Short-term (<8 weeks) high-intensity interval training in diseased cohorts.

James E M Blackwell[1-2], Brett Doleman[1-2], Philip J J Herrod[1-2], Samuel Ricketts[1], Bethan E Phillips[1], J N Lund[1-2], John P Williams[1-2]

University of Nottingham, UK[1], Royal Derby Hospital, UK[2]

Corresponding author:

Dr James Blackwell
Email: james.blackwell@nhs.net
Mobile: 07878182529

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Abstract:

Background & Aim:

Exercise training regimes can lead to improvements in measures of cardiorespiratory fitness (CRF), improved general health, and reduced morbidity and overall mortality risk. High intensity interval training (HIIT) offers a time-efficient approach to improve CRF in healthy individuals, but the relative benefits of HIIT compared to traditional training methods are unknown in across different disease cohorts.

Methods:

This systematic review and meta-analysis compares CRF gains in randomised controlled trials of short-term (<8 weeks) HIIT vs. either no exercise control (CON) or moderate continuous exercise training (MCT) within diseased cohorts. Literature searches of the following databases were performed: MEDLINE, EMBASE, CINAHL, AMED, and PubMed (all from inception to 1st December 2017), with further searches of Clinicaltrials.gov and citations via Google Scholar. Primary outcomes were effect upon CRF variables; VO_{2peak} and Anaerobic Threshold (AT).

Results:

Thirty-nine studies met the inclusion criteria. HIIT resulted in a clinically significant increase in VO_{2peak} compared with CON (mean difference (MD) 3.32 $ml \cdot kg^{-1} \cdot min^{-1}$; 95% CI 2.56 to 2.08). Overall HIIT provided added benefit to VO_{2peak} over MCT (MD 0.79 $ml \cdot kg^{-1} \cdot min^{-1}$; 95% CI 0.20 to 1.39). The benefit of HIIT was most marked in patients with cardiovascular disease when compared to MCT (VO_{2peak} (MD 1.66 $ml \cdot kg^{-1} \cdot min^{-1}$; 95% CI 0.60 to 2.73); AT (MD 1.61 $ml \cdot kg^{-1} \cdot min^{-1}$; 95% CI 0.33 to 2.90)).

Conclusions:

HIIT elicits improvements in objective measures of CRF within 8 weeks in diseased cohorts compared to no intervention. When compared to MCT, HIIT imparts statistically significant additional improvements in measures of CRF, with clinically important additional improvements in VO_{2peak} in cardiovascular patients. Comparative efficacy of HIIT vs MCT combined with an often reduced time commitment may warrant HIIT's promotion as a viable clinical exercise intervention.

Key Words: HIIT, VO_{2peak}, anaerobic threshold, clinical, short-term.

Introduction:

Objective measures of cardiorespiratory fitness (CRF) (e.g. VO_{2peak} and anaerobic threshold (AT)) predict whole-body health, morbidity and mortality (1–4). These measures of CRF can be altered via participation in exercise training regimens, which in turn may improve general health. Traditionally endurance based aerobic activity or 'moderate continuous training' (MCT) has been employed to improve CRF (5) and exercise tolerance (6).

Despite MCT (150 minutes of moderate aerobic activity every week) forming the primary basis of almost all public health exercise-based recommendations (7,8), greater attention has recently been paid to the utility of higher intensity exercise (75 minutes of vigorous activity every week) as an alternative to MCT (7) in the context of 'exercise-for-health' (9) as the latter is more time efficient, which may improve compliance (10).

Patients can have modification of disease risk factors through exercise interventions (e.g. reduction of blood pressure in those at risk of stroke) (11) and exercise can also be used to help optimise patients prior to a planned intervention (e.g. patients with suspected cancer or those awaiting urgent elective surgery for malignancy) (12). For those having major surgical procedures perioperative outcome is in large part dependent upon preoperative CRF (2). An ability to rapidly improve CRF would therefore be attractive if deliverable in the short time available between the suspicion of cancer and initiation of primary treatment (13).

Often however, there is not an extended period available from clinical suspicion of cancer before first definitive treatment to complete exercise programmes: for example, in the United Kingdom the National Cancer Action Team imposes two cancer waiting time service standards (13). The first is a 62 day target from initial GP referral for suspected cancer or urgent referral from NHS screening program, whilst the second is a 31-day window from the decision to treat to primary treatment (surgery, drug treatment or radiotherapy) of the cancer (13). These standards have led to increasing interest in novel exercise interventions to improve CRF within truncated timeframes. It has been suggested that exercise regimens such as high intensity interval training (HIIT) may deliver clinically important improvements in CRF within a clinically relevant time frame with minimal time commitment from the patient.

HIIT, defined as brief intermittent bursts of vigorous activity interspersed with periods of rest or low-intensity exercise (14), can bring more pronounced improvements in objective measures of CRF than MCT in healthy individuals over an equivalent number of weeks (15). It is unknown whether individuals with disease will benefit from HIIT in the same way. In any exercise intervention it is essential that there are high levels of adherence and compliance to maximise benefit, especially given that co-morbid patients have been shown to be poor compliers with exercise interventions (16). HIIT has previously been reported to be more enjoyable than MCT (17). Time pressure has been identified as one of the most commonly cited barriers to exercise adherence (10). HIIT's reduced time commitment and training volume makes it an attractive option for rapidly achieving maximal gains in CRF.

