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Meta-Analysis

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The Effect of High-intensity Interval Training vs Moderate-intensity Continuous Training on Liver Fat: A Systematic Review and Meta-Analysis

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Abbreviations: ^{1}H-MRS, proton magnetic resonance spectroscopy; CI, confidence interval; CON, control; GRADE, grading of recommendations, assessment, development, and evaluation; HIIT, high-intensity interval training; MD, mean difference; MICT, moderate-intensity continuous training; MRI, magnetic resonance imaging; NAFLD, nonalcoholic fatty liver disease; SD, standard deviation.

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Abstract

Context: Non-alcoholic fatty liver disease, characterized by excess fat accumulation in the liver, is considered the hepatic manifestation of metabolic syndrome. Recent findings have shown that high-intensity interval training (HIIT) can reduce liver fat but it is unclear whether this form of exercise is superior to traditional moderate-intensity continuous training (MICT).

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Objective: The aim of this systematic review was to determine the effect of HIIT vs MICT on liver fat in adults. A secondary aim was to investigate the interaction between total weekly exercise volume and exercise-related energy expenditure and change in liver fat.

Methods: Relevant databases were searched up to December 2020 for randomized trials, comparing HIIT to control, MICT to control, or HIIT to MICT. Studies were excluded if they did not implement 2 or more weeks' intervention or assess liver fat using magnetic resonance-based techniques. Weighted mean differences and 95% CIs were calculated. Regression analyses were undertaken to determine the interaction between weekly exercise volume in minutes and kilocalories (kcal) with change in liver fat content.

Results: Of the 28 268 studies screened, 19 were included involving 745 participants. HIIT and MICT both elicited moderate reductions in liver fat content when compared to control (HIIT: –2.85%, 95% CI, –4.86 to –0.84, $P = .005$, $I^2 = 0\%$, n = 114, low-certainty evidence; MICT: –3.14%, 95% CI, –4.45 to –1.82, $P < .001$, $I^2 = 5.2\%$, n = 533, moderate-certainty evidence). There was no difference between HIIT and MICT (–0.34%, 95% CI, –2.20 to 1.52, $P = .721$, $I^2 = 0\%$, n = 177, moderate-certainty evidence). Neither total exercise volume in minutes ($\beta = .0002$, SE = 0.0017, $Z = 0.13$, $P = .89$) nor exercise-related energy expenditure in kcal ($\beta = .0003$, SE = 0.0002, $Z = 1.21$, $P = .23$) were related to changes in liver fat content.

Conclusion: HIIT elicits comparable improvements in liver fat to MICT despite often requiring less energy and time commitment. Further studies should be undertaken to assess the relative importance of aerobic exercise prescription variables, such as intensity, on liver fat.

Key Words: physical activity, aerobic exercise, HIIT, MICT, obesity, nonalcoholic fatty liver disease

Obesity poses a unique threat to health as it is an independent risk factor for the development of conditions such as heart disease, type 2 diabetes, and a variety of cancers (1, 2). Interestingly, there are individuals who despite being considered categorically obese, do not present with significant health complications and are considered otherwise "metabolically healthy" (3). Recently, central obesity, characterized by fat accumulation in the abdominal region, has emerged as a greater indicator of cardiometabolic risk than overall obesity (4), with fat accumulation in the liver being closely linked to the development, progression, and severity of various diseases, including type 2 diabetes (5).

Nonalcoholic fatty liver disease (NAFLD) is one of the most prevalent liver diseases in the world, affecting approximately 20% to 30% of the population (6). Characterized as excess fat accumulation in the liver, NAFLD increases the rates of de novo lipogenesis and gluconeogenesis. If untreated, this eventually overwhelms the capacity of the mitochondria in myocytes and hepatocytes to metabolize nutrients, thus posing an increased threat to individuals with already compromised metabolic health such as those with type 2 diabetes (7).

Owing to the lack of effective therapies, lifestyle interventions targeting weight loss continue to be the primary approach for the management of NAFLD (8). However, meaningful weight loss and maintenance of weight loss is rarely achieved (9). As a result efficacious therapies that are weight loss–independent continue to be explored. Previous systematic reviews have highlighted the utility of aerobic exercise as a therapy for NAFLD, for which benefits are often incurred in the absence of significant weight loss (10-12). While exercise interventions can incorporate aerobic or resistance components, aerobic interventions have been shown to elicit greater reductions in liver fat when compared to resistance training (12). However, these reviews often incorporate exercise interventions varying in modality, intensity, and volume, and as a result, optimal aerobic exercise prescriptions for NAFLD remain elusive.

A recent evidence summary by the European Association for the Study of Obesity stated that there is a high-level of evidence supporting the efficacy of aerobic, resistance, and high-intensity interval training (HIIT) for liver fat reduction, yet the summary did not provide specific exercise recommendations (13). Due to the lack of condition-specific exercise recommendations, individuals with NAFLD may be provided exercise prescriptions based on generic recommendations that can include large volumes of exercise. For example, the World Health Organization recommends that adults should aim to achieve a minimum of 150 to 300 minutes of moderate-intensity exercise per week or 75 to 150 minutes of vigorous-intensity exercise per week (14). However, exercise at these volumes may be unnecessarily time burdensome as recent reports have shown that cardiometabolic benefits, including liver fat reduction, can be achieved with significantly less exercise training time by incorporating variations of aerobic exercise such as HIIT (15, 16). While available data suggest HIIT may be effective for reducing liver fat, it is unclear whether this form of training is superior to traditional aerobic exercise involving moderate-intensity continuous training (MICT). Similarly, it is also unclear as to whether an optimal aerobic exercise prescription exists and if so, which prescription variables (eg, time, intensity, volume) contribute to its effectiveness. Therefore, the primary aim of this systematic review and meta-analysis was to determine whether aerobic exercise interventions involving MICT are superior to HIIT for liver fat reduction. A secondary aim was to determine whether exercise prescriptions conforming to current exercise guidelines are more effective than those that do not. The third aim was to determine the relative importance of total weekly exercise volume and energy expenditure in predicting liver fat reduction.

Materials and Methods

This systematic review was prospectively registered on the Prospero International Prospective Register of Systematic Reviews (CRD42021240061) and conforms to the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (17).

Search

An online literature search was performed by one reviewer (A.S.) in CINAHL (EBSCO Host), Embase (Ovid), Medline (Ovid), Scopus, and SPORTDiscus (EBSCO Host) from the earliest record up to December 2020. Search terms included key words and Medical Subject Headings (MeSH) to find literature involving exercise and liver fat. Specifically, the database searches were conducted using the following terms: (exercise OR HIIT OR high-intensity interval* OR high intensity interval* OR aerobic interval* OR HIT OR aerobic exercise OR endurance exercise OR aerobic training OR endurance training OR cardio training OR physical endurance OR physical exertion OR moderate intensity continuous training OR MICT OR sprint interval*) AND (liver fat OR intrahepatic* OR non-alcoholic fatty liver disease OR NAFLD OR fatty liver OR hepatic steatosis OR hepatic OR liver OR steatohepatitis OR non-alcoholic steatohepatitis OR NASH OR aminotransferase OR AST OR ALT).

Where possible, searches were limited to humans. All articles related to the search terms from each database were exported to a central database, where studies were screened against the inclusion and exclusion criteria. Randomized trials were included, whereas nonrandomized trials, and cross-sectional studies were excluded. Studies were excluded if not published in the English language. Studies were also excluded if they were book sections, theses, film/broadcast, opinion articles, observational studies, reviews, and conference presentation abstracts.

Interventions

Studies incorporating aerobic exercise training interventions of moderate or greater intensity and lasting 2 or more weeks were included. Studies involving sprint interval training (> 100 maximal oxygen consumption, or equivalent) were excluded. Studies involving concurrent resistance training, diet, or drug therapy with aerobic training were excluded. Studies involving high-intensity interval training and/or moderate-intensity continuous training were included in the review if they were compared to each other or individually compared to a control (CON) group.

Training and Intensity Classification

HIIT is characterized by single or repeated bouts of high-intensity aerobic exercise interspersed with active or passive rest periods (18). Studies that involved intermittent exercise at intensities ranging from 80% to 100% maximal/peak heart rate or maximal/peak oxygen consumption (or equivalent) were classified as HIIT. Studies incorporating sprint interval training involving “all-out” efforts were not included in this review because of the large nonoxidative energy contributions to this form of exercise training (18).

MICT is often referred to as “traditional” aerobic exercise training, during which aerobic exercise is performed continuously at a steady state for a set duration (typically 20-60 min) (19). Studies that involved continuous exercise at an intensity of 45% or greater but less than 80% maximal/peak heart rate or maximal/peak oxygen uptake (or equivalent) were classified as MICT.

Participants

Studies involving adult human content (aged ≥ 18 years) were included. Studies involving participants who consumed excessive amounts of alcohol or had alcoholic fatty liver disease were excluded.

