of leisure time physical activity was also investigated. Patients were randomly allocated into one of the two arms of the study (HIIT or CT). The authors found that HIIT aquatic resistance training program is effective at decreasing fat mass four months after intervention, as well as improving walking speed calculated as m/s (1.74 ± 0.15 , 1.83 ± 0.16 and 1.82 ± 0.14 for HIIT at baseline, four and 12 months, respectively, 1.73 ± 0.17 , 1.76 ± 0.17 and 1.77 ± 0.13 for CT, at baseline, four and 12 months, respectively) in post-menopausal women with mild knee OA. Furthermore, daily leisure time physical activity (recorded as any type of activity and self-perceived intensity of each activity, i.e. low, moderate or high) over the 16-month period had a significant effect on fat mass loss but no effect on walking speed.

Calatayud et al. [59] evaluated the effectiveness of a 8-week (3/week) HIIT preoperative resistance training program in patients waiting for total knee arthroplasty (TKA). Fifty patients were randomly allocated to the HIIT group or CT. The main finding of this study was that high-intensity pre-operative training improved strength: isometric knee flexion measured in kg (9.2 and 9.1 at baseline, 9.4 and 4.4 three months after surgery for HIIT and CT, respectively), isometric knee extension measured in kg (23.5 and 23.5 at baseline, 22.8 and 14.3 three months after surgery for HIIT and CT, respectively) and hip abduction

measured in kg (7.3 and 7.2 at baseline, 7.8 and 5.0 three months after surgery for HIIT and CT, respectively), active knee range of motion (knee flexion was 104.0° and 104.2° at baseline, 101.2° and 96.4° at three months after surgery for HIIT and CT, respectively, while knee extension was 14.4° and 14.0° at baseline, 8.2° and 13.9° at three months after surgery for HIIT and CT, respectively) and functional measures such as the timed up and go test measured in seconds (8.6 and 8.5 at baseline, 7.0 and 8.7 at three months after surgery for HIIT and CT, respectively), as well as reduced pain measured with WOMAC (54.0 and 53.2 at baseline, 25.0 and 30.7 at three months after surgery for HIIT and CT, respectively) and length of hospitalization in the early post-operative periods compared with CT. Adherence was generally very good throughout the studies (the drop-out rate was of 0%, 8%, 2% after 16 weeks and 13% after 12-months, and 12%, respectively). No adverse events were reported throughout the studies.

HIIT vs LIT vs CT

Two studies evaluated the effects of HIIT vs LIT vs CT for knee OA.

A recent study by Messier et al. [60] was performed to determine whether strength HIIT reduces knee pain and knee joint compressive forces more than strength LIT and more than CT in patients with knee OA. A total of 377 participants were randomized into strength HIIT or LIT or CT. The exercise protocols for both HIIT and LIT were performed for 18 months (3x/week). Among participants with knee OA, strength HIIT did not significantly reduce WOMAC knee pain or knee joint compressive forces at 18 months compared with strength LIT or with an attention CT group. Some improvements were reported in the mean knee flexor strength that was statistically significantly greater in both exercise groups than in the CT group at 18 months measured in Nm (35.0 ± 20.1 , 38.2 ± 20.3 , and 38.1 ± 22.5 at baseline, 51.5, 52.6 and 43.8 at 18-month follow-up for HIIT, LIT and CT, respectively), and in the proportion of participants using pain medication that declined across the 18-month intervention period (45%, 34% and 55% for HIIT, LIT and CT, respectively), with no statistical difference among the groups at the 18-month follow-up.

Another study by Jan et al. [44] compare the effects of resistance strength HIIT and strength LIT in elderly subjects with knee OA. One-hundred and two participants were randomized into HIIT, LIT, and CT groups, and trained for eight weeks (3/week). The authors reported that both HIIT and low-intensity resistance strength trainings reduced pain measured with WOMAC pain subscale (8.5 ± 3.8 and 4.8 ± 3.5 in the HIIT group at baseline and after eight weeks, 7.8 ± 3.3 and 4.8 ± 2.7 in the LIT group at baseline and after eight weeks, 8.3 ± 4.6 and 7.1 ± 3.4 in the CT group at baseline and after eight weeks) and improved function measured with WOMAC physical function subscale (26.4 ± 9.0 and 14.7 ± 8.5 in the HIIT group at baseline and after eight weeks, 26.1 ± 8.1 and 14.8 ± 9.2 , in the LIT group at baseline and after eight weeks, 25.4 ± 11.3 and 22.5 ± 10.9 in the CT group at baseline and after eight weeks) in patients with knee OA. Although HIIT strength training demonstrated effect sizes that consistently were slightly greater than those achieved with low-intensity resistance strength training, the differences in improvement between the HIIT and low-intensity groups were not significant.