Previous reviews in distinct disease groups exploring the efficacy of HIIT over longer time durations (median 12 weeks) have reported benefits of HIIT over MCT in cardio-metabolic disease (19) and possible improved efficacy in patients with chronic obstructive pulmonary disease (COPD) (20). Whereas, equal effects on CRF have been seen in HIIT and MCT in patients with coronary artery disease during cardiac rehabilitation (21). In general within disease groups, 8 – 16 week exercise programmes involving HIIT have been shown to be as effective as MCT(22), while uncontrolled studies have shown large increases in CRF following HIIT across co-morbidities as varied as cardiac disease (23), diabetes (24), obesity (25) and asthma (26). HIIT retains the advantage of requiring significantly less time commitment than MCT.

The aim of this review was to compare the effect of HIIT to no exercise control (CON) or MCT on cardiorespiratory fitness (VO_{2peak}/AT) in differing disease states over short timeframes (≤8 weeks). We also aimed to identify conditions where HIIT might be particularly effective compared to CON or MCT.

Methods:

Study design

This systematic review was prospectively registered with PROSPERO (registration number CRD42016042299) and performed according to the PRISMA statement (27). Only randomised control trials (RCT's) evaluating HIIT vs. CON or HIIT vs. MCT were included. Other inclusion criteria were participants aged >17 years old with disease, an intervention duration of 8 weeks or less and trials where outcome data was reported pre and post intervention. Trials involving a drug treatment or dietary supplementation were excluded. We classified trials as delivering high-intensity interval training if they satisfied the following criteria: i) high intensity efforts interspersed with reduced or no effort recovery periods, and ii) high intensity bouts >85% predicted heart rate or heart rate reserve, or iii) high intensity bouts >85% of peak power output or peak power achieved at baseline exercise test. Studies using 'supra-maximal' loading of >100% Wattage max at CPET or similar loading criteria were not included.

Literature search

Literature searches were carried out by a research team member (BD) using the following databases: MEDLINE, EMBASE, CINAHL, AMED, and PubMed, all searched from their inception to 1st December 2017, with no language restriction. A detailed search for unpublished studies was carried out on Clinicaltrials.gov. The Cochrane library of systematic reviews was searched for relevant previous reviews, whilst previous systematic reviews of related topics were also searched for relevant primary studies. References of all identified potentially relevant primary studies were hand-searched for further relevant studies. Finally, we searched for studies citing the identified potentially relevant primary studies on Google Scholar to identify any further work potentially meeting the inclusion criteria.

Medical subject headings (MeSH) included the terms ‘HIIT’, ‘HIT’ and ‘EXERCISE’. Free-text words included ‘exercise’, ‘high AND intensity’ and ‘interval’. Abstracts of identified studies were screened by two authors independently (JB and BD). Full text versions of potentially relevant primary studies were then independently screened against the inclusion and exclusion criteria by two authors (JB and SR) and agreement to inclusion reached by consensus.

Data extraction

Study characteristics (authors and year of publication, mean age (years), % female individuals, training intervention duration (weeks), number of planned exercise sessions in total, disease state, individual exercise protocols and country of origin) were extracted by one author (JB) with outcome data (VO_{2peak}, AT, SBP, DBP, 6-MWT, QoL questionnaires, adherence data) independently extracted and verified by two authors (JB and SR). Risk of bias for included studies was assessed using the Cochrane Collaboration tool for assessing risk of bias. This was performed independently by two authors (JB and BD), with any disagreement resolved by consensus with a third party author (PH). When outcome data was only reported in graphical form, data were extracted using WebPlotDigitizer (Version 3.12, Austin, Texas, USA).

Statistical analysis

To facilitate meta-analysis of change variables when standard deviations (SD) of change were not reported, SDs were imputed using recommended methods described in the Cochrane Handbook (28). First, studies that reported data as SD of the difference between pre versus post values were used to calculate correlation coefficients, these were then averaged for each outcome and used these to calculate change SDs from reported baseline and final SDs. Outcomes were aggregated using a random-effects model. Changes in VO_{2peak} and AT are presented as mean difference (MD) with 95% confidence intervals (CI), in the unit $ml \cdot kg^{-1} \cdot min^{-1}$. All other continuous outcomes are also reported as MD. Minimal clinically significant improvements were defined as follows: change in VO_{2peak} and AT >1.5 $ml \cdot kg^{-1} \cdot min^{-1}$ (12), six minute walk test (6-MWT) >17-23 meters (29,30), <systolic/ diastolic blood pressure (BP) of 10mmHg/ 5mmHg(11).