Outcome Measures

Studies were included if they quantified liver fat content via proton magnetic resonance spectroscopy (^{1}H-MRS) or magnetic resonance imaging (MRI).

Weekly exercise volume was calculated using moderate-intensity and vigorous-intensity physical activity definitions from the American College of Sports Medicine's Guidelines for Exercise Testing and Prescription (20), with 1 minute of vigorous-intensity exercise equal to 2 minutes of moderate-intensity exercise as per the current World Health Organization Guidelines on Physical Activity and Sedentary Behavior (14).

Weekly exercise-related energy expenditure was calculated as the sum of the reported or calculated energy expenditure during exercise sessions per week. Where studies did not report energy expenditure, the average energy expenditure per session was calculated by converting power output, heart rate, or rate of perceived exertion to oxygen consumption using methodology reported elsewhere (21-23).

Selection of Studies

After eliminating duplicates, search results were screened by 2 independent researchers (L.B. and A.A.) against the eligibility criteria, and studies that could not be eliminated by title or abstract were retrieved and assessed for eligibility. Disagreements were resolved by a third researcher (A.S.). Reference lists of included studies were manually searched for potentially eligible papers that were not identified in the database search. On occasions where the identified studies reported insufficient data, attempts were made to contact authors to acquire the required information, and if no response was received, the study was excluded.

Data Extraction

Data from all eligible studies were independently extracted to relevant tables by 2 reviewers (A.S. and L.B.). Graphical data were extracted and converted into numerical format using appropriate software (Graph Data Extractor, Version 0.0.0.1., Dr A. J. Matthews). Where applicable, data were converted to mean and standard deviation (SD) using the RevMan calculator.

Data Analysis

Data are presented as mean or effect size ± SD or 95% confidence interval (CI). Random-effects meta-analyses and meta-regressions were conducted using Comprehensive Meta-Analysis version 3 software (Biostat Inc). Significance was set at P less than .05. Effect sizes were calculated from preintervention to postintervention scores between 2 groups for change in liver fat and expressed as Hedge's g with 95% CIs around the estimated effect size. If postintervention scores were not available, the absolute or relative mean change scores were used to calculate effect sizes. Pooled mean difference in liver fat percentage with 95% CIs was calculated using data from all but one study that reported liver fat in arbitrary units (24).

Univariate meta-regression analyses were performed to examine possible predictors that may have influenced the change in liver fat content. The moderators selected included total estimated or reported weekly energy expenditure and total exercise volume in minutes per week with 1 minute of vigorous-intensity exercise equal to 2 minutes of moderate-intensity exercise.

Statistical heterogeneity between studies was quantified using the Cochran Q and I^2 statistic, both of which provide estimates of the degree of heterogeneity resulting from between-study variance, rather than by chance. Cochran Q with a P value of less than .05 was classified as significant heterogeneity, and I^2 of more than 75% was indicative of considerable heterogeneity, I^2 of 25% to 75% was indicative of moderate heterogeneity, and an I^2 of less than 25% was indicative of low heterogeneity. Publication bias was tested using the Begg and Mazumdar test, with a P value of less than .05 suggesting the presence of bias (25, 26). Where significant bias was detected, a Duval and Tweedie trim-and-fill analysis (27) was conducted to recalculate the pooled effect size after removing any studies that may introduce publication bias (ie, small studies with large effect sizes from the positive side of the funnel plot).

The primary analyses involved pooling data to determine the effect of HIIT vs MICT, HIIT vs CON, and MICT vs CON for change in liver fat content. Further subgroup analyses, determined a priori, were undertaken to determine whether exercising at levels below or meeting/exceeding the physical activity guidelines (14) would lead to significant reductions in liver fat when compared to CON. Finally, a regression analysis was undertaken to determine the relationship between change in liver fat content and total weekly exercise volume in minutes and energy expenditure in kcal.

Study Quality Assessment

Study quality was assessed independently by 2 researchers (A.S. and C.B.) using a modified Downs and Black checklist (28). The scale was modified to include criteria for adequate description of controls and whether the exercise sessions were supervised. If an item was unable to be determined, a "no" was given. Scores were compared and disagreements resolved by a third reviewer (S.K.).

Risk of Bias Assessment and Level of Certainty

Studies were independently assessed for bias by 2 reviewers (C.B. and A.A.) using the Cochrane Risk of Bias 2 tool, which is structured into a fixed set of domains of bias, including selection bias, performance bias, detection bias, attrition bias, reporting bias, and other bias (29). Other bias was judged by assessing whether studies incorporated supervised or monitored exercise interventions and whether they reported exercise adherence. The studies are rated across domains on a scale of low, unclear, or high risk of bias. Scores were compared and disagreements resolved by a third reviewer (A.S.). Studies were not excluded based on their bias assessment. The certainty of the evidence was assessed using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) framework (30) by one reviewer (M.A.).

Results

Identification of Studies

The search returned a total of 28 262 studies, with a further 6 studies identified through other sources. After the removal of duplicates and screening based on the eligibility criteria, 19 studies were included (Fig. 1). Of these, 3 studies compared HIIT vs MICT vs CON (15, 31, 32), 4 studies compared HIIT vs MICT (24, 33-35), 2 studies compared HIIT vs CON (36, 37), and the remaining 10 studies compared MICT vs CON (38-47).

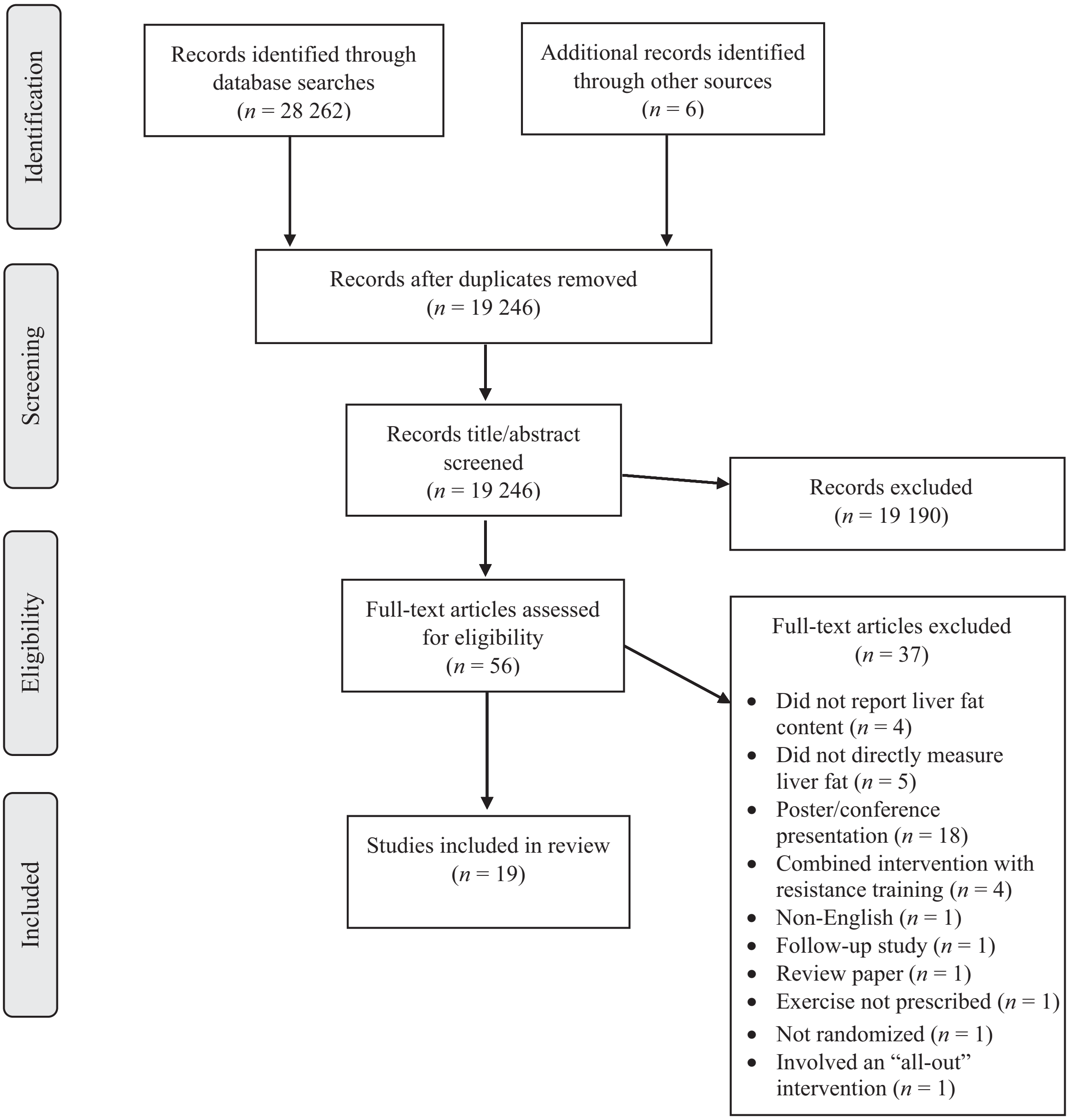


Figure 1. Search strategy and outcome flowchart.

