Clinical Efficacy of HIIT in Prevention and Management of Depressive Symptoms

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Abstract [**Objectives**] To assess the effects of high-intensity interval training (HIIT) in reducing or preventing depression. [**Methods**] A systematic electronic searching of the PubMed, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science, SPORTSDiscus, PsyCINFO, SCOPUS and CINAHL (EBSCOhost) was initially performed up to June 25, 2024. Randomized controlled trials (RCTs) were included if they contained data on depression taken before and after HIIT treatment. Data were extracted by 2 independent coders. Estimates were examined by using random-effects meta-analysis. [**Results**] 14 independent samples (493 participants) were included. There was a statistically significant reduction in depression symptom following HIIT compared with both continuous training (CT) and control conditions (CON) (HIIT vs. CT; standardized mean difference [SMD] = -0.35, 95% confidence interval [CI] -0.66 to -0.04, p = 0.025; CON; CI = -0.49, 95% CI = -0.92 to -0.07, p = 0.022). There were no statistically significant differences between groups in anxiety symptom (HIIT vs. CT; CI = CI

1 Introduction

Depression, with a significant and lasting low mood as the main clinical symptom, is a main type of mood disorder. It can affect a person's feelings, cogitation, behavior, cognitive funCTion, and physical conditions, which might be caused by a variety of factors such as mood disorders, heredity and so on [1]. With an aggravating trend of aging population in many countries, late-life depression cannot be neglected. Moreover, many chronic physical conditions, such as diabetes, cancer, cardiovascular diseases, chronic pain, and respiratory diseases, give rise to the concurrent depression^[2-3]. At present, medication, including selective serotonin reuptake inhibitors regarded as the first-line option, is the main treatment of depression^[4]. However, there are many side effects brought by antidepressants, including postural hypotension, cardiovascular and cerebrovascular events, gastrointestinal disorders, epilepsy, and even increased suicide risk^[5-6]. To date, more attention has been paid to the contribution of exercise and behavioral therapy in preventing and treating mental illnesses. A meta-analysis including fifty studies found a significant effect (r = -0.14; 95% CI = 0.19 to = 0.10) of exercise on depression^[7]. Studies that included a measure of both increased physical activity (PA) frequency and intensity demonstrated stronger associations with depressive symptoms than those that used measures of intensity alone[8].

High-intensity interval training (HIIT), a new strategy that maximizes exercise intensity through short bursts of concentrated effort, has been proposed as a time-efficient exercise intervention that may bring about similar or more effective benefits compared to traditional moderate-intensity aerobic exercise for healthy adults^[9] and patients with specific cardiovascular pathologies including cor-

onary artery disease (CAD)^[10], heart transplantation^[11], and heart failure(HF)^[12]. Clinically, HIIT has been found to improve depression and anxiety in a variety of chronic diseases. However, there has been no quantitative assessment of the HIIT in preventing both disorders. The aim of this systematic review is therefore to quantify the effect of HIIT for alleviating symptoms of depression compared with CT and CON using meta-analysis.

2 Methods

- 2.1 Search strategy A systematic electronic searching of the PubMed, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), Web of Scicience, SPORTSDiscus was initially performed up to June 25, 2024 with no publication date limits. We used a combination of MeSH and free text terms, including HIIT, HIIE, high intensity interval training, high-intensity interval training, high intensity interval exercise, high-intensity interval exercise and depress *, mood, stress, panic, emotions, nervousness, obsession, apprehension, fear, schizophrenia * (a serious mental health condition that affects how people think, feel and behave, posttraumatic, mental health, mental disorders, PTSD. The truncation symbol " * " were used so that the variations would be returned to expand the search scope.
- **2.2 Inclusion and exclusion criteria** The article was subsequently read and thoroughly assessed for following inclusion or exclusion criteria: (i) study design: all randomized controlled trials and randomized crossover trials; (ii) intervention: a detailed description of the exercise intervention, including intensity, duration and frequency; HIIT is always performed on devices (e. g., treadmill, cycling) or through other activities such as swimming or walking. Studies would be excluded if HIIT was applied in combination with another intervention (e. g., psychotherapy and physical factors therapy); (iii) control: continuous training, no any exercise intervention or no specific exercise intervention were used in the control group; (iv) outcomes: Studies must have included

at least one or more well-being measures of depression before and after the exercise intervention using validated scales, including the Beck Depression Inventory (BDI), Hospital Anxiety and Depression Scale (HADS), HDCDS, the Hamilton Rating Scale for Depression (HRSD) or Profile of Mood States (POMS) scale. Conference abstract, case reports, observational studies and studies without available data were excluded.