The I^2 statistic was used to quantify statistical heterogeneity, with values above 50% taken as evidence of statistical heterogeneity. Publication bias was assessed qualitatively using funnel plots and quantitatively using Egger's linear regression test ($p<0.05$ as evidence of imprecise study effects). We investigated heterogeneity using a random effects, restricted maximum likelihood meta-regression. Covariates included mean age of participants, duration of intervention (weeks) and disease cohort. For disease cohorts, we created dummy variables and used the least effective subgroup as the reference category. We report the between-study heterogeneity explained by the model (R^2 analogue) with a corresponding p-value. The Knapp-Hartung modification was used as the variance estimator. To assess the quality of evidence, the GRADE approach (28) was used with evidence downgraded to moderate, low or very low quality owing to concerns over unexplained heterogeneity, indirectness of evidence, possible publication bias, imprecision in effect estimates and concerns over risk of bias. All calculations were carried out using STATA 15 (StataCorp, Texas USA).

Results:

Search results

A total of 2612 abstracts were screened for inclusion; 2570 from the initial literature search and 42 from the reference lists of other identified studies, Google Scholar citations and other systematic reviews. Of the 2612 abstracts screened, 2559 were excluded as not being relevant or duplicates, leaving 53 studies for full-text review. Of the 53 studies undergoing full text review, 14 were excluded, leaving 39 studies for inclusion in the qualitative analysis and 34 studies for quantitative analysis (Figure 1 – PRISMA Flow Chart (27))(12,23,31–64).

Study characteristics

The characteristics of the included studies can be found in the online supplementary tables (See Tables, Supplementary Digital Content 1 (HIIT vs. CON) and 2 (HIIT vs. MCT). The earliest study meeting the inclusion criteria was published in 1999 and the latest in 2016. All studies were published as journal articles. The interventions studied were HIIT vs. CON or HIIT vs. MCT. Three studies were included in both analyses which compared HIIT vs. CON vs MCT (37,38,64).

Risk of bias

All included studies were at high risk of bias in at least one domain (See Figure, Supplementary Digital Content 3, which shows risk of bias summary chart). The majority of studies were at high risk of bias due to the innate difficulties in blinding participants to a physical activity intervention. A large number of studies did not describe their random sequence allocation or allocation concealment in sufficient detail to be judged as low risk of bias, and many did not describe blinding of their outcome assessment. Many studies were at risk of reporting bias and some may have suffered from attrition bias.

Data synthesis

There were sufficient studies to perform independent meta-analysis for VO_{2peak}, AT, SBP and DBP for both HIIT vs. CON and HIIT vs. MCT interventions.

VO_{2peak}

Of 11 study groups from 11 trials analysed for the comparison of HIIT vs. CON, comprising 153 individuals in the HIIT groups and 124 CON participants, HIIT produced a clinically significant increase in VO_{2peak} compared with CON (MD 3.38 $ml\cdot kg^{-1}\cdot min^{-1}$; 95% CI 2.7 to 4.05; I^2=47.8%) (Figure 2). Of 25 study groups from 24 trials comparing HIIT to MCT, comprising 359 individuals in the HIIT groups and 341 MCT participants, HIIT provided additional mean increase in VO_{2peak} compared with MCT (MD 0.79 $ml\cdot kg^{-1}\cdot min^{-1}$; 95% CI 0.20 to 1.39; I^2=50.5%) (Figure 3). However, this improvement did not meet our a priori target of clinical significance (>1.5 $ml\cdot kg^{-1}\cdot min^{-1}$). Cardiovascular patients showed the greatest improvement, with clinically significant mean increases in VO_{2peak} following HIIT (MD 1.66 $ml\cdot kg^{-1}\cdot min^{-1}$; 95% CI 0.60 to 2.73, I^2=43.8%) when compared to MCT (Figure 3).

On meta-regression analysis, duration of intervention showed significance for HIIT vs. CON (R^2=53.0%, p=0.04) but non-significant for HIIT vs. MCT (R^2=5.54%, p=0.245). For HIIT vs. CON, longer duration of interventions led to larger increases in VO_{2peak}. Neither HIIT vs. CON nor HIIT vs MCT showed significant interaction for age (R^2=0%, p=0.637 and R^2=0%, p=0.529 respectively). On meta-regression analysis of HIIT vs. MCT, HIIT was more effective in cardiovascular patients (R^2=4.46%, p=0.057) than respiratory patients.

There was no evidence of publication bias in either analysis (p=0.16 and p=0.91). The quality of evidence of VO_{2peak} data was regarded as moderate for HIIT vs. CON (downgraded owing to concerns over risk of bias) and low for HIIT vs. MCT (downgraded owing to concerns over risk of bias and unexplained heterogeneity) using GRADE criteria (65).

AT

A single study reported AT following HIIT vs. CON, showing a mean improvement in AT following HIIT vs. CON (MD 1.5 ml·kg^{-1}·min^{-1}; 95% CI 0.18 to 2.82). There was no further data available for meta-analysis to be performed in relation to anaerobic threshold for HIIT vs CON.

HIIT provided additional increase in AT compared with MCT of borderline statistical but not clinical significance (MD 1.26 ml·kg^{-1}·min^{-1}; 95% CI -0.02 to 2.54, I^2=38.3%) in 6 study groups from 5 trials, comprising 84 individuals receiving HIIT and 79 MCT. Cardiovascular patients showed the greatest mean improvement in AT following HIIT in comparison with MCT (MD 1.61 ml·kg^{-1}·min^{-1}; 95% CI 0.33 to 2.90, I^2=39.8%) (Figure 4). The quality of evidence of AT data for HIIT vs. MCT was regarded as low using GRADE criteria (downgraded owing to concerns over risk of bias and imprecision) (65).