Table 1. Participant characteristics

Study	Group (n)	% Male	Age, y	BMI	Condition
HIIT vs MICT vs CON					
Abdelbasset et al, 2020	HIIT (16)	63	54.4 (5.8)	36.3 (4.5)	Adults with diabetes, obesity, and NAFLD
	MICT (15)	53	54.9 (4.7)	36.7 (3.4)	
	CON (16)	56	55.2 (4.3)	35.9 (5.3)	
Sabag et al, 2020	HIIT (12)	58	56.9 (7.3)	37.5 (5.5)	T2D
	MICT (12)	42	54.8 (8.3)	34.3 (3.8)	
	CON (11)	64	51.9 (4.6)	35.8 (5.6)	
Winn et al, 2018	HIIT (8)	NR	41.0 (14.0)	33.8 (4.1)	Adults with obesity and liver steatosis
	MICT (8)		46.0 (9.0)	40.3 (5.2)	
	CON (5)		51.0 (13.0)	30.3 (1.7)	
HIIT vs MICT					
Oh et al, 2017	HIIT (20)	100	48.6 (8.0)	28.4 (4.0)	Adults with obesity and NAFLD
	MICT (13)	100	48.2 (8.3)	28.8 (4.0)	
Ryan et al, 2020	HIIT (16)	33	32.0 (7.0)	32.4 (2.5)	Adults with obesity
	MICT (15)	43	30.0 (6.0)	34.1 (3.3)	
Sasaki et al, 2014	HIIT (12)	100	NR	24.3 (2.4)	Sedentary males
	MICT (12)	100		23.4 (2.8)	
Taylor et al, 2020	HIIT (19)	79	65.0 (7.0)	27.7 (4.2)	Adults in cardiac rehabilitation
	MICT (23)	83	63.0 (7.0)	28.3 (4.0)	
HIIT vs CON					
Cassidy et al, 2016	HIIT (12)	83	61.0 (9.0)	31.0 (5.0)	T2D
	CON (11)	73	59.0 (9.0)	32.0 (6.0)	
Hallsworth et al, 2015	HIIT (11)	NR	54.0 (10.0)	31.0 (4.0)	NAFLD
	CON (12)		52.0 (12.0)	31.0 (5.0)	
MICT vs CON					
Cheng et al, 2017	MICT (29)	21	59.0 (4.4)	27.3 (3.6)	NAFLD
	CON (29)	24	60.0 (3.4)	27.1 (2.9)	
Cuthbertson et al, 2016	MICT (30)	77	50.0 (16.8)	30.7 (5.4)	Adults with obesity and NAFLD
	CON (20)	80	52.0 (14.8)	29.7 (6.6)	
Finucane et al, 2010	MICT (50)	56	71.4 (NR)	27.4 (4.9)	Healthy older adults
	CON (50)			26.9 (3.6)	
Johnson et al, 2009	MICT (12)	65	49.1 (8.0)	32.2 (2.8)	Sedentary adults with obesity
	CON (7)		47.3 (9.5)	31.1 (2.9)	
Keating et al, 2015	MICT (12)	42	45.5 (8.0)	33.9 (3.1)	Inactive adults with overweight/obesity
	CON (12)	25	39.1 (10.0)	32.2 (4.8)	
Pugh et al, 2013	MICT (6)	54	45.0 (5.0)	31.0 (1.9)	NAFLD
	CON (5)		51.0 (3.0)	30.0 (5.7)	
Shojaee-Moradie et al, 2007	MICT (10)	100	47.0 (9.5)	27.6 (1.9)	Sedentary adults with overweight.
	CON (7)	100	55.0 (10.6)	27.6 (2.4)	
Sullivan et al, 2012	MICT (12)	33	48.6 (7.6)	37.1 (3.8)	Adults with obesity and NAFLD
	CON (6)	17	47.5 (7.6)	40.0 (5.4)	
Sun et al, 2018	MICT (11)	100	72.0 (5.9)	22.1 (3.1)	Healthy older adults
	CON (11)	100	69.0 (6.7)	23.6 (2.5)	
Zhang et al, 2016	MICT (73)	30	54.4 (7.4)	28.1 (3.3)	Adults with obesity and NAFLD
	CON (74)	38	54.0 (6.8)	28.0 (2.7)	

Data reported as mean ± SD unless stated otherwise.

Abbreviations: BMI, body mass index; CON, control; HIIT, high-intensity interval training; MICT, moderate-intensity continuous training; NAFLD, nonalcoholic fatty liver disease; NR, not reported; T2D, type 2 diabetes.

Participant Characteristics

Participant characteristics are detailed in Table 1. Briefly, there were a total of 745 participants, of whom 67% were male with an average (mean ± SD) age of 53 ± 10 years, body mass index of 30.9 ± 4.4, and liver fat content of 11.5 ± 6.2%. Four studies exclusively recruited male participants (24, 33, 44, 46), while 2 studies did not report sex (32, 37). Thirteen studies involved participants with obesity (15, 31-34, 36, 37, 39, 41-43, 45, 47), 5 with overweight (24, 35, 38, 40, 44), and 1 with normal

Table 2. Details of exercise interventions

Study	Group	Mode of intervention	Body mass Δ, kg	Frequency	Exercise session details	Weekly exercise energy expenditure	Converted weekly exercise volume	Intervention duration
	HIIT vs MICT vs CON							
Abdelbasset et al, 2020	HIIT	Cycle ergometer	NR	3/7	Warm up: 5 min Work: 3 × 4 min at 80%-85% VO_{2max} Interset recovery: 2 min at 50% VO_{2max} Cool down: 5 min Total exercise time: 26 min Estimated average energy expenditure: 140 kcal	420 kcal	84 min	8 wk
	MICT	Cycle ergometer	NR	3/7	Warm up: 5 min Work: 40-50 min at 60%-70% HR_{max} Cool down: 5 min Average exercise time: 45 min Estimated average energy expenditure: 344 kcal	1032 kcal	135 min	
	CON	NA	NR	NA	NA			
Sabag et al, 2020	HIIT	Cycle ergometer	–0.6	3/7	Warm up: 10 min at 50% VO_{2peak} Work: 1 × 4 min at 90% VO_{2peak} Cool down: 5 min 50% VO_{2peak} Total exercise time: 19 min Estimated energy expenditure: 128 kcal	384 kcal	69 min	12 wk
	MICT	Cycle ergometer	–0.3	3/7	Warm up: 5 min at 50% VO_{2peak} Work: 45 min at 60% VO_{2peak} Cool down: 5 min at 50% VO_{2peak} Total exercise time: 55 min Estimated energy expenditure: 440 kcal	1320 kcal	165 min	
	PLA	Various	1.5	0.5/7	Warm up: 5 min at 50% VO_{2peak} Work: fit ball exercise and upper and lower body stretches Cool down: 5 min at 50% VO_{2peak} Total exercise time: 25 min			
Winn et al, 2018	HIIT	Treadmill	– 0.3	4/7	Warm up: NR Work: repetitions of 4 min at 80% VO_{2peak} until 400 kcal/session achieved Interset recovery: 3 min at 50% VO_{2peak} Cool down: NR Average exercise time: ~ 55 min Reported energy expenditure: 396 kcal	1600 kcal	264 min	4 wk
	MICT	Treadmill	–1.0	4/7	Warm up: NR	1600 kcal	232 min	

Table 2. Continued

Study	Group	Mode of intervention	Body mass Δ, kg	Frequency	Exercise session details	Weekly exercise energy expenditure	Converted weekly exercise volume	Intervention duration
					Work: continuous cycling at 55% VO_{2peak} until 400 kcal/session achieved Cool down: NR 55% VO_{2peak} Average exercise time: ~ 58 min Reported energy expenditure: 407 kcal			
	CON	NA	−0.3	NA	NR			
	HIIT vs MICT							
Oh et al, 2017	HIIT	Cycle ergometer	0.2	3/7	Warm up: NR Work: 3 × 3 min at 80%-85% VO_{2max} Interset recovery: 2 min at 50% VO_{2max} Cool down: NR Total exercise time: 15 min Reported energy expenditure: 180 kcal	540 kcal	72 min	12 wk
	MICT	Cycle ergometer	−0.5	3/7	Warm up: NR Work: 40 min at 60%-65% VO_{2max} Cool down: NR Total exercise time: 40 min Reported energy expenditure: 360 kcal	1080 kcal	120 min	
Ryan et al, 2020	HIIT	Choice of aerobic modalities including running, cycling, rowing, or elliptical	NR	4/7	Warm up: 3 min at ~ 65% HR_{max} Work: 10 × 1 min at 90% HR_{max} Interset rest: 1-min recovery at 50% HR_{max} Cool down: 3 min at ~ 65% HR_{max} Total exercise time: 26 min Reported energy expenditure: 150 kcal	600 kcal	140 min	12 wk
	MICT	Choice of aerobic modalities including running, cycling, rowing, or elliptical	NR	4/7	Warm up: NR Work: 45 min at 70% HR_{max} Cool down: NR Total exercise time: 45 min Reported energy expenditure: 250 kcal	1000 kcal	180 min	
Sasaki et al, 2014	HIIT	Cycle ergometer	NR	3/7	Warm up: NR Work: 10 × 1 min at 85% VO_{2max} Interset rest: 30 s Cool down: NR Total exercise time: 10 min Estimated energy expenditure: 150 kcal	450 kcal	60 min	4 wk

