Rationale and optimising of outcomes in high-intensity interval training for health and disease

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Abstract High-intensity interval training (HIIT) research has drastically increased globally in the last decade. This might be owing to the application of HIIT in various fields such as among cardiovascular disease and cancer populations, and its increasing popularity in the media and fitness industries. It is crucial to realize the substantial benefits of HIIT, keeping safety in mind, for these target groups. In this narrative review, HIIT is discussed from multifaceted perspectives. First, I describe the rationale behind the improvement in aerobic and metabolic capacity with HIIT requiring less time compared to moderate-intensity continuous training, as well as the enjoyable and affective factors and the broad applicability of HIIT due to the “relative” high-intensity training. Second, I describe ways to maximize the effects of HIIT, which include optimising a potential genetic factor in HIIT responder, decreasing non-responders by attaining a targeted intensity, and adhering to the exercise intensity and unsupervised long-term participation. Recent development of HIIT/sprint interval training protocols and several unique clinical studies in the world have helped overcome the barriers against high adherence. Finally, safety and potential risks were only discussed briefly due to insufficient available data. In conclusion, to utilise the benefits of HIIT effectively and safely for unfit subjects with lifestyle-related and chronic diseases, optimising HIIT protocols to include high adherence to exercise intensity and long-term participation should be considered.

Keywords: HIIT, sprint interval training, cardiac, health, chronic disease, safety

Introduction

The number of published papers on research of “high-intensity interval training” (HIIT) has dramatically increased globally in the last decade according to PubMed search results (Fig. 1). Numbers have increased in Japan and globally, following a similar trend, with the increasing popularity of HIIT among physically active individuals1. This positive trend might partly reflect the increase in research conducted in fields that have adapted HIIT.

Since 1990, HIIT has been adapted for individuals with obesity, sedentary, and cardio-metabolic risk factors1, as well as those with cardiovascular diseases such as ischemic heart disease (angina pectoris and old myocardial infarction [MI]) and chronic heart failure (CHF)3-5. In the last decade, HIIT has also been applied to patients with other chronic diseases such as cancer6-7, cerebral or cognitive disorders8, and mental disorders (particularly depression)9,10. This universal application11 might lead to the increase in the volume of published literature on HIIT.

The American College of Sports Medicine (ACSM)’s Health & Fitness Journal12 presents the annual results of its worldwide fitness trends survey, in its 14th year in 202013.

Over 3,000 health and fitness professionals ranked 38 possible trends on a scale of 1 (least likely to be