Six minute walk test

A single study reported 6-MWT outcomes for HIIT vs CON with an effect size of 66 meters following HIIT (p=0.001) (66). For the comparison of HIIT vs. MCT, six study groups from 6 trials were analysed, comprising 151 individuals in the HIIT groups and 149 participants in the MCT group. HIIT delivered an increase in 6-MWT distance compared with MCT (MD 11.67 meters; 95% CI 1.28 to 22.06; I^2=38.9%). Cardiovascular patients showed a greater, yet clinically insignificant improvement (MD 16.64 meters; 95% CI 5.22 to 28.07; I^2=31.9%) compared to respiratory patients (MD 2.05 meters; 95% CI -12.57 to 16.66; I^2=0%).The quality of evidence 6-MWT was regarded as low using GRADE criteria (downgraded owing to concerns over risk of bias and imprecision)(65).

Blood Pressure

When analysing blood pressure changes in HIIT vs CON 6 study groups from 6 trials reported systolic blood pressure (SBP) results, whereas only 5 trials presented data for analysis of diastolic blood pressure (DBP) changes due to unreliable data in one study (47). These studies comprised 79 individuals for SBP in the HIIT groups (DBP 66 individuals) and 67 individuals for SBP in the CON groups (DBP 57 individuals). Compared to CON, HIIT provided a non-significant reduction in SBP (MD -4.48 mmHg; 95% CI -11.13 to 2.18; I^2=58.8%) and a statistically significant reduction in DBP (MD -3.05 mmHg; 95% CI -5.41 to -0.69; I^2=0%), which however did not meet our a priori target of clinical significance (DBP -5mmHg).

When analysing BP changes in HIIT vs. MCT, for SBP and DBP 8 study groups from 8 trials were included. These studies comprised 116 individuals for both SBP and DBP in the HIIT groups and 113 individuals for SBP and DBP in the CON groups. HIIT provided no additional benefit in either SBP (MD 0.48 mmHg; 95% CI -2.01 to 2.97; I^2=0.0%) or DBP (MD -0.51 mmHg; 95% CI -2.53 to 1.50; p=0.136; I^2=36.8%) compared to MCT. The quality of evidence for blood pressure was regarded as moderate to low using GRADE criteria (downgraded owing to concerns over risk of bias and imprecision for some analyses)(65).

Quality of life

There was marked variation in both instrument selection and reporting of quality of life (QoL) qualitative measures and questionnaire outcomes were equivocal between both HIIT vs CON and HIIT vs MCT (See Tables, Supplementary Digital Content 4 (HIIT vs. CON) and 5 (HIIT vs. MCT), which shows quality of life questionnaire outcomes). The most commonly reported QoL questionnaire was SF-36 (67). Studies including SF-36 data did so either with a total score (overall scores) or by domains (summary scores) of the full questionnaire (i.e: Physical Health, Perceived Health, Mental Health). Dunne *et al.* (2016) reported that HIIT prehabilitation was associated with improvements in overall SF-36 QoL and SF-36 mental health scores (change of +11 p=0.028 and +11 p=0.037 respectively) (12). Gloeckl *et al.* (2012) reported increased overall SF-36 scores following both HIIT and MCT, however only the physical health summary score in the MCT group (MD 4.3 $p<0.05$) and the mental health summary score in the HIIT group (MD 9.7 $p<0.05$) improved significantly (43). Freese *et al.* (2014) reported clinically meaningful improvements in role-physical scores, bodily pain, vitality, social functioning, mental health and total SF-36 score following 6 weeks HIIT (41). Jaureguizar *et al.* (2016) reported significant increases in the role emotional, mental health, self-reported health status and the mental health index following HIIT only (48). Other quality of life questionnaires used in more than one study are summarized in supplementary digital content tables 4 and 5 as above.

Anxiety / Mood

Questionnaires used for anxiety and mood can be seen in the supplementary tables (See Tables, Supplementary Digital Content 4 (HIIT vs. CON) and 5 (HIIT vs. MCT), which shows quality of life questionnaires used within studies). The most commonly reported questionnaire to determine anxiety and mood was the Hospital Anxiety and Depression Scale (HADS). Again due to paucity of studies reporting values no meta-analysis was performed across HIIT vs. CON or HIIT vs. MCT. Flemmen *et al.* (2014) showed a significant reduction in anxiety favouring CON ($p<0.05$) and a significant reduction in depression following HIIT ($p<0.05$), with no significant difference in reported insomnia (40). For HIIT vs. MCT both studies showed improvements in the HADS anxiety and depression domains however with no significant benefit between intervention arms (42,57).

Adherence

Due to widespread lack of reporting and insufficient information included within published papers, we deemed it inappropriate to analyse adherence from the number of drop-outs to each intervention, as very few studies reported the direct reason for participants dropping out in HIIT or MCT groups. Disparity in duration of exercise (weeks) led to varying numbers of scheduled sessions per study. Overall, adherence to scheduled sessions was high in both groups (See Table, Supplementary Digital Content 6, which shows reported adherence to HIIT vs. MCT protocols).