Table 2. Continued

Study	Group	Mode of intervention	Body mass Δ, kg	Frequency	Exercise session details	Weekly exercise energy expenditure	Converted weekly exercise volume	Intervention duration
	MICT	Cycle ergometer	NR	3/7	Warm up: NR Work: 22 min at 45% VO_{2max} Cool down: NR Total exercise time: 22 min Estimated energy expenditure: 150 kcal	450 kcal	66 min	
Taylor et al, 2020	HIIT	Various aerobic exercise equipment	–1.0	3/7	Warm up: 4 min Work: 4 × 4 min at 85%-95% HR_{peak} Interset recovery: 3 min at 65%-75% HR_{peak} Cool down: 3 min Total exercise time: 24 min Reported energy expenditure: 250 kcal	750 kcal	123 min	12 wk
	MICT	Various aerobic exercise equipment	–1.8	3/7	Warm up: 3-min warm up Work: 34 min at 65%-75% HR_{peak} Cool down: 3 min Total exercise time: 34 min Reported energy expenditure: 250 kcal	750 kcal	102 min	
	HIIT vs CON							
Cassidy et al, 2016	HIIT	Cycle ergometer	–1.0	3/7	Warm up: 5 min at RPE 9-13 Work: 5×2-4 min at 15-18 RPE Interset rest: 3 min Cool down: NR Average exercise time: 20 min Estimated energy expenditure: 136 kcal	408 kcal	102 min	12 wk
	CON	NA	1.0	NA	NR			
Hallsworth et al, 2015	HIIT	Cycle ergometer	NR	3/7	Warm up: 5 min at RPE 9-13 Work: 5 × 2-4 min at 15-18 RPE Inter-set rest: 3 min Cool down: NR Total exercise time: 20 min Estimated energy expenditure: 136 kcal	408 kcal	102 min	12 wk
	CON	NA	NR	NA	Usual care			
	MICT vs CON							
Cheng et al, 2017	MICT	Various modalities	NR	2-3/7	Warm up: 5 min Work: 30-60 min at 60%-75% VO_{2max} Cool down: 5 min Average exercise time: 45 min Estimated energy expenditure: 166 kcal	415 kcal	225 min	8.6 mo
	CON	NA	NR	NA	Usual care			

Table 2. Continued

Study	Group	Mode of intervention	Body mass Δ, kg	Frequency	Exercise session details	Weekly exercise energy expenditure	Converted weekly exercise volume	Intervention duration
Cuthbertson et al, 2016	MICT	Varied: treadmill, cross-trainer, bike ergometer, rower	–2.5	3-5/7	Warm up: NR Work: up to 30-45 min at 30-60% HRR Cool down: NR Average exercise time: ≤ 38 min Estimated energy expenditure: 191 kcal	764 kcal	114 min	12 wk
	CON	NA	0.2	NA	Usual care			
Finucane et al, 2010	MICT	Cycle ergometer	NR	3/7	Warm up: NR Work: ≤ 60 min at 50%-70% W_{max} Cool down: NR Total exercise time: 60 min Estimated energy expenditure: 387 kcal	1161 kcal	180 min	12 wk
	Con	NA	NR	NA	Usual care			
Johnson et al, 2009	MICT	Cycle ergometer	NR	3/7	Warm up: NR Work: 30-45 min at 50%-70% VO_{2peak} Cool down: NR Average exercise time: 38 min Estimated energy expenditure: 287 kcal	861 kcal	114 min	4 wk
	CON	Stretching	NR	3/7	Warm up: NR Work: 30 min whole-body stretching Cool down: NR Total exercise time: 30 min			
Keating et al, 2015	MICT	Cycle ergometer and walking	NR	4/7	Warm up: NR Work: 45-60 min at 50% VO_{2peak} Cool down: NR Average exercise time: 57 min Estimated energy expenditure: 344 kcal	1376 kcal	228 min	8 wk
	CON	Stretching	NR	3/7	Warm up: NR Work: Stretching, massage, and fit ball program Cool down: NR Total exercise time: NR			
Pugh et al, 2013	MICT	NR	–2.3	3-5/7	Warm up: NR Work: 30-45 min at 30%-60% HRR Cool down: NR Average exercise time: ≤ 38 min Estimated energy expenditure: 210 kcal	840 kcal	152 min	16 wk
	CON	NA	–0.7	NA	Usual care			

Table 2. Continued

Study	Group	Mode of intervention	Body mass Δ, kg	Frequency	Exercise session details	Weekly exercise energy expenditure	Converted weekly exercise volume	Intervention duration
Shojaee-Moradie et al, 2007	MICT	NR	NR	3/7	Warm up: NR Work: 20 min at 60%-85% VO_{2max} Cool down: NR Total exercise time: ≤ 20 min Estimated energy expenditure: 196 kcal	588 kcal	120 min	6 wk
	CON	NR	NR	NA	Usual care			
Sullivan et al, 2012	MICT	Treadmill	NR	5/7	Warm up: NR Work: 30-60 min at 45%-55% of VO_{2peak} Cool down: NR Average exercise time: 45 min Estimated energy expenditure: 264 kcal	1320 kcal	225 min	16 wk
	CON	NA	NR	NA	Usual care			
Sun et al, 2018	MICT	NR	0.3	3/7	Warm up: NR Work: 30-45 min at 60%-75% of VO_{2peak} Cool down: NR Average exercise time: ≤ 39 min Estimated energy expenditure: 200 kcal	600 kcal	234 min	5 wk
	CON	NA	0.5	NA	Usual care			
Zhang et al, 2016	MICT	Walking	–2.6	5/7	Warm up: NR Work: 30 min at 45%-55% of HR_{max} Cool down: NR Total exercise time: 30 min Estimated energy expenditure: 168 kcal	840 kcal	150 min	12 mo
	CON	NA	–1.1	NA	Usual care			

Abbreviations: CON, control; HIIT, high-intensity interval training; HR_{max}, maximal heart rate; HR_{peak}, peak heart rate; HRR, heart rate reserve; kcal, kilocalorie; MICT, moderate-intensity continuous training; NA, not applicable; NR, not reported; PLA, placebo; RPE, rate of perceived exertion; VO_{2max}, maximal oxygen consumption; VO_{2peak}, peak oxygen consumption; W_{max}, maximal power output.

weight (46). The majority of studies involved participants with average liver fat content consistent with a diagnosis of NAFLD (ie, > 5.5%) with the exception of 3 studies (40, 44, 46).

Intervention Characteristics

Intervention characteristics are summarized in Table 2. The intervention duration ranged from 2 to 52 weeks, with 12-week interventions being the most common