Adherence was generally good throughout the studies (the drop-out rate was 25% and 4%, respectively). There were 87 non-serious adverse events in the study by Messier et al. [60]: 53 in the HIIT, 30 in the LIT, and 4 in the CT groups. Of those, 29 were related to the program: 20 in the HIIT, 9 in the LIT, none in the CT groups. No adverse effects related to the program were reported in the study by Jan et al. [44].

Discussion

HIIT gained significant popularity worldwide as a fitness trend, and recent research has demonstrated its potential in reducing disability in people with different chronic musculoskeletal disorders such as fibromyalgia [36], axial spondylarthritis [61] and chronic non-specific low back pain [62–65]. In our review, we examined the effects of HIIT on knee OA as a standalone exercise modality or in comparison to training modalities with other exercise intensities such as MICT and LIT, or to CT. To the best of our knowledge, this is the first review that assessed the potential role of HIIT in mitigating symptoms associated with knee OA.

HIIT showed good outcomes in improving pain, physical functioning, muscle strength, cardiorespiratory fitness and QoL, when evaluated alone or compared with CT [14,31,45,49,57–59]. However, HIIT was shown to have similar effects in improving pain, function and strength when compared with other exercise intensity, especially LIT. The included studies utilized various exercise modalities ranging from resistance training to aquatic treadmill training, with all exercise intensities showing superiority over no exercise.

Exercise therapy is known to provide significant improvements to patients suffering from chronic musculoskeletal pain conditions (including OA). This improvement is thought to occur through different possible underlying mechanisms, including the reconceptualization of pain-related fears, a hypo-analgesic effect, and changes in the immune system, ultimately leading to better pain control, functional ability, and overall well-being [23,66,67].

According to Beckwée et al. [68], several explanatory models can be described for exercise-induced improvement of knee OA related symptoms, which can be categorized in five main components: neuromuscular, peri-articular, intra-articular, psychosocial components, and general fitness and health. The authors suggest that the clinical benefits of exercise therapy observed in patients with knee OA are likely due to a combination of these underlying mechanisms, and that future exercise studies taking all possible pathways into consideration should help in providing more targeted exercise recommendations for patients suffering by knee OA.

Furthermore, Runhaar et al. [69] stated that an increase of upper leg strength, a decrease of extension impairments and improvement in proprioception were identified as possible mediators in the positive association between physical exercise and OA symptoms.

Although several studies investigated optimal training parameters for resistance training in patients with knee OA, no uniform training dose can be proposed due to the great heterogeneity in training protocols limiting a direct comparison. In the included studies, resistance training treatment duration ranged from six weeks to 18 months and was performed using different kinds of equipment. For instance, de Zwart et al. [54], Thorstensson et al. [57], Waller et al. [58], and Messier et al. [60] used resistance bands in their protocols, resulting in improvements in knee OA symptoms, muscle strength and physical functioning. Foroughi et al. [55] and Jan et al. [44] used machines such as leg press and leg extension/flexion, finding improvements in knee OA symptoms and muscle strength.

Regarding cardiorespiratory exercise training, the included studies mainly used cycling as a modality, and treatment duration ranged from six to 12 weeks. Golightly et al. [49] and Smith-Ryan et al. [31] found benefits in knee symptoms and cardiorespiratory fitness with cycling, as well as Keogh et al. [50], who found improvements in health-related QoL and physical function, and Mangione et al. [56] who found benefits in physical function, overall pain and aerobic capacity. In a recent review, Zeng et al. [23] stated that low-intensity aerobic exercise is better for patients with severe knee OA, while high-intensity aerobic exercise is more suitable for patients with mild knee OA. In contrast, for mild knee OA patients with chronic diseases, HIIT was found to be

better, so it might be advocated that physicians should choose the most appropriate treatment basing on each single patient's health status.