Discussion:

In this review of the current literature exploring the effectiveness of short duration HIIT in disease cohorts, we found that HIIT elicits clinically important improvements (>1.5 ml·kg^{-1}·min^{-1}) in VO_{2peak} within 8 weeks or less when compared to non-intervention control subjects.

This is in keeping with previous data in both healthy young and older individuals (>60 years), where HIIT has been shown to improve aspects of fitness. In healthy young individuals completing sprint interval training (4-6 intervals, 30 second all-out sprints), similar adaptations in human skeletal muscle oxidative capacity and exercise performance to those undertaking MCT (90-120 minutes continuous cycling at 65% VO_{2peak}) were seen in as little as 2-weeks, despite a vastly reduced time commitment and training volume (approximately 90% lower vs. MCT) (68). Similarly, in healthy older individuals HIIT has been shown to increase VO_{2peak} (+8%) and reduce systolic blood pressure (-9%) in just 6-weeks (69). Moreover, in a separate study of healthy older individuals, HIIT has also recently been shown to elicit clinically significant improvements in CRF within just 31-days (70), a time-frame which is compliant with the aforementioned UK National Cancer Action Team policy on time from decision-to-treat to surgery. In addition to the reduced time-frame and training volume required by HIIT to elicit improvements in CRF, HIIT may also have the added advantage of rapid adaptation at the level of skeletal muscle, resulting in fewer negative training symptoms (e.g. delayed onset muscle soreness (DOMS) (22), which is postulated to lead to increased adherence.

HIIT is at least as effective as MCT over short time periods across all groups. Subgroup analysis showed additional benefit in cardiovascular patients versus other patient groups following HIIT. To exemplify, cardiovascular patients showed additional increases in VO_{2peak} and AT following HIIT when compared with MCT. It is likely that the rapid benefit shown in this review is a result of peripheral adaptations such as mitochondrial oxidative enzyme upregulation and increased buffering capacity (68) as it is only in longer-term training programs (≥12 weeks) that improvements in cardiac structure and systolic function have been shown (71). In response to HIIT the contribution of cardiac change may be underestimated due to the research focus primarily being upon mitochondrial upregulation, with potential cardiac changes being understudied.

A small number patients with cancer were included in this review, with varying outcomes. Lung, colon and breast cancer groups all showed improvement in CRF with HIIT when compared to no exercise. There was no added benefit of HIIT over MCT. Blunted adaptation in these cancer groups (shown as a lack of CRF improvement in response to HIIT compared to the overall effect of HIIT vs. CON) may be explained by blunted mitochondrial enzyme activity whilst cancers remain in situ (72). In addition, colorectal cancer patients presenting for resection have lower CRF than age-matched controls whilst the cancer is still in situ. However, removal the cancer facilitates a return toward normal CRF (73). Taken together, these studies may lead to a suggestion that tumour presence hinders adaptive capacity to exercise training, at least in this cancer type. Adjuvant chemotherapy has negative effects upon cardiorespiratory fitness preoperatively in colorectal cancer patients (74) and have resulted in higher rates of heart failure and cardiomyopathy following breast cancer chemotherapy (75), as such these confounding drug regimens must be considered when interpreting trainability within these groups.

The beneficial psychological effects of exercise *per se* are well known but it is unclear whether HIIT is superior to MCT in improving QoL from this review. This lack of clarity is due to the heterogeneity of tools used, small numbers of studies reporting QoL outcomes and lack of suitable comparisons for many of the questionnaires.

Beyond mechanistic propositions based on small-scale non-RCTs in distinct disease groups, reasons why certain pathological subgroups might not show CRF improvements with HIIT is far from clear. One possible explanation for certain subgroups is that exercise intervention studies mainly report mean improvements in CRF parameters as $ml \cdot kg^{-1} \cdot min^{-1}$, rendering obese patients at a relative disadvantage for demonstrating improvement over short periods; as in the authors' experience individuals normally remain weight-stable during short-term HIIT protocols (often due to increased lean muscle mass and fat mass reductions). A recent meta-analysis in obesity concluded that HIIT was superior to traditional exercise to improve CRF and reduce body fat percentage. Notably the median duration of training protocol for this meta-analysis was 12 weeks, with a wide range of 2-52 weeks (76), which is does not comply with clinical time-frames for cancer surgery. In contrast, but in agreement with this review, another recently published meta-analysis found no clinical benefit of HIIT versus MCT in reduction of total body fat or fat mass over shorter training duration (<12 weeks) (77).

To achieve benefit from HIIT it is thought that a minimal dose of exercise expenditure, or training load is required to significantly disturb intracellular homeostasis and stimulate mitochondrial biogenesis (14). This may explain why the respiratory patients seem to gain less benefit versus other pathological groups as respiratory limitation may result in low maximal exercise scores and therefore lower training loads, given that most protocols prescribe the training load as a percentage of VO_{2peak} or maximal wattage achieved at CPET.