- 2.3 Risk of bias Methodological quality of the each RCT was independently assessed by two authors according to the *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (*PRIS-MA*) recommendations. The first part of the tool assesses seven specific domains, namely sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting and other issues. The second part assigns a judgement relating to the risk of bias for each domain which includes "low risk" of bias, "high risk" of bias or "unclear risk" of bias. Decisions were compared and discussed to achieve consensus. A third reviewer was consulted if disagreement persisted.
- **2.4 Data extraction** A data extraction sheet based on the *Cochrane Handbook for Systematic Reviews*. The data extraction form includes study (author, year, country), sample (number of participant, type of disease), exercise (frequency, intensity of intervention, duration, type) according to the American College of Sports Medicine (ACSM)^[13], type of control group (continuous training, care-as-usual, no activity, placebo pill, or other control), and outcome (pre- and post-treatment depression scores). If the primary outcomes (means \pm SDs) were not available, we used the changes from baseline (also called a change score), if provided within the study. Moreover, if the study reported results at multiple time points, we chose the final follow up data for several reasons. When more than one rating scale were used in a single study, we would select the most common across studies or the one which data was more reasonable.
- **2.5 Statistical analysis** Stata V. 18.0 was used to conduct the meta-analyses. Since depression and anxiety score were continuous outcomes, we chose *SMD* as summary statistics used for meta-analysis. And the random effects model was selected due to the similar but identical rating scale across studies. Separate analyses were performed for the following comparisons: (i) Change in depression after HIIT compared to CT; (ii) Change in depression after HIIT compared to CON.

In the meta-analyses of each outcome, we did pre-planned subgroup analyses restricted to trials to compare exercise response according to condition of mental illness risk. We classified it into high risk, moderate risk and low risk based on the mean baseline score measured by respective depression or anxiety scale in the two groups. To assess the robustness of our results, sensitivity analyses were subsequently performed: (i) computing the effects of exercise on depression using fixed effects model or random effects model; (ii) comparing exercise response according to study design (RCT, RCD), mode of exercise, measure time (post intervention, follow-up); (iii) by removing each study in turn. We used the $\it I^2$ test to assess the statistical heterogeneity of the treat-

ment effect among studies, and the values greater than 50% were regarded as being indicative of moderate-to-high heterogeneity. The trim-and-fill computation was used to estimate the effect of publication bias on the interpretation of the results.

Results and analysis

- **3.1 Studies retrieved** A flow chart detailing the study selection process is given in Fig. 1. A total of 14 RCTs (493 patients) were eligible for inclusion in meta-analysis. The initial searches returned a total of 2 631 articles, of which 1 531 were duplicated articles. Of these, 45 did not fulfill the inclusion criteria and the remaining 14 studies were analyzed. Table 1 summarizes the descriptive characteristics of the 14 studies that met inclusion criteria for the review.
- 3.2 Characteristics of included studies 14 RCTs (3 studies are RCD) were included in the review. Of these studies, 14 reported the change of depression symptom and 10 on anxiety. The scales used to assess depression were varied: HADS (n = 5); POMS (n=3); ZDRS (n=1); GDS (n=1); HDCDS (n=1); (SCL-90) (n=1); DASS21 (n=1) and VAS (n=1). According to the baseline level in the HIIT group, we classified the risk of mental illness to high (n = 1), moderate (n = 3) and low (n = 1)10). The range of participants' ages from the studies was 24 - 65 years, with the majority having a mean age in the 50 sec or 60 sec. Of the 14 controlled trials, 8 (57%) had a CT group, and 6(43%) a CON group. Mode of exercise varied widely between both HIIT and CT interventions. Mode of HIIT intervention included cycle ergometer (n = 8), treadmill (n = 3) and walking (n=2). The interval time (range 30 sec – 4 min) and total time (range 15 - 60 min) as well as weekly frequency (range 3 - 7 times) and duration (range 2 - 24 weeks) varied widely between studies. CT intervention ranged from 20 to 45 min per session at intensities between 60% and 80% VO2 max/HRmax. Anti-depressants and anxiety medication use was not reported in any study. The outcome was measured after up to 2 years^[23] and 5 years^[15] in two of the trials and post-treatment in 12 trials. There were statistically significant differences in the baseline of depression between HIIT and control group in three studies [11,19,21].
- 3.3 Risk of bias in individual studies Risk of bias for efficacy analysis for each included RCT is shown in Table 2. Three studies, rated as low risk at not less than six of the seven criteria, were regarded as high quality finally. Only one study was rated as low quality as they met less than three of the criteria. The remaining were rated as moderate quality as they met three to five of the seven criteria. Dimeo et al. [26] and Chrysohoou et al. [14] assessed and found that there was at high risk of bias in random sequence generation due to allocating participants according to the time of hospitalization and condition of patients. Three studies $^{[16,23-24]}$ clearly mentioned that the people engaged in assignment did not participate in the study. Therefore these studies were assessed to be at low risk of bias in blinding of participants and personnel. The rest of literature had an unknown risk of bias because of unclear information concerning blinding of assignments and assessors. All 14 RCTs reported whole expected outcome.