Table 3. Effect of aerobic exercise interventions on liver fat

Study	Group (n)	Liver fat assessment technique	Preintervention	Postintervention	Absolute %Δ	Relevant %Δ
HIIT vs MICT vs CON						
Abdelbasset et al, 2020	HIIT (16)	MRI	12.4 (4.5)	10.1 (1.3)	NR	NR
	MICT (15)	MRI	12.9 (4.2)	10.5 (1.5)		
	CON (16)	MRI	11.2 (5.1)	11.1 (5.2)		
Sabag et al, 2020	HIIT (12)	^{1}H-MRS	9.7 (8.3)	8.0 (7.6)	–1.7 (3.8)	NR
	MICT (12)	^{1}H-MRS	9.4 (6.9)	8.6 (7.3)	–0.9 (2.4)	
	CON (11)	^{1}H-MRS	11.8 (7.6)	13.0 (9.0)	1.2 (1.7)	
Winn et al, 2018	HIIT (8)	^{1}H-MRS	18.9 (11.7)	12.5 (13.4)	NR	–37.0 (12.4)
	MICT (8)	^{1}H-MRS	19.6 (9.7)	16.1 (9.6)		–20.1 (6.6)
	CON (5)	^{1}H-MRS	5.8 (4.7)	6.7 (5.9)		17.3(14.5)
HIIT vs MICT						
Oh et al, 2017	HIIT (20)	^{1}H-MRS	NR	NR	–4.9 (8.9)	NR
	MICT (13)	^{1}H-MRS			–0.3 (12.1)	
Ryan et al, 2020	HIIT (16)	MRI	8.7 (7.5)	7.5 (5.4)	NR	NR
	MICT (15)	MRI	10.4 (10.0)	9.0 (7.3)	NR	NR
Sasaki et al, 2014	HIIT (12)	^{1}H-MRS	44.5 (16.3)	46.6 (14.9)	NR	NR
	MICT (12)	^{1}H-MRS	49.9 (21.5)	46.8 (24.9)		
Taylor et al, 2020	HIIT (19)	^{1}H-MRS	7.3 (8.9)	5.1 (7.5)	–2.8 (2.7)	NR
	MICT (23)	^{1}H-MRS	4.8 (4.1)	3.3 (4.3)	–1.4 (2.4)	
HIIT vs CON						
Cassidy et al, 2016	HIIT (12)	^{1}H-MRS	6.9 (6.9)	4.2 (3.6)	NR	NR
	CON (11)	^{1}H-MRS	7.1 (6.8)	7.7 (6.9)		
Hallsworth et al, 2015	HIIT (11)	^{1}H-MRS	10.6 (4.9)	7.8 (2.4)	NR	NR
	CON (12)	^{1}H-MRS	10.3 (4.4)	10.4 (3.9)		
MICT vs CON						
Cheng et al, 2017	MICT (29)	^{1}H-MRS	17.7 (13.1)	12.2 (10.5)	NR	–24.4 (67.0)
	CON (29)	^{1}H-MRS	16.0 (10.5)	18.8 (10.5)		20.9 (69.5)
Cuthbertson et al, 2016	MICT (30)	^{1}H-MRS	19.4 (6.3)	10.1 (15.3)	–9.3 (10.9)	NR
	CON (20)	^{1}H-MRS	16.0 (17.0	14.6 (13.7)	–2.5 (8.4)	
Finucane et al, 2010	MICT (50)	^{1}H-MRS	3.7 (6.2)	2.4 (4.1)	NR	NR
	CON (50)	^{1}H-MRS	3.6 (5.1)	3.5 (8.6)		
Johnson et al, 2009	MICT (12)	^{1}H-MRS	8.6 (8.7)	6.8 (6.6)	NR	NR
	CON (7)	^{1}H-MRS	9.2 (10.1)	9.4 (10.3)		
Keating et al, 2015	MICT (12)	^{1}H-MRS	9.4 (6.9)	6.8 (4.8)	–2.6 (3.5)	NR
	CON (12)	^{1}H-MRS	7.7 (9.0)	8.8 (11.1)	1.1 (2.1)	
Pugh et al, 2013	MICT (6)	^{1}H-MRS	25.1 (27.1)	14.2 (15.1)	–13.0 (6.5)	NR
	CON (5)	^{1}H-MRS	22.4 (11.8)	18.5 (13.1)	–6.5 (5.2)	
Shojaee-Moradie et al, 2007	MICT (10)	^{1}H-MRS	4.0 (16.0)	4.3 (8.1)	NR	NR
	CON (7)	^{1}H-MRS	3.9 (5.0)	5.2 (7.9)		
Sullivan et al, 2012	MICT (12)	^{1}H-MRS	20.4 (13.9)	17.6 (9.4)	NR	NR
	CON (6)	^{1}H-MRS	21.4 (21.8)	23.9 (23.5)		
Sun et al, 2018	MICT (11)	^{1}H-MRS	2.9 (4.3)	2.5 (4.6)	–0.22 (1.37)	NR
	CON (11)	^{1}H-MRS	2.6 (4.3)	2.4 (4.6)	–0.14 (1.24)	
Zhang et al, 2016	MICT (73)	^{1}H-MRS	18.0 (9.9)	NR	–7.2 (6.8)	NR
	CON (74)	^{1}H-MRS	17.5 (11.0)		–2.2 (6.6)	

Data reported as mean ± SD unless stated otherwise.

Abbreviations: CON, control; HIIT, high-intensity interval training; ^{1}H-MRS, proton magnetic resonance spectroscopy; MICT, moderate-intensity continuous training; MRI, magnetic resonance imaging; NR, not reported.

(15, 33-37, 39, 40). The frequency of exercise sessions ranged from 2 to 5 times per week, with most studies implementing a training frequency of 3 times per week (15, 24, 31, 33, 35-37, 40, 41, 44, 46). The intensity of the interventions were reported as percentage of maximal/peak oxygen consumption in 11 studies (15, 24, 31-33, 38, 41, 42, 44-46), percentage of heart rate maximum/reserve in 5 studies (34, 35, 39, 43, 47), rate of perceived exertion in 2 studies (36, 37), and as a percentage of maximum power output in 1 study (40).

Effect of Aerobic Exercise on Liver Fat

The effects of aerobic exercise interventions on liver fat are summarized in Table 3. A total of 20 studies provided sufficient data to enable calculation of effect size and 95% CI. When compared to CON, all aerobic exercise interventions showed an effect size favoring aerobic exercise for change in liver fat, ranging from –0.04 to –0.85.

Study Quality, Risk of Bias, and Certainty of Evidence

The assessment of study quality is summarized in Supplementary Table 1 (48). Quality was assessed as a score out of 23 with a mean score of 18.8 ± 3.13 (minimum 11, maximum 23). All included studies specified their main outcomes, main findings, interventions, variability estimates and statistical tests. Two studies reported absolute change in liver fat but no postintervention scores (33, 47). One study reported liver fat in arbitrary units (24).

The results of the risk of bias assessment are summarized in Fig. 2. Five of 19 studies scored an unclear or high risk of bias on 5 or more items (24, 37, 43, 44, 46), 2 of 19 studies scored an unclear or high risk of bias on 4 or more items (34, 41), and the remaining studies scored an unclear or high risk of bias on 2 or fewer items (Supplementary Table 2) (48). All studies scored a high risk of bias for performance bias, which is expected in exercise trials.

The level of certainty of the results produced are detailed in Table 4. There was a moderate certainty of evidence showing that HIIT probably results in little to no difference in reducing liver fat content when compared to MICT. There was a low certainty of evidence showing that HIIT may reduce liver fat content when compared to CON. There was a moderate level of certainty that MICT probably reduces liver fat content when compared to CON.

Primary Analyses

Effect of high-intensity interval training vs moderate-intensity continuous training on liver fat

The between-group analysis for HIIT vs MICT is summarized in Fig. 3. Seven studies reported sufficient data to determine the pooled effect of HIIT vs MICT (15, 24, 31-35). There was no effect of HIIT when compared to MICT for change in liver fat ($g = -0.05$, 95% CI, –0.32 to 0.22, $P = .702$, $I^2 = 0\%$, n = 201) (Fig. 3). One study reported liver fat in arbitrary units and was excluded from the weighted mean difference analysis of HIIT vs MICT (24), which showed no difference between interventions (MD = –0.34%, 95% CI, –2.20 to 1.52, $P = .721$, $I^2 = 0\%$, n = 177, moderate-certainty evidence)(Fig. 4). Visual appraisal of funnel plots indicated no publication bias.

Effect of high-intensity interval training vs control on liver fat

Five studies reported sufficient data to determine the pooled effect and weighted mean difference of HIIT vs CON for change in liver fat (15, 31, 32, 36, 37). There was a moderate

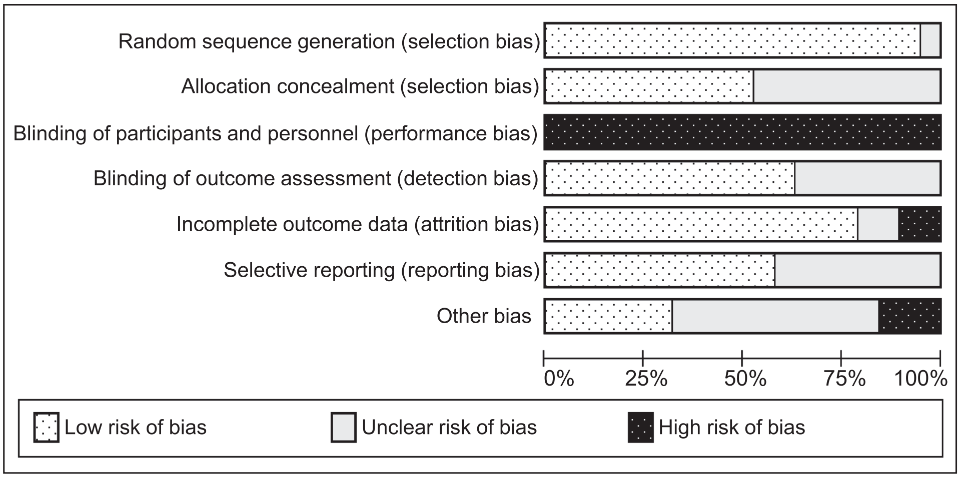


Figure 2. Risk of bias summary.