HIIT can represent a time efficient training method by which to improve CRF, potentially removing the commonly cited "lack of time" as a barrier to exercise (10). Time efficiency can be due to two facets, reduced work duration within a session and/or individual session time. For example, one of the most commonly employed HIIT protocols within studies in this review employed 10 intervals of 1-minute with 1-minute rest periods in between (32,49,52,58,59,62,66,78) totalling a session duration of ~20 minutes. However, another frequently used HIIT protocol employed 4 intervals of 4-minutes high intensity work with 3 minute rest periods in between each bout, which led to sessions typically lasting >30-minutes (12,31,32,36,40,44,55,79) including a work duration of 16-minutes (vs. 10-minutes in the aforementioned example). Herein we show that, excluding warm-up and end of session recovery periods, median work duration during a HIIT session was half of that for MCT protocols (16-minutes vs. 30-minutes). In addition, a number of studies in this review (34,41,42,46,48,49,51,53,54,58–63) used low volume HIIT protocols, involving 10 minutes (or less) total work duration (80). Indeed, CRF improvements have been shown in as little as ten percent of the training volume with HIIT when compared to MCT (81). Taken in combination, reductions in regime duration, total volume of training and weekly time commitment represent important drivers for enhancing adherence and reducing costs associated with patient training. However, further work is required to elucidate the optimal work-to-rest ratios within HIIT protocols, which may further reduce the total time commitment for the individual. It is also worth noting whilst the majority (>90%) of studies within this review utilised a static cycle-ergometer for HIIT other training modalities (e.g. running) maybe viable. However further work is needed to assess the efficacy and tolerability when compared to cycle ergometry within certain patient groups.

Quality of life and mood outcomes analysed in this review were pre-to-post training program questionnaires; mostly global QoL scores or disease specific questionnaires. These outcomes are not specific enough to draw conclusions as to whether individuals preferred HIIT or MCT. However as there were no significant differences in the number of non-compliers, adherence to scheduled sessions (See Table, Supplementary Digital Content 6) or reported serious adverse events leads us to believe that neither HIIT nor MCT are inferior for enjoyment, acceptability or safety when compared.

Limitations

The studies in this review have a high risk of bias, some of which is unavoidable because of the nature of exercise intervention studies and the inability to blind participants (See Figure, Supplementary Digital Content 3, which shows risk of bias summary chart). There is also a risk of contamination between HIIT and non-intervention controls. In addition, heterogeneity amongst HIIT protocols, training duration, chronological age and pathology leads to uncertainty about the true effectiveness of interventions (82) (See Tables, Supplementary Digital Content 1, 2, 7 and 8, which show paper characteristics and training protocols / durations).

Conclusions

We have shown that HIIT leads to clinically significant improvements in CRF within 8 weeks in patients with disease, when compared to no intervention. HIIT also resulted in statistically significant improvements in CRF compared to MCT, with clinically significant benefit seen in cardiovascular patients. Due to the reduced exercise volume and improved efficacy (versus MCT) in certain clinical groups, HIIT can be promoted as a viable clinical exercise intervention to rapidly improve CRF.

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Figure Captions:

Figure 1: PRISMA Flow Diagram

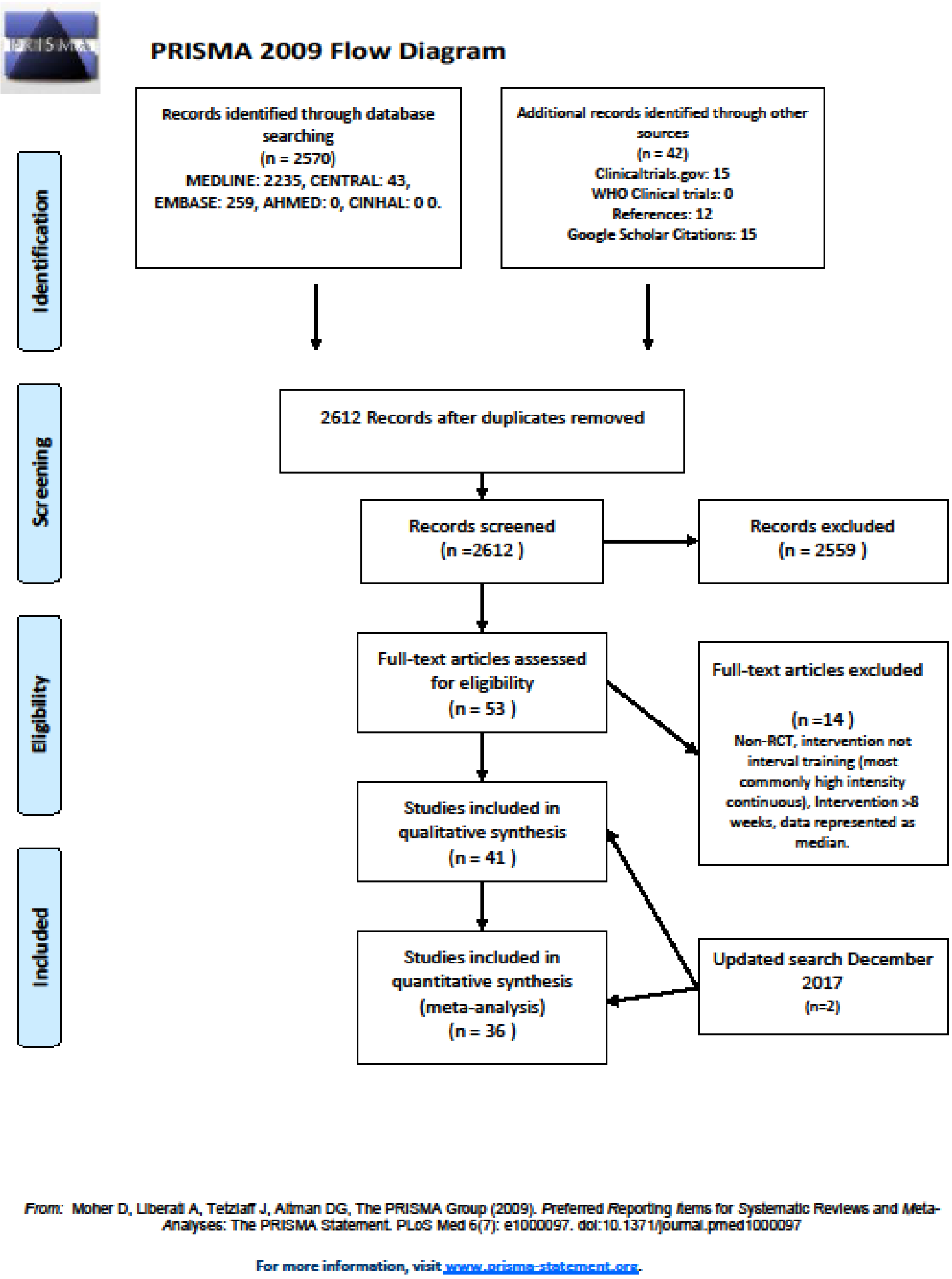

Figure 2: Forest plot showing meta-analysis of VO2peak data for HIIT vs CON (WMD ml·kg^{-1}·min^{-1}). Diamonds to the right of the plot show benefit with HIIT.