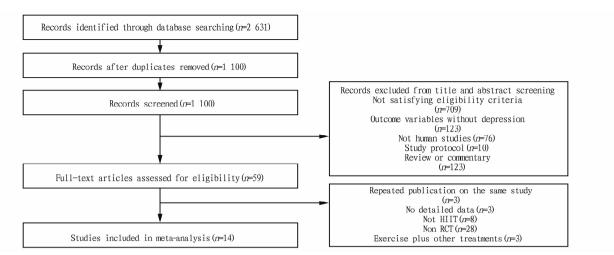


Fig. 1 PRISMA flowchart diagram of the search process

Table 1 Studies included in the analysis

	participants	Control	Mode	HIIT intervention Intervals Total			— Duration	Treatment focus/	Mental illness
Author, year, country									
				High Recovery		time//min		outcomes	risk
Chrysohoou et al. [14], 2014, Greece	CHF; 60 years old (nHIIT = 33, nCON = 39)	CON Usual care(RCT)	Cycle ergometer	30 sec at 100% max workload	30 sec rest	45	3 d a week/12 weeks	ZDRS	Low
Yardley et al. ^[15] , 2017, Norway	HTx; 50 years old (n HIIT = 21, n CON = 20)	CON Usual care (RCT)	Treadmill	4 × 4 min at 85% - 95% HRmax)	3 min at 6 - 20 RPE	38	3 d a week/8 weeks	BDI, HADS	Low
Sanudo <i>et al.</i> ^[16] , 2015, Spain	FM; 56 years old (n HIIT = 16, n CON = 12)	CON Usual care (RCT)	Walking	6 × 1.5 min at 75% - 80% HRmax	1 min rest	15	2 d a week/24 weeks	VAS	Moderate
Dall et al. [11], 2015, Denmark	HTx; 52 years old (n HIIT = 16, n CT = 16)	CT 45 min at 60% - 70% VO ₂ peak (RCD)	Cycle ergometer	1,2,4 min at $> 80\%$ VO ₂ peak	2 min at 60% VO ₂ peak	30	3 d a week/12 weeks	HADS	Low
Freese et al. ^[17] , 2014, Athens	MetS; 52 years old (n HIIT = 23, n CON = 24)	CON Non-exercising (RCT)	Cycle ergometer	4-8 ×30 sec at 9% of fat-free mass	4 min active re- covery with no resistance	23 -41	3 d a week/6 weeks	POMS	Low
Freyssin et al. ^[18] , 2012, France	CHF; 54 years old (n HIIT = 12, n CT = 14)	CT 45 min at the heart rate in VT1 (RCT) $$		12×30 sec at 60% – 80% the maximal power	1 min rest	18	5 d a week/8 weeks	HADS	Low
Smart et al. [19], 2012, Australia	CHF; 60 years old (n HIIT = 10, n CT = 13)	CT 30 min at 60% - 70% VO ₂ peak	Cycle ergometer	60 sec at 70% VO ₂ peak	60 sec rest	60	3 d a week/16 weeks	HDCDS	High
Oliveira <i>et al.</i> [20], 2013, Spain	Health; 24 years old (n HIIT = 15, nCT = 15)	CT 24 min at 72% VO ₂ peak (RCD)	Treadmill	$6-7 \times 2$ min at 100% VO_2 peak	57 sec rest	19.2	1-3 d a week/ $2-3$ weeks	POMS	Low
Chapman et al. ^[21] , 2017, Australia	Mental illness; 38 years old (n HI-IT = 9, n CT = 10)	CT 30-min at 65% - 75% HR-max (RCT)	Treadmill	3 × 4 min at 85% - 95% HRmax	3 min at 60% - 70% HRmax	18	3 d a week/12weeks	DASS21	Moderate
Arnardottir <i>et al.</i> ^[22] , 2007, Sweden	COPD; 65 years old $(nHIIT = 28, nCT = 32)$	CT 27 min at \geq 65% Wpeak (RCT)	Cycle ergometer	5×3 min at $\geq 80\%$ Wpeak	3 min at 30% - 40% Wpeak	27	Twice a week/16 weeks	HADS	Low
Uc et al. ^[23] , 2014, America	PD; 65 years old (n HIIT = 18, n CT = 17)	CT 45 min at 70% - 80% HR- max (RCT)	Walking	3 min at 80% - 90% of HRmax	3 min at 60% - 70% HRmax	45	3 d a week/6 weeks	GDS	Low
Neunhauserer <i>et al.</i> ^[24] , 2016, Australia	COPD; 64 years old $(nHIIT = 29, nCT = 29)$	CT 8 – 15 repetitions of strength training exercises (RCD)	-	7×1 min at 70% -80% peak work rate	2 min at 50% peak work rate	21	3 d a week/6 weeks	HADS	Low
Goldstein et al. ^[25] , 2001, the United States	HIV-seropositive; 35 years old (nHIIT = 13, nCON = 10)	CON Non-exercising (RCT)	Cycle ergometer	3 min at 70% – 80% HRmax	2 min at < 70% HRmax	45	3 d a week/12 weeks	BDI, POMS	Moderate
Dimeo et al. ^[26] , 1999, Germany	Cancer; 40 years old (n HIIT = 27, n CON = 32)	CON Non-exercising (RCT)	Cycle ergometer	1 min at >50% HRR	1 min rest	30	Daily	POMS, SCL-90-R	Low