Strengths and limitations

A strength of this narrative review is the use of the CERT tool [48], which provides a systematic and clear display of all relevant exercise components, which supports the reproducibility of exercise modalities, and thus patient outcomes. CERT can be used in all types of exercise interventions, and has a good inter-rater agreement in musculoskeletal exercise interventions [70]. The main limitation of this review is the small number of relevant studies found in the scientific literature about the effects of HIIT for knee OA. Furthermore, in the included studies there was a great heterogeneity of exercise programs in terms of modality and duration, making it difficult to compare the effects of the exercise programs. However, both short-term and long-term programs showed that HIIT is a feasible and effective strategy for lowering pain and improving function, with minimal to no adverse events.

Clinical implications

Given the great variety in applicability of the HIIT protocol, the authors recommend adapting the exercise modality to the patient's preferences and available equipment of the physical therapist to maximize patient's motivation and exercise adherence. Moreover, physical therapists should choose together with the patient between cardiorespiratory or resistance training, given the evidence that the application of one of the exercise modalities is superior to a mixed program in patients suffering from knee OA [71].

Future recommendations

Given the promising results of the articles included in this review, more high-quality research should be performed for a further understanding of the beneficial effects of HIIT in patients with knee OA., since there is still too little knowledge about its effectiveness. The evaluation of the effects of a multimodal HIIT program (i.e. resistance training in combination with cardiorespiratory training) [72], patient profiling in order to prescribe a tailored HIIT program [73], and the evaluation of the effects of HIIT on other important outcome measures in knee OA such as depression, inflammation, sleep quality, etc [74], should be considered as topics of interest for future research.

Conclusion

In conclusion, it is possible to state that HIIT showed promising results as a therapeutic exercise for patients with knee OA. However, the actual quality of evidence remains very low, and further high evidence studies (such as RCTs) are needed to confirm the promising outcomes reported in this review.

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References

1. Johnson VL, Hunter DJ. The epidemiology of osteoarthritis. *Best Pract Res Clin Rheumatol.* 2014 Feb;28(1):5–15.
2. Neogi T, Zhang Y. Epidemiology of osteoarthritis. *Rheum Dis Clin North Am.* 2013 Feb;39(1):1–19.