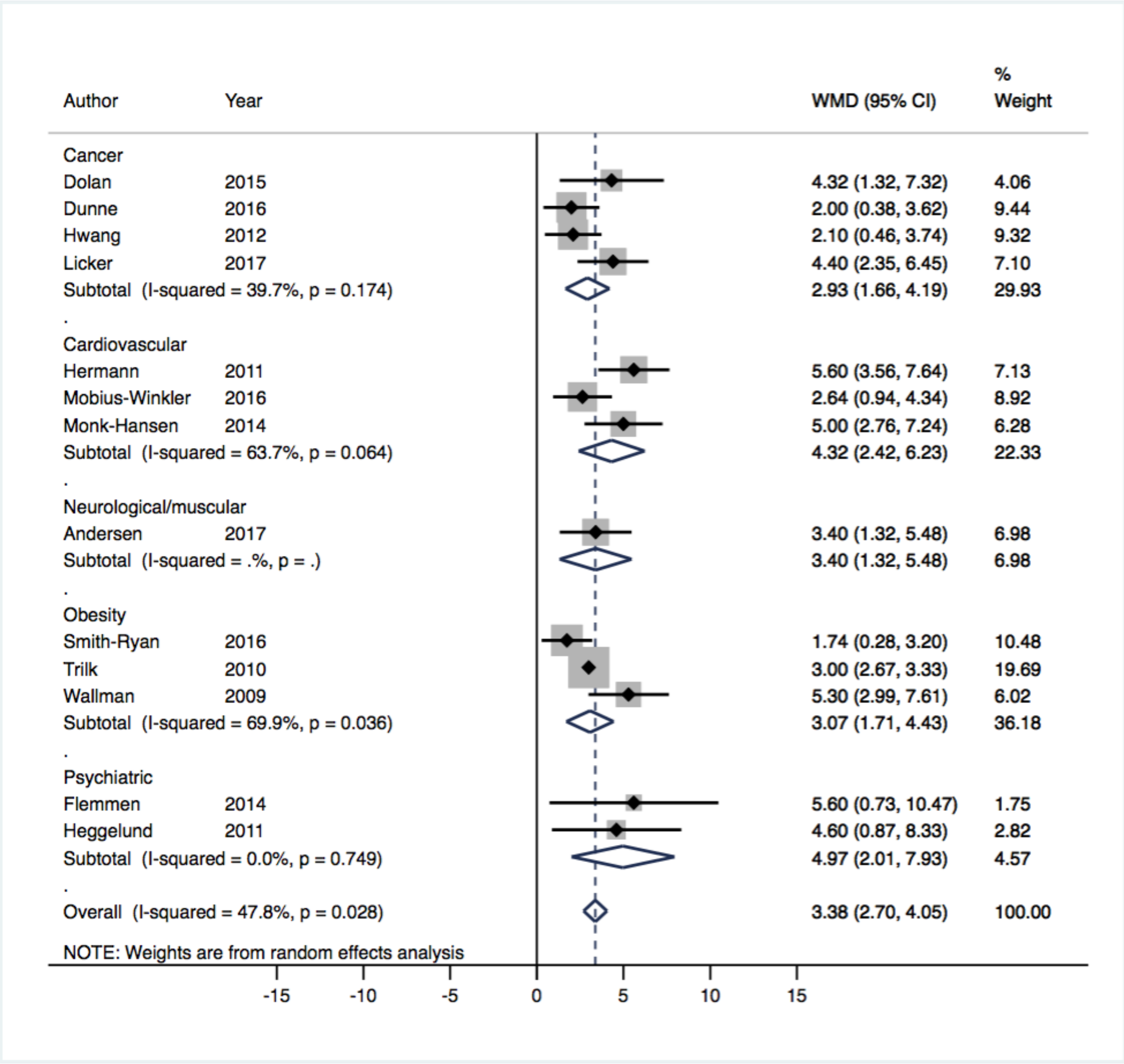

Figure 3: Forest plot showing meta-analysis of VO2peak data for HIIT vs MCT (WMD ml·kg^{-1}·min^{-1}). Diamonds to the right of the plot show benefit with HIIT.

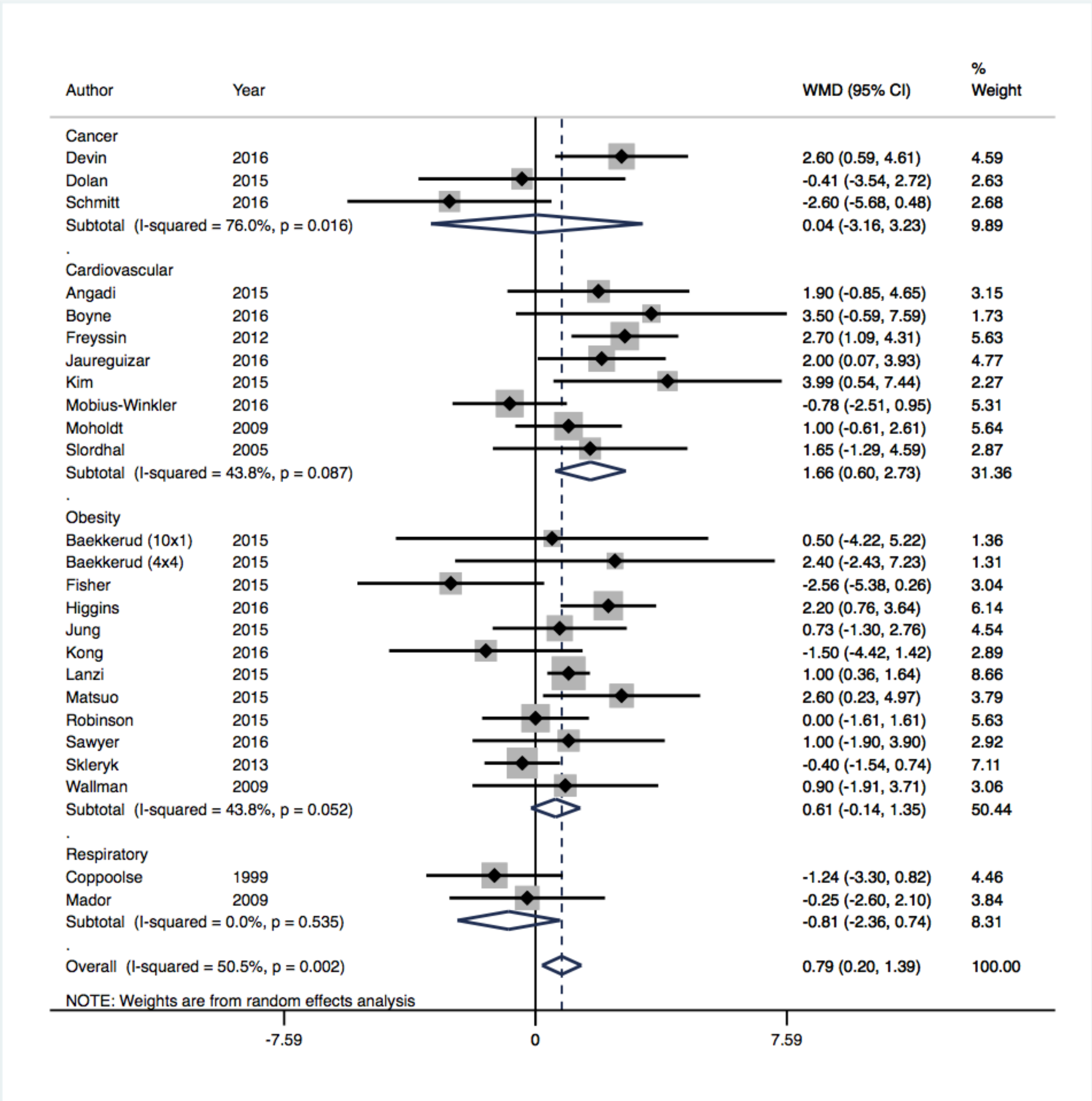

Figure 4: Forest plot showing meta-analysis of AT data for HIIT vs MCT (WMD $ml \cdot kg^{-1} \cdot min^{-1}$). Diamonds to the right of the plot show benefit with HIIT.