Table 4. Summary of assessment of certainty of evidence

HIIT compared to MICT for liver fat reduction
Patient or population: adults
Setting: supervised or unsupervised exercise
Intervention: HIIT
Comparison: MICT

Outcomes	**Anticipated absolute effects[a] (95% CI)**		**No. of participants (studies)**	Certainty of evidence (GRADE)	Comments
	Score with MICT	Score with HIIT			
Liver fat assessed via MRI or ^{1}H-MRS	Mean liver fat = 7.71 percent	MD 0.34 percent **lower** (2.2 lower to 1.52 higher)	201 (7 RCTs)	⊕⊕⊕◯ moderate[b]	HIIT probably results in little to no difference in reducing liver fat compared to MICT

HIIT compared to CON for liver fat reduction
Patient or population: adults
Setting: supervised or unsupervised exercise
Intervention: HIIT
Comparison: CON

Outcomes	**Anticipated absolute effects[a](95% CI)**		**No. of participants (studies)**	**Certainty of evidence (GRADE)**	**Comments**
	Score with CON	**Score with HIIT**			
Liver fat assessed via MRI or ^{1}H-MRS	Mean liver fat = 9.78 percent	MD 2.85 percent **lower** (4.86 lower to 0.84 lower)	114 (5 RCTs)	⊕⊕◯◯ low[c,d]	HIIT may result in reduction in liver fat compared to CON

MICT compared to CON for liver fat reduction
Patient or population: adults
Setting: supervised or unsupervised exercise
Intervention: MICT
Comparison: CON

Outcomes	**Anticipated absolute effects[a](95% CI)**		**No. of participants (studies)**	**Certainty of evidence (GRADE)**	**Comments**
	Score with CON	**Score with MICT**			
Liver fat assessed via MRI or ^{1}H-MRS	Mean liver fat = 11.33 percent	MD 3.14 percent **lower** (4.45 lower to 1.82 lower)	533 (13 RCTs)	⊕⊕⊕◯ moderate[e]	MICT probably results in reduction in liver fat compared to CON

High certainty: We are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.

Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

Abbreviations: ^{1}H-MRS, proton magnetic resonance spectroscopy; CON, control; HIIT, high-intensity interval training; GRADE, Grading of Recommendations, Assessment, Development, and Evaluation; MD, mean difference; MICT, moderate-intensity continuous training; MRI, magnetic resonance imaging; RCT, randomized clinical trials.

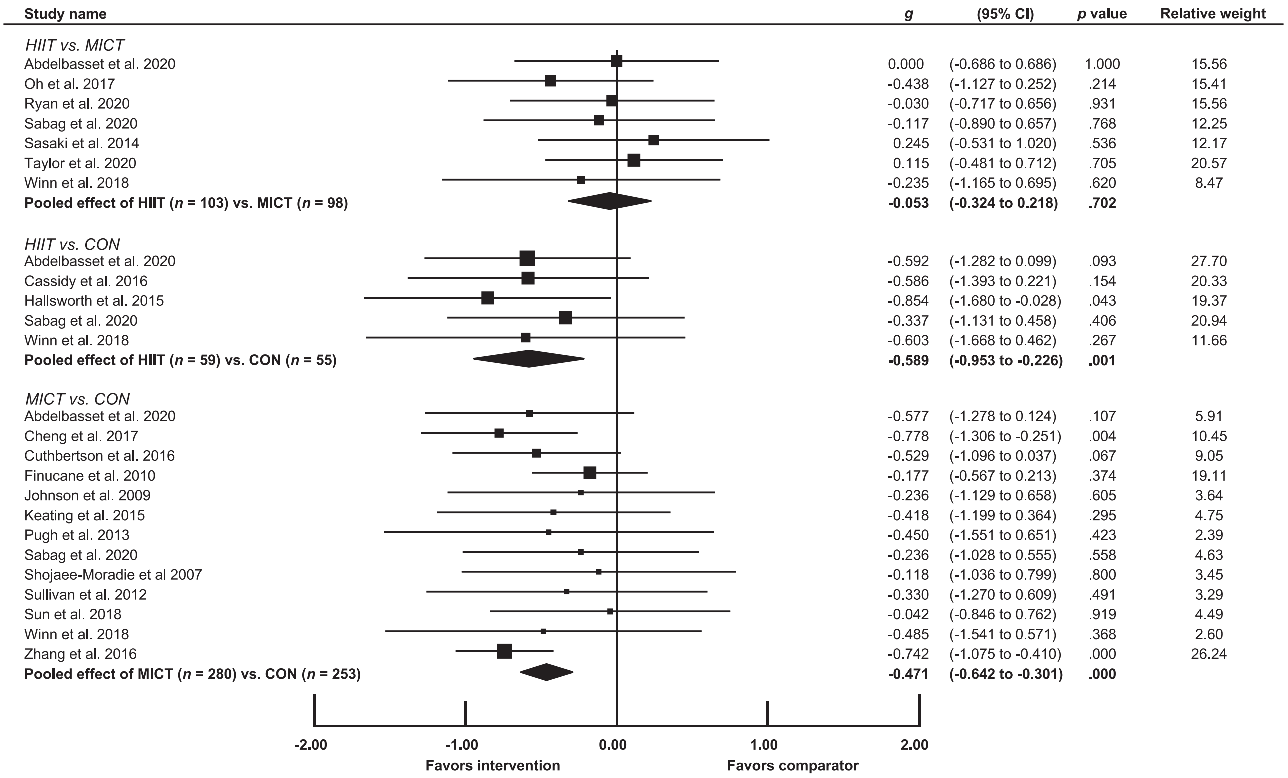
[a] The score in the intervention group (and its 95% CI) is based on the assumed score in the comparison group.

[b] Downgraded one level for serious risk of bias: Two of the 7 studies had an unclear risk of bias for allocation concealment, and 2 had an unclear risk of detection bias.

[c] Downgraded one level for serious risk of bias: Two of the 5 included studies were at unclear risk of bias for selection bias, and 1 was unclear for detection bias.

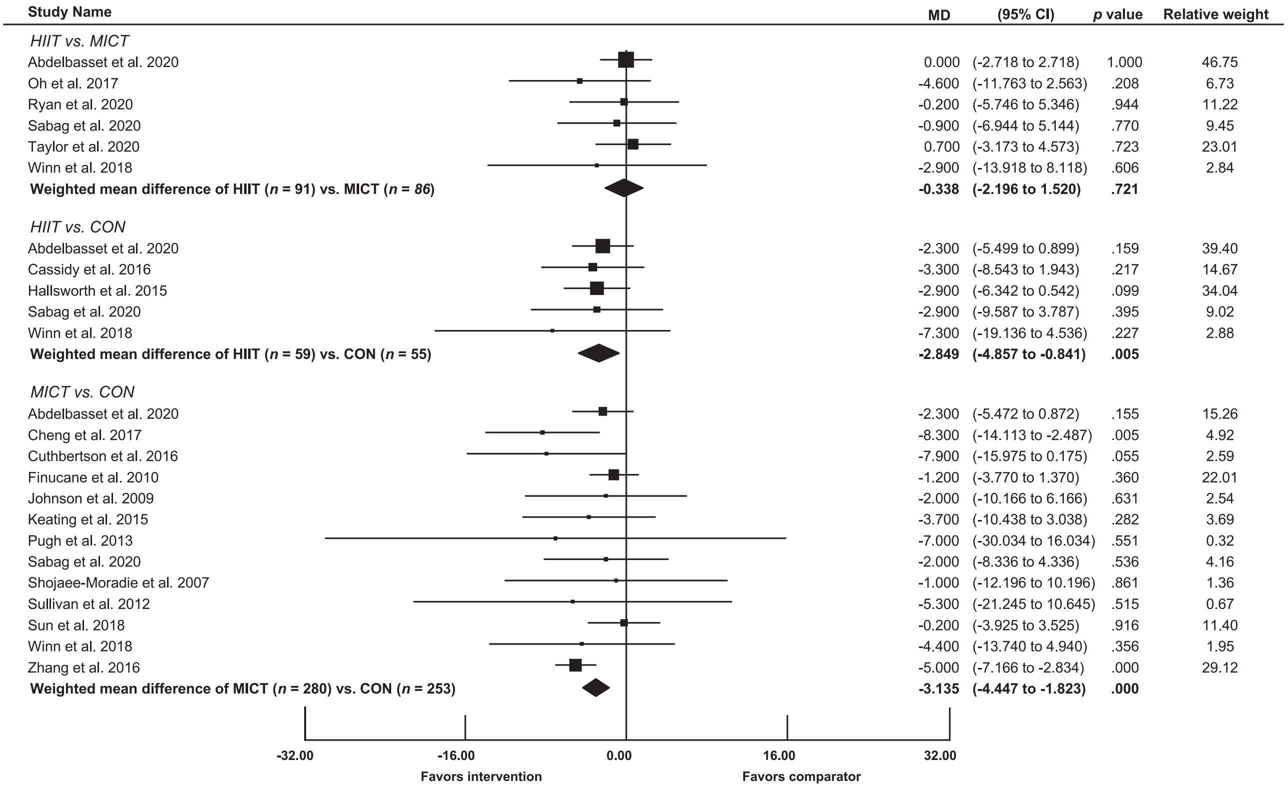
[d] Downgraded one level for serious imprecision: small sample size.