3. Murray CJL, Vos T, Lozano R, Naghavi M, Flaxman AD, Michaud C, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet Lond Engl*. 2012 Dec 15;380(9859):2197-223.
4. Woolf AD, Pfleger B. Burden of major musculoskeletal conditions. *Bull World Health Organ*. 2003;81(9):646-56.
5. Vos T, Flaxman AD, Naghavi M, Lozano R, Michaud C, Ezzati M, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet Lond Engl*. 2012 Dec 15;380(9859):2163-96.
6. Cui A, Li H, Wang D, Zhong J, Chen Y, Lu H. Global, regional prevalence, incidence and risk factors of knee osteoarthritis in population-based studies. *EClinicalMedicine*. 2020 Dec;29-30:100587.
7. Aamot IL, Karlsen T, Dalen H, Støylen A. Long-term Exercise Adherence After High-intensity Interval Training in Cardiac Rehabilitation: A Randomized Study. *Physiother Res Int*. 2016;21(1):54-64.
8. Gibala MJ. High-intensity Interval Training: A Time-efficient Strategy for Health Promotion? *Curr Sports Med Rep*. 2007 Aug;6(4):211-3.
9. Fransen M, McConnell S, Harmer AR, Van der Esch M, Simic M, Bennell KL. Exercise for osteoarthritis of the knee. *Cochrane Database Syst Rev*. 2015 Jan 9;1:CD004376.
10. Nelson AE, Allen KD, Golightly YM, Goode AP, Jordan JM. A systematic review of recommendations and guidelines for the management of osteoarthritis: The chronic osteoarthritis management initiative of the U.S. bone and joint initiative. *Semin Arthritis Rheum*. 2014 Jun;43(6):701-12.
11. Wisløff U, Støylen A, Loennechen JP, Bruvold M, Rognum Ø, Haram PM, et al. Superior cardiovascular effect of aerobic interval training versus moderate continuous training in heart failure patients: a randomized study. *Circulation*. 2007 Jun 19;115(24):3086-94.
12. Persoon S, Kersten MJ, ChinAPaw MJ, Buffart LM, Burghout H, Schep G, et al. Design of the EXercise Intervention after Stem cell Transplantation (EXIST) study: a randomized controlled trial to evaluate the effectiveness and cost-effectiveness of an individualized high intensity physical exercise program on fitness and fatigue in patients with multiple myeloma or (non-) Hodgkin's lymphoma treated with high dose chemotherapy and autologous stem cell transplantation. *BMC Cancer*. 2010 Dec 6;10(1):671.
13. Knowles MA, Hurst CD. Molecular biology of bladder cancer: new insights into pathogenesis and clinical diversity. *Nat Rev Cancer*. 2015 Jan;15(1):25-41.
14. Bressel E, Wing JE, Miller AI, Dolny DG. High-Intensity Interval Training on an Aquatic Treadmill in Adults With Osteoarthritis: Effect on Pain, Balance, Function, and Mobility. *J Strength Cond Res*. 2014 Aug;28(8):2088-96.
15. Fransen M, McConnell S. Exercise for osteoarthritis of the knee. *Cochrane Database Syst Rev*. 2008 Oct 8;(4):CD004376.
16. Farr JN, Going SB, Lohman TG, Rankin L, Kastle S, Cornett M, et al. Physical activity levels in patients with early knee osteoarthritis measured by accelerometry. *Arthritis Rheum*. 2008 Sep 15;59(9):1229-36.
17. Wallis JA, Webster KE, Levinger P, Taylor NF. What proportion of people with hip and knee osteoarthritis meet physical activity guidelines? A systematic review and meta-analysis. *Osteoarthritis Cartilage*. 2013 Nov;21(11):1648-59.
18. Aglamış B, Toraman NF, Yaman H. Change of quality of life due to exercise training in knee osteoarthritis: SF-36 and WOMAC. *J Back Musculoskelet Rehabil*. 2009;22(1):43-5, 47-8, 46.
19. Tucker JM, Welk GJ, Beyler NK. Physical Activity in U.S. Adults: Compliance with the Physical Activity Guidelines for Americans. *Am J Prev Med*. 2011 Apr 1;40(4):454-61.
20. Kolasinski SL, Neogi T, Hochberg MC, Oatis C, Guyatt G, Block J, et al. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Management of Osteoarthritis of the Hand, Hip, and Knee. *Arthritis Care Res*. 2020 Feb;72(2):149-62.
21. Fransen M, McConnell S. Land-based exercise for osteoarthritis of the knee: a metaanalysis of randomized controlled trials. *J Rheumatol*. 2009 Jun;36(6):1109-17.
22. Golightly YM, Allen KD, Caine DJ. A comprehensive review of the effectiveness of different exercise programs for patients with osteoarthritis. *Phys Sportsmed*. 2012 Nov;40(4):52-65.
23. Zeng CY, Zhang ZR, Tang ZM, Hua FZ. Benefits and Mechanisms of Exercise Training for Knee Osteoarthritis. *Front Physiol*. 2021 Dec 16;12:794062.
24. Hall M, Hinman RS, Wrigley TV, Kasza J, Lim BW, Bennell KL. Knee extensor strength gains mediate symptom improvement in knee osteoarthritis: secondary analysis of a randomised controlled trial. *Osteoarthritis Cartilage*. 2018 Apr;26(4):495-500.
25. Singh NA, Clements KM, Fiatarone MA. A randomized controlled trial of progressive resistance training in depressed elders. *J Gerontol A Biol Sci Med Sci*. 1997 Jan;52(1):M27-35.
26. Otterness IG, Eskra JD, Bliven ML, Shay AK, Pelletier JP, Milici AJ. Exercise protects against articular cartilage degeneration in the hamster. *Arthritis Rheum*. 1998 Nov;41(11):2068-76.
27. Van den Hoogen BM, van de Lest CH, van Weeren PR, Lafeber FP, Lopes-Cardozo M, van Golde LM, et al. Loading-induced changes in synovial fluid affect cartilage metabolism. *Br J Rheumatol*. 1998 Jun;37(6):671-6.
28. Ferenczi MA, Bershtitsky SY, Koubassova NA, Kopylova GV, Fernandez M, Narayanan T, et al. Why muscle is an efficient shock absorber. *PLoS One*. 2014;9(1):e85739.
29. Overview | Osteoarthritis in over 16s: diagnosis and management | Guidance | NICE [Internet]. NICE; 2022 [cited 2023 Mar 5]. Available from: <https://www.nice.org.uk/guidance/ng226>