OTE CHF; chronic heart failure; HTx; heart transplantation; FM; fibromyalgia; MetS; metabolic syndrome; COPD; chronic obstructive pulmonary disease; PD; Parkinson disease; HIV; human immunodeficiency virus; HIIT; high-intensity interval training; CON; non-exercising control group; CT; continuous training group; RCT; randomized controlled trial; RCD; randomized crossover design; Wpeak; peak exercise capacity; VT1; first ventilatory threshold; HRmax; maximum heart rate; VO₂ peak; peak oxygen consumption; RPE; rated perceived exertion; HRR; heart rate reserve; ZDRS; Zung Depression Rating Scale; BDI; Beck's Depression Inventory; HADS; Hospital Anxiety and Depression Scale; VAS; Visual Analogue Scale; HDCDS; The Hare-Davis Cardiac Depression Scale; DASS21; Depression Anxiety Stress Scale; GDS, Geriatric Depression Scale; POMS; Profile of Mood States; SCL-90-R; Symptom Check List.

Table 2 Risk of bias in individual studies

Study	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data addressed	Selective outcome reporting	Other bias	Decision
Arnardottir et al. [22]	Low	Low	Unclear	Unclear	Low	Low	Unclear	Moderate quality
Chapman et al. [21]	Low	Low	Unclear	Unclear	Low	Low	Low	Moderate quality
Chrysohoou et al. [14]	High	Unclear	Unclear	Unclear	Low	Low	Low	Moderate quality
Dall et al. $[11]$	Low	Low	Unclear	Unclear	Low	Low	Low	Moderate quality
Dimeo et al. [26]	High	High	Unclear	Unclear	Unclear	Low	Low	Low quality
Freese et al. [17]	Low	Unclear	Unclear	Unclear	Low	Low	Low	Moderate quality
Freyssin et al. [18]	Low	Unclear	Unclear	Unclear	Low	Low	Unclear	Moderate quality
Goldstein et al. [25]	Low	Unclear	Unclear	Unclear	Low	Low	Unclear	Moderate quality
Neunhauserer et al. [24]	Low	Low	Low	Low	Low	Low	Low	High quality
Oliveira et al. [20]	Low	Unclear	Unclear	Unclear	Low	Low	Unclear	Moderate quality
Sanudo et al. [16]	Low	Low	Low	Low	Low	Low	Unclear	High quality
Smart et al. [19]	Low	Unclear	Unclear	Unclear	Low	Low	Unclear	Moderate quality
Uc et al. [23]	Low	Low	Low	Low	Low	Low	Low	High quality
Yardley et al. [15]	Low	Unclear	Unclear	Unclear	Low	Low	Low	Moderate quality