[e] Downgraded one level for serious risk of bias: Six of the included studies had an unclear risk of bias for selection bias, and 3 studies had an unclear risk for detection bias.



Study name	*g*	(95% CI)	*p* value	Relative weight
HIIT vs. MICT				
Abdelbasset et al. 2020	0.000	(-0.686 to 0.686)	1.000	15.56
Oh et al. 2017	-0.438	(-1.127 to 0.252)	.214	15.41
Ryan et al. 2020	-0.030	(-0.717 to 0.656)	.931	15.56
Sabag et al. 2020	-0.117	(-0.890 to 0.657)	.768	12.25
Sasaki et al. 2014	0.245	(-0.531 to 1.020)	.536	12.17
Taylor et al. 2020	0.115	(-0.481 to 0.712)	.705	20.57
Winn et al. 2018	-0.235	(-1.165 to 0.695)	.620	8.47
Pooled effect of HIIT (*n* = 103) vs. MICT (*n* = 98)	**-0.053**	**(-0.324 to 0.218)**	**.702**	
HIIT vs. CON				
Abdelbasset et al. 2020	-0.592	(-1.282 to 0.099)	.093	27.70
Cassidy et al. 2016	-0.586	(-1.393 to 0.221)	.154	20.33
Hallsworth et al. 2015	-0.854	(-1.680 to -0.028)	.043	19.37
Sabag et al. 2020	-0.337	(-1.131 to 0.458)	.406	20.94
Winn et al. 2018	-0.603	(-1.668 to 0.462)	.267	11.66
Pooled effect of HIIT (*n* = 59) vs. CON (*n* = 55)	**-0.589**	**(-0.953 to -0.226)**	**.001**	
MICT vs. CON				
Abdelbasset et al. 2020	-0.577	(-1.278 to 0.124)	.107	5.91
Cheng et al. 2017	-0.778	(-1.306 to -0.251)	.004	10.45
Cuthbertson et al. 2016	-0.529	(-1.096 to 0.037)	.067	9.05
Finucane et al. 2010	-0.177	(-0.567 to 0.213)	.374	19.11
Johnson et al. 2009	-0.236	(-1.129 to 0.658)	.605	3.64
Keating et al. 2015	-0.418	(-1.199 to 0.364)	.295	4.75
Pugh et al. 2013	-0.450	(-1.551 to 0.651)	.423	2.39
Sabag et al. 2020	-0.236	(-1.028 to 0.555)	.558	4.63
Shojaee-Moradie et al 2007	-0.118	(-1.036 to 0.799)	.800	3.45
Sullivan et al. 2012	-0.330	(-1.270 to 0.609)	.491	3.29
Sun et al. 2018	-0.042	(-0.846 to 0.762)	.919	4.49
Winn et al. 2018	-0.485	(-1.541 to 0.571)	.368	2.60
Zhang et al. 2016	-0.742	(-1.075 to -0.410)	.000	26.24
Pooled effect of MICT (*n* = 280) vs. CON (*n* = 253)	**-0.471**	**(-0.642 to -0.301)**	**.000**	

Figure 3. Effect of aerobic exercise modalities on liver fat. Forest plot for effect of moderate-intensity continuous training (MICT) vs high-intensity interval training (HIIT) (n = 201), HIIT vs control (CON) (n = 114), and an MICT vs CON (n = 533) on liver fat. Graph depicts effect size in Hedge's *g* and 95% CI for individual studies and the pooled estimates.



Study Name	MD	(95% CI)	*p* value	Relative weight
HIIT vs. MICT				
Abdelbasset et al. 2020	0.000	(-2.718 to 2.718)	1.000	46.75
Oh et al. 2017	-4.600	(-11.763 to 2.563)	.208	6.73
Ryan et al. 2020	-0.200	(-5.746 to 5.346)	.944	11.22
Sabag et al. 2020	-0.900	(-6.944 to 5.144)	.770	9.45
Taylor et al. 2020	0.700	(-3.173 to 4.573)	.723	23.01
Winn et al. 2018	-2.900	(-13.918 to 8.118)	.606	2.84
Weighted mean difference of HIIT (*n* = 91) vs. MICT (*n* = *86*)	**-0.338**	**(-2.196 to 1.520)**	**.721**	
HIIT vs. CON				
Abdelbasset et al. 2020	-2.300	(-5.499 to 0.899)	.159	39.40
Cassidy et al. 2016	-3.300	(-8.543 to 1.943)	.217	14.67
Hallsworth et al. 2015	-2.900	(-6.342 to 0.542)	.099	34.04
Sabag et al. 2020	-2.900	(-9.587 to 3.787)	.395	9.02
Winn et al. 2018	-7.300	(-19.136 to 4.536)	.227	2.88
Weighted mean difference of HIIT (*n* = 59) vs. CON (*n* = 55)	**-2.849**	**(-4.857 to -0.841)**	**.005**	
MICT vs. CON				
Abdelbasset et al. 2020	-2.300	(-5.472 to 0.872)	.155	15.26
Cheng et al. 2017	-8.300	(-14.113 to -2.487)	.005	4.92
Cuthbertson et al. 2016	-7.900	(-15.975 to 0.175)	.055	2.59
Finucane et al. 2010	-1.200	(-3.770 to 1.370)	.360	22.01
Johnson et al. 2009	-2.000	(-10.166 to 6.166)	.631	2.54
Keating et al. 2015	-3.700	(-10.438 to 3.038)	.282	3.69
Pugh et al. 2013	-7.000	(-30.034 to 16.034)	.551	0.32
Sabag et al. 2020	-2.000	(-8.336 to 4.336)	.536	4.16
Shojaee-Moradie et al. 2007	-1.000	(-12.196 to 10.196)	.861	1.36
Sullivan et al. 2012	-5.300	(-21.245 to 10.645)	.515	0.67
Sun et al. 2018	-0.200	(-3.925 to 3.525)	.916	11.40
Winn et al. 2018	-4.400	(-13.740 to 4.940)	.356	1.95
Zhang et al. 2016	-5.000	(-7.166 to -2.834)	.000	29.12
Weighted mean difference of MICT (*n* = 280) vs. CON (*n* = 253)	**-3.135**	**(-4.447 to -1.823)**	**.000**	

Figure 4. Mean difference of aerobic exercise modalities on liver fat. Forest plot depicting the effect of moderate-intensity continuous training (MICT) vs high-intensity interval training (HIIT) (n = 177), HIIT vs control (CON) (n = 114), and an MICT vs CON (n = 533) on absolute liver fat change. Graph depicts mean difference and 95% CI for individual studies and the pooled estimates.

effect favoring HIIT vs CON ($g = -0.59$, 95% CI, –0.95 to –0.23, $P = .001$, $I^2 = 0\%$, n = 114) (Fig. 3), which saw liver fat content reduced by –2.85% (95% CI, –4.86 to –0.84, $P = .005$, $I^2 = 0\%$, n = 114, low-certainty evidence) (Fig. 4). Visual appraisal of funnel plots indicated no publication bias.

Effect of moderate-intensity continuous training vs control on liver fat

Thirteen studies reported sufficient data to determine the pooled effect of MICT vs CON for change in liver fat (15, 31, 32, 38-47). There was a moderate effect favoring MICT interventions vs CON ($g = -0.47$, 95% CI, –0.64 to –0.30, $P < .001$, $I^2 = 0\%$, n = 533) (Fig. 3), which saw liver fat content reduced by –3.14% (95% CI, –4.45 to –1.82, $P < .001$, $I^2 = 5.2\%$, n = 533, moderate-certainty evidence) (see Fig. 4). Visual appraisal of funnel plots indicated no publication bias.

Secondary Analyses

Effect of guideline-conforming interventions vs control on liver fat

There were a total of 9 studies that compared interventions conforming to the current physical activity guidelines (14) to CON (15, 32, 38, 40, 42, 43, 45-47). One study involved a 3-armed design in which both exercise groups incorporated prescriptions conforming to the current physical activity guidelines (32). Of the 10 groups analyzed, 9 involved MICT interventions. There was a moderate effect favoring guideline-adherent interventions vs CON for liver fat reduction (MD = –3.28, 95% CI, –5.04 to –1.51, $P < .001$, $I^2 = 20.1\%$, n = 429).