30. Raposo F, Ramos M, Lúcia Cruz A. Effects of exercise on knee osteoarthritis: A systematic review. *Musculoskeletal Care*. 2021 Dec;19(4):399–435.
31. Smith-Ryan AE, Blue MNM, Anderson KC, Hirsch KR, Allen KD, Huebner JL, et al. Metabolic and physiological effects of high intensity interval training in patients with knee osteoarthritis: A pilot and feasibility study. *Osteoarthr Cartil Open*. 2020 Dec 1;2(4):100083.
32. MacInnis MJ, Gibala MJ. Physiological adaptations to interval training and the role of exercise intensity. *J Physiol*. 2017 May 1;595(9):2915–30.
33. Fleg JL. Salutory effects of high-intensity interval training in persons with elevated cardiovascular risk. *F1000Research* [Internet]. 2016 Sep 7 [cited 2021 Jun 16];5. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5017287/>
34. Gibala MJ, Little JP, Macdonald MJ, Hawley JA. Physiological adaptations to low-volume, high-intensity interval training in health and disease. *J Physiol*. 2012 Mar 1;590(5):1077–84.
35. Wen D, Utesch T, Wu J, Robertson S, Liu J, Hu G, et al. Effects of different protocols of high intensity interval training for VO₂max improvements in adults: A meta-analysis of randomised controlled trials. *J Sci Med Sport*. 2019 Aug;22(8):941–7.
36. Botta RM, Palermi S, Tarantino D, Botta RM, Palermi S, Tarantino D. High-intensity interval training for chronic pain conditions: a narrative review. *J Exerc Rehabil*. 2022 Feb 24;18(1):10–9.
37. Smith-Ryan AE, Trexler ET, Wingfield HL, Blue MNM. Effects of high-intensity interval training on cardiometabolic risk factors in overweight/obese women. *J Sports Sci*. 2016 Nov;34(21):2038–46.
38. Smith-Ryan AE, Melvin MN, Wingfield HL. High-intensity interval training: Modulating interval duration in overweight/obese men. *Phys Sportsmed*. 2015 May;43(2):107–13.
39. Helgerud J, Høydal K, Wang E, Karlsen T, Berg P, Bjerkaas M, et al. Aerobic High-Intensity Intervals Improve V_O2max More Than Moderate Training. *Med Sci Sports Exerc*. 2007 Apr;39(4):665–71.
40. Milanović Z, Sporiš G, Weston M. Effectiveness of High-Intensity Interval Training (HIT) and Continuous Endurance Training for VO₂max Improvements: A Systematic Review and Meta-Analysis of Controlled Trials. *Sports Med Auckl NZ*. 2015 Oct;45(10):1469–81.
41. Whyte LJ, Gill JMR, Cathcart AJ. Effect of 2 weeks of sprint interval training on health-related outcomes in sedentary overweight/obese men. *Metabolism*. 2010 Oct;59(10):1421–8.
42. Am K, P H, C E, N S, Fm G. Impact of low-volume, high-intensity interval training on maximal aerobic capacity, health-related quality of life and motivation to exercise in ageing men. *Age Dordr Neth* [Internet]. 2015 [cited 2022 Nov 8];37(2). Available from: <https://pubmed.ncbi.nlm.nih.gov/25773069/>
43. Sharma L, Dunlop DD, Cahue S, Song J, Hayes KW. Quadriceps strength and osteoarthritis progression in malaligned and lax knees. *Ann Intern Med*. 2003 Apr 15;138(8):613–9.
44. Jan MH, Lin JJ, Liau JJ, Lin YF, Lin DH. Investigation of clinical effects of high- and low-resistance training for patients with knee osteoarthritis: a randomized controlled trial. *Phys Ther*. 2008 Apr;88(4):427–36.