3.4 Main analysis

- **3.4.1** Depression. 14 studies reported baseline and post-treatment data from depression scales. Of these, 8/14 had a CON group and 6/14 had a CT group. In a pooled analysis of all 14 trials, the HIIT intervention led to a mean greater reduction in depression score than any other treatment strategy, without statistically significant between-study heterogeneity (Fig. 2). Visual interpretation of funnel plots suggested no obvious evidence of asymmetry. In this analysis there was publication bias on Begg's Test (p = 0.743) and Egger test (p = 0.912), indicating no evidence of publication bias. The trim-and-fill computation showing no trimming performed and data was unchanged.
- **3.4.2** HIIT versus CT. Compared to CT intervention, HIIT showed statistically significant difference (SMD = -0.35, 95% CI 0.66 to -0.04, p = 0.025) in the analysis of two high quality studies and six moderate quality studies (with a total of 223 participants) (Fig. 2). We detected no significant heterogeneity between the trials ($I^2 = 37.4\%$, $Tau^2 = 0.072$, p = 0.131). We made sensitivity analysis where random or fixed effects model were used respectively. This did not significantly change the results (Table 3). We did another sensitivity analysis for study design, measure time and intervention type. These also failed to explain heterogeneity. Heterogeneity was still constant when each study was removed in turn. But result changed significantly (p = 0.07, SMD = -0.29, 95% CI = 0.61 to 0.02, $I^2 = 35\%$) after Smart et al. [19] was excluded.
- **3.4.3** HIIT versus CON. Compared to CON group, HIIT intervention showed statistically significant difference (SMD = -0.49, 95% CI 0.92 to -0.07, p = 0.022) in the analysis of one high quality study, four moderate quality studies and one low quality study (with a total of 270 participants), as shown in Fig. 3. The heterogeneity between the trials was substantial indicated by the I^2

test ($I^2 = 64.4\%$, $Tau^2 = 0.176$, p = 0.015). The sensitivity analyses showed on Table 3. Results were robust when random or fixed effects model was applied in analysis. And the heterogeneity decrease to 0% after one study (Chrysohoou *et al.* [14]) was excluded. But the result still showed a significant difference (p = 0.062, SMD = -0.27, CI = 0.55 to 0.01). We supposed that the high risk of this study in random sequence generation could contribute to it. Mean age and HIIT characteristics (duration, interval intensity and weekly frequency, time) did not predict the change in depression.