Effect of guideline-nonconforming interventions vs control on liver fat

There were a total of 7 studies that compared interventions that did not conform to the current physical activity guidelines (14) to CON (15, 31, 36, 37, 39, 41, 44). One study involved a 3-armed design in which both exercise groups incorporated prescriptions that did not conform to the current physical activity guidelines (31). Four of 8 studies involved HIIT interventions. There was a moderate effect favoring nonguideline-adherent interventions vs CON (MD = –2.75, 95% CI, –4.38 to –1.13, $P = .001$, $I^2 = 0\%$, n = 218).

Regression Analysis

The meta-regression analysis found that neither the total weekly exercise volume in minutes (N = 18, $B = 0.0002$, SE = 0.0017, $Z = 0.13$, $P = .89$) nor the total energy expenditure in kcal (N = 18, $B = 0.0003$, SE = 0.0002, $Z = 1.21$, $P = .23$) were related to changes in liver fat.

Discussion

This systematic review and meta-analysis assessed the effects of varying aerobic exercise modalities on liver fat. The primary analyses included 19 studies of moderate to high quality and involved 745 participants. Two studies assessed liver fat content via MRI (31, 34), while the remaining studies assessed liver fat content via ^{1}H-MRS. The results showed that HIIT probably results in little to no difference in reducing liver fat compared to MICT (moderate level of certainty of evidence). MICT probably results in a reduction in liver fat compared to CON (moderate level of certainty of evidence). While HIIT was also shown to significantly reduce liver fat, there was a low level of certainty of evidence for this analysis, which was largely due to the small sample sizes of the studies included. The results from the subanalyses revealed that aerobic exercise interventions were effective for reducing liver fat whether or not the interventions conformed to current physical activity guidelines. The results of the regression analysis revealed that weekly exercise energy expenditure and training volume were not associated with change in liver fat. Together, these results suggest that aerobic exercise interventions incorporating either HIIT or MICT are effective for improving NAFLD.

Recent reviews have highlighted the comparable effects of HIIT to MICT for improving an array of cardiometabolic outcomes such as cardiorespiratory fitness and blood pressure (19, 49). The results of this study add to the findings of previous reviews (12, 16) by showing that HIIT is at least as effective as MICT for reducing liver fat. Furthermore, this study goes beyond previous reviews by directly comparing the effect of HIIT vs MICT for liver fat reduction as well as by determining the association between change in liver fat and weekly exercise volume and energy expenditure. The findings from this study, which are supported by those from previous reviews, highlight that HIIT interventions may be particularly efficacious for individuals who are time poor as they often involve prescriptions requiring lower time commitment and energy expenditure than MICT.

The current physical activity guidelines recommend that adults should aim to undertake 150 to 300 minutes of moderate intensity physical activity, or 75 minutes to 150 minutes of vigorous physical activity, per week (14). The analyses performed in this study showed that there were minimal differences for change in liver fat between studies implementing interventions that conformed with the guidelines and those that did not when compared to CON (MD = –3.28% and MD = –2.75% for guideline conforming and guideline nonconforming interventions, respectively). Importantly, these findings do not imply that the current physical activity guidelines are unnecessarily high, rather that individuals with compromised health may achieve cardiometabolic benefits, which in this case is a reduction in liver fat, at lower volumes than once thought required. This may be especially true for interventions involving HIIT, as half of the studies that did not conform to the guidelines implemented HIIT, while 90% of guideline-conforming studies involved MICT.

While explanatory mechanisms for the findings reported in this review are not completely understood, the results of the regression analysis suggest that differences in total exercise time and energy expenditure are not associated with change in liver fat. Importantly, these results do not nullify the importance of key exercise prescription variables such as exercise volume for achieving health benefits, including body weight management. However, the observations hint at the importance of a combination of factors such as energy expenditure, total exercise volume (ie, time), and exercise intensity as predictors of cardiometabolic adaptations with the relative importance of each parameter currently unknown. Future studies should assess the relative importance of exercise prescription variables by comparing groups with equal training volumes but different exercise intensities and vice versa.

Available evidence suggests that the pathogenesis of NAFLD is caused by, in part, the sustained and elevated influx of free fatty acids to the liver, resulting from or contributed to by obesity and/or insulin resistance (50). This process eventually overwhelms the capacity of the liver to handle free fatty acids (eg, via triglyceride export and/or mitochondrial oxidation), causing intracellular buildup of fatty acid by-products, such as ceramides and diacylglycerol (50). Consequently, there are multiple potential mechanistic pathways by which aerobic exercise may improve liver fat content: 1) increases in cardiorespiratory fitness and ensuing improvements in mitochondrial content and function and fatty-acid handling capacity of hepatocytes and skeletal muscle (18); 2) changes in lipolytic and antilipolytic hormones, such as growth hormone, that can reduce visceral adipose tissue and the subsequent influx of fatty acids to the liver via the portal vein (51), and insulin action that potently reduces lipolysis (52, 53). Importantly, changes in cardiorespiratory fitness and lipolytic hormone secretion and action are affected by both exercise intensity and volume (20, 51). As cardiorespiratory fitness is closely related to mitochondrial content and function as well as the regulation of exercise-related changes in lipolytic hormones, improving cardiorespiratory fitness may be a useful therapeutic target for individuals with NAFLD.

Quality of Available Evidence

Given the stringent inclusion criteria, it is unsurprising that the studies included in this review were of moderate to high methodological quality. However, there are some considerations that should be taken into account when designing future exercise trials for NAFLD. For example, many studies did not report adherence to the exercise interventions. Additionally, while it is not possible to blind participants to group allocation, future studies should incorporate blinded assessors to decrease the risk of detection bias. Furthermore, although HIIT elicited significant improvements in liver fat, the level of certainty for this analysis was low partly because of the low sample sizes of studies involving HIIT interventions. Finally, given the majority of studies involved supervised exercise interventions in controlled environments where exercise prescription variables were closely monitored, further studies are required to determine the efficacy of accessible and unsupervised exercise interventions for adults with or at risk of NAFLD.

Practical Recommendations

The results of this study highlight the efficacy of aerobic exercise for the management of NAFLD. Adults with or at risk of NAFLD should aim to undertake regular moderate-to-vigorous intensity aerobic exercise, which can include either MICT or HIIT. While interventions that did not conform to the current physical activity guidelines elicited significant improvements in liver fat, slightly greater improvements were observed among interventions that met or exceeded the guidelines. Consequently, individuals should aim to undertake a minimum of 150 minutes of moderate-intensity aerobic exercise, 75 minutes of high-intensity aerobic exercise, or a combination of both, to optimize reductions in liver fat.

Strengths

This is the first systematic review to determine the effect of aerobic exercise on liver fat by solely incorporating studies that assessed liver fat via gold-standard noninvasive measurement techniques such as ^{1}H-MRS and MRI. Furthermore, by reporting the effect size and weighted MD, the results showed not only that aerobic exercise elicits moderate effects on liver fat reduction when compared to CON, but also that these improvements are likely clinically significant (–2.85% for HIIT vs CON and –3.14% MICT vs CON). Finally, the risk of bias, methodological quality, and certainty of evidence assessments allow for a more thorough interpretation of the results.

Limitations

This study has several limitations that should be considered when interpreting the results. First, mean changes were assessed from pooled data of randomized trials that incorporated HIIT and MICT interventions varying in exercise duration, frequency, measures of intensity, and intervention length. Second, the included studies incorporated adults varying in training status, health status, and sex. Consequently, the effect of the interventions on liver fat and the association of exercise prescription parameters (such as weekly exercise volume and energy expenditure) with liver fat change may have been augmented by these factors. However, although there were no condition-specific inclusion criteria, all but one study (46) involved individuals with overweight or obesity. Similarly, all but 3 studies (40, 44, 46) had average liver fat scores consistent with a diagnosis of NAFLD. One study reported liver fat in arbitrary units (24) and as a result, it was not possible to determine whether the participants, on average, had liver fat scores consistent with NAFLD. Third, this study, by nature, assessed the effect of aerobic exercise on liver fat and not measures of metabolic function such as glucose control or the rate of hepatic glucose production. As such, the results produced may not reflect the effect of exercise on these outcomes. Fourth, the studies included in this review involved free-living adults and as such, additional factors such as changes in diet and physical activity levels, outside the prescribed interventions, may have affected the results of this study. Finally, as highlighted previously, the majority of studies involved supervised exercise interventions and as such, the efficacy of accessible, nonsupervised, and community-based exercise interventions on liver fat reduction require further elucidation.

Conclusions

The results of this study confirm the therapeutic effect of aerobic exercise for the reduction of liver fat and demonstrate that comparable improvements are observed following HIIT or MICT interventions. Given that HIIT interventions often involve less energy expenditure and require less time commitment, this modality may be particularly efficacious for individuals who are time poor.

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