45. King LK, Birmingham TB, Kean CO, Jones IC, Bryant DM, Giffin JR. Resistance training for medial compartment knee osteoarthritis and malalignment. *Med Sci Sports Exerc*. 2008 Aug;40(8):1376–84.
46. Hurkmans E, van der Giesen FJ, Vliet Vlieland TP, Schoones J, Van den Ende ECHM. Dynamic exercise programs (aerobic capacity and/or muscle strength training) in patients with rheumatoid arthritis. *Cochrane Database Syst Rev*. 2009 Oct 7;(4):CD006853.
47. Baker KR, Nelson ME, Felson DT, Layne JE, Sarno R, Roubenoff R. The efficacy of home based progressive strength training in older adults with knee osteoarthritis: a randomized controlled trial. *J Rheumatol*. 2001 Jul;28(7):1655–65.
48. Slade SC, Dionne CE, Underwood M, Buchbinder R. Consensus on Exercise Reporting Template (CERT): Explanation and Elaboration Statement. *Br J Sports Med*. 2016 Dec;50(23):1428–37.
49. Golightly YM, Smith-Ryan AE, Blue MNM, Alvarez C, Allen KD, Nelson AE. High-Intensity Interval Training for Knee Osteoarthritis: A Pilot Study. *ACR Open Rheumatol*. 2021 Oct;3(10):723–32.
50. Keogh JW, Grigg J, Vertullo CJ. Is high-intensity interval cycling feasible and more beneficial than continuous cycling for knee osteoarthritic patients? Results of a randomised control feasibility trial. *PeerJ*. 2018;6:e4738.
51. Alkatan M, Baker JR, Machin DR, Park W, Akkari AS, Pasha EP, et al. Improved Function and Reduced Pain after Swimming and Cycling Training in Patients with Osteoarthritis. *J Rheumatol*. 2016 Mar 1;43(3):666–72.
52. Rewald S, Mesters I, Emans PJ, Arts JJC, Lenssen AF, de Bie RA. Aquatic circuit training including aqua-cycling in patients with knee osteoarthritis: A feasibility study. *J Rehabil Med*. 2015 Apr;47(4):376–81.
53. Salacinski AJ, Krohn K, Lewis SF, Holland ML, Ireland K, Marchetti G. The Effects of Group Cycling on Gait and Pain-Related Disability in Individuals With Mild-to-Moderate Knee Osteoarthritis: A Randomized Controlled Trial. *J Orthop Sports Phys Ther*. 2012 Dec;42(12):985–95.
54. de Zwart AH, Dekker J, Roorda LD, van der Esch M, Lips P, van Schoor NM, et al. High-intensity versus low-intensity resistance training in patients with knee osteoarthritis: A randomized controlled trial. *Clin Rehabil*. 2022 Jul;36(7):952–67.
55. Foroughi N, Smith RM, Lange AK, Singh MAF, Vanwanseele B. Progressive resistance training and dynamic alignment in osteoarthritis: A single-blind randomised controlled trial. *Clin Biomech Bristol Avon*. 2011 Jan;26(1):71–7.
56. Mangione KK, McCully K, Gloviak A, Lefebvre I, Hofmann M, Craik R. The effects of high-intensity and low-intensity cycle ergometry in older adults with knee osteoarthritis. *J Gerontol A Biol Sci Med Sci*. 1999 Apr;54(4):M184–190.
57. Thorstensson CA, Roos EM, Petersson IF, Ekdahl C. Six-week high-intensity exercise program for middle-aged patients with knee osteoarthritis: a randomized controlled trial [ISRCTN20244858]. *BMC Musculoskelet Disord*. 2005 May 30;6:27.