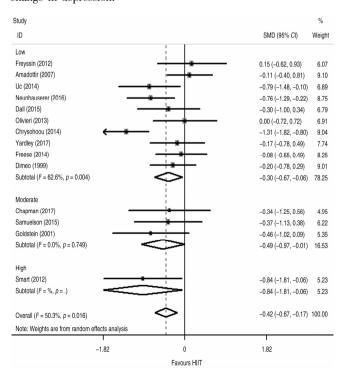


Fig. 2 Change in depression after HIIT

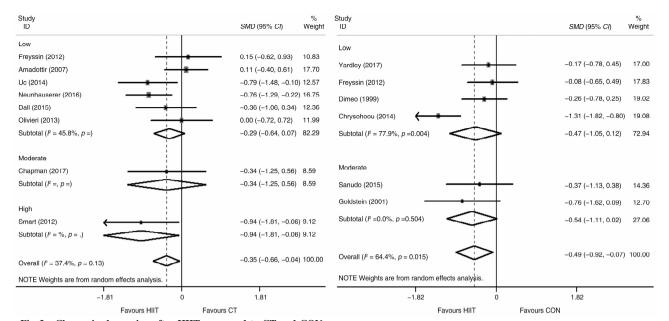


Fig. 3 Change in depression after HIIT compared to CT and CON

Table 3 Sensitivity analyses on depression

Outcome	Analysis	RCTs (n)	SMD	95% CI	<i>p</i> -value	I^2	Trim and fill effect size (95% CI)
HIIT VS CT on depression	Model						
	Random	8	-0.35	[-0.66, -0.04]	0.025	37.4%	Unchanged
	Fixed	8	-0.34	[-0.58, -0.10]	0.005	37.4%	Unchanged
	Design						
	RCD	3	-0.43	[-0.87, 0.02]	0.059	30.1%	
	RCT	5	-0.31	[-0.76, 0.14]	0.176	47.8%	Unchanged
	Time-point						
	Post intervention	7	-0.28	[-0.61, 0.04]	0.086	35.7%	Unchanged
	Follow-up	1	-0.79	[-1.48, -0.10]	0.025	0	N/A
	Mode						
	Cycle ergometer	4	-0.19	[-0.64, 0.26]	0.400	40.5%	Unchanged
	Treadmill	2	-0.12	[-0.68, 0.44]	0.680	0%	Unchanged
	Walking	1	-0.79	[-1.48, -0.10]	0.025	0%	N/A
HIIT VS CON on depression	Model						
	Random	6	-0.49	[-0.92, -0.07]	0.022	64.4%	-0.60[-0.99, -0.21]
	Fixed	6	-0.51	[-0.76, -0.26]	0.000	64.4%	-0.61[-1.00, -0.21]
	Time-point						
	Post intervention	5	-0.56	[-1.05, -0.07]	0.026	68.3%	Unchanged
	Follow-up	1	-0.17	[-0.78, 0.45]	0.594	0	N/A
	Mode						
	Cycle ergometer	4	-0.60	[-1.20,0.00]	0.051	75.6%	Unchanged
	Treadmill	1	-0.17	[-0.78, 0.45]	0.594	0%	N/A
	Walking	1	-0.37	[-1.13, 0.38]	0.334	0%	N/A

4 Discussion

As far as we are aware, this is a systematic review and meta-analysis that has specifically focused on examining the effectiveness of HIIT at improving symptoms of depression compared with continuous exercise and a non-exercising control group. Physical activity (muscle resistance, coordination, occupational, sports, conditioning and balance training) can decrease fatigue, depressive symp-

toms, sleep disorders^[27], but has no effect on anxiety in Parkinson's disease (PD)^[28-29]. As showed in figures above, our review is consistent with those references. The potential explanation is that young people more easily suffer from anxiety disorders^[1]. But the majority of the included studies have a mean age of 50 years old, which means that the evidence base is scarce for the young. In spite of this, the HIIT intervention can be consid-

ered an effective non-pharmacological treatment for depression in older adults due to the fact that late-life depression is becoming a major social burden with increased health care costs and risk of suicide, morbidity. It is worth mentioning that the effects of HIIT on depression in chronic conditions, such as heart disease, cancer, PD and COPD, might be smaller than effect sizes in populations just with anxiety or mood disorders. Because the depression may be caused by poor physical conditions or potential side-effects of medical treatments in these chronic disease patients, the symptoms of depression are hard to be relieved before the primary affections get treated. In addition, the patients suffered from cancer, chronic pain or other medical conditions with a low level of anxiety or depression at pre-treatment may show a relatively smaller degree of improvement after treatment than those with a high level at pretreatment, which is consistent that majority of included studies' baseline level of depression or anxiety was low in this review.

Although there was only one study rated as low quality, majority of studies were rated as moderate quality due to the unclear risk with insufficient information about allocation concealment, blinding of participants and outcome assessment, which limited the reliability of results. Begg's test and Egger test indicated no evidence of publication bias in the pooled analysis. But we need to be cautious about it due to the small amounts of included studies and high heterogeneity between different control groups. There were differences in participants, scales of assessment, types of interventions across studies and the heterogeneity indicated significant in some comparisons. Therefore, it is questionable whether pooling studies in meta-analyses is appropriate in this review. We did preplanned subgroup analyses according to pre-treatment condition of mental illness risk. No further subgroups could be created given the lack of studies, such as type of disease. Sensitivity analyses could also be performed in the limited comparison (study design, exercise type), which showed that the high heterogeneity could be caused by few studies in some comparison. After two studies were omitted, heterogeneity has a significant reduction, but this did not reverse the results. In addition, we used a random-effects model throughout to incorporate heterogeneity into our analyses. The sensitivity analysis, however, showed that there was no statistically significant difference between random effects model and fixed effects model. Although we have tried to minimize the effects of heterogeneity, results in this review should still be treated with caution. In the regression analysis, the primary modifiable elements of HIIT protocols, defined here as duration, interval intensity and weekly frequency, time spent at high-intensity, did not significantly predict the change in depression and anxiety.

5 Conclusions

Some limitations of our review should be noted. Firstly, we limited the review to RCTs. It is possible, however, that study designs other than RCTs would have given valuable insight. Secondly, there were only 3 studies were assessed as high quality and wide heterogeneity between participants, making it difficult to generalize conclusions. Thirdly, only two studies reported follow-up results. There were no sufficient follow-up data to demonstrate the longer

lasting effects on improvement in depression and anxiety symptoms following HIIT. Despite these limitations, we have demonstrated that HIIT conveys benefits to psychological health which in the case of improving depression symptom may be superior to the effect of traditional continuous training and inactivity, especially for the elderly.

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