58. Waller B, Munukka M, Rantalainen T, Lammontausta E, Nieminen MT, Kiviranta I, et al. Effects of high intensity resistance aquatic training on body composition and walking speed in women with mild knee osteoarthritis: a 4-month RCT with 12-month follow-up. *Osteoarthritis Cartilage*. 2017 Aug;25(8):1238–46.
59. Calatayud J, Casaña J, Ezzatvar Y, Jakobsen MD, Sundstrup E, Andersen LL. High-intensity preoperative training improves physical and functional recovery in the early post-operative periods after total knee arthroplasty: a randomized controlled trial. *Knee Surg Sports Traumatol Arthrosc Off J ESSKA*. 2017 Sep;25(9):2864–72.
60. Messier SP, Mihalko SL, Beavers DP, Nicklas BJ, DeVita P, Carr JJ, et al. Effect of High-Intensity Strength Training on Knee Pain and Knee Joint Compressive Forces Among Adults With Knee Osteoarthritis: The START Randomized Clinical Trial. *JAMA*. 2021 Feb 16;325(7):646–57.
61. Sveaas SH, Bilberg A, Berg IJ, Provan SA, Rollefstad S, Semb AG, et al. High intensity exercise for 3 months reduces disease activity in axial spondyloarthritis (axSpA): a multicentre randomised trial of 100 patients. *Br J Sports Med*. 2020 Mar;54(5):292–7.
62. Verbrugghe J, Agten A, Stevens S, Hansen D, Demoulin C, O Eijnde B, et al. Exercise Intensity Matters in Chronic Nonspecific Low Back Pain Rehabilitation. *Med Sci Sports Exerc*. 2019 Dec;51(12):2434–42.
63. Verbrugghe J, Agten A, Stevens S, Hansen D, Demoulin C, Eijnde BO, et al. High Intensity Training to Treat Chronic Nonspecific Low Back Pain: Effectiveness of Various Exercise Modes. *J Clin Med*. 2020 Aug;9(8):2401.
64. Agten A, Verbrugghe J, Stevens S, Eijnde BO, Timmermans A, Vandenabeele F. High Intensity Training Increases Muscle Area Occupied by Type II Muscle Fibers of the Multifidus Muscle in Persons with Non-Specific Chronic Low Back Pain: A Pilot Trial. *Appl Sci*. 2021 Jan;11(8):3306.
65. Verbrugghe J, Hansen D, Demoulin C, Verbunt J, Roussel NA, Timmermans A. High Intensity Training Is an Effective Modality to Improve Long-Term Disability and Exercise Capacity in Chronic Nonspecific Low Back Pain: A Randomized Controlled Trial. *Int J Environ Res Public Health*. 2021 Oct 14;18(20):10779.
66. Kroll HR. Exercise therapy for chronic pain. *Phys Med Rehabil Clin N Am*. 2015 May;26(2):263–81.
67. Smith BE, Hendrick P, Bateman M, Holden S, Littlewood C, Smith TO, et al. Musculoskeletal pain and exercise-challenging existing paradigms and introducing new. *Br J Sports Med*. 2019 Jul;53(14):907–12.
68. Beckwée D, Vaes P, Cnudde M, Swinnen E, Bautmans I. Osteoarthritis of the knee: why does exercise work? A qualitative study of the literature. *Ageing Res Rev*. 2013 Jan;12(1):226–36.
69. Runhaar J, Luijsterburg P, Dekker J, Bierma-Zeinstra SMA. Identifying potential working mechanisms behind the positive effects of exercise therapy on pain and function in osteoarthritis; a systematic review. *Osteoarthritis Cartilage*. 2015 Jul;23(7):1071–82.
70. Slade SC, Finnegan S, Dionne CE, Underwood M, Buchbinder R. The Consensus on Exercise Reporting Template (CERT) applied to exercise interventions in musculoskeletal trials demonstrated good rater agreement and incomplete reporting. *J Clin Epidemiol*. 2018 Nov;103:120–30.
71. Goh SL, Persson MSM, Stocks J, Hou Y, Welton NJ, Lin J, et al. Relative Efficacy of Different Exercises for Pain, Function, Performance and Quality of Life in Knee and Hip Osteoarthritis: Systematic Review and Network Meta-Analysis. *Sports Med Auckl NZ*. 2019 May;49(5):743–61.
72. Sharp T, Grandou C, Coutts AJ, Wallace L. The Effects of High-Intensity Multimodal Training in Apparently Healthy Populations: A Systematic Review. *Sports Med - Open*. 2022 Mar 29;8(1):43.
73. Edwards RR, Dworkin RH, Turk DC, Angst MS, Dionne R, Freeman R, et al. Patient phenotyping in clinical trials of chronic pain treatments: IMMPACT recommendations. *Pain*. 2016 Sep;157(9):1851–71.
74. Aguiar GC, Do Nascimento MR, De Miranda AS, Rocha NP, Teixeira AL, Scalzo PL. Effects of an exercise therapy protocol on inflammatory markers, perception of pain, and physical performance in individuals with knee osteoarthritis. *Rheumatol Int*. 2015 Mar;35(3):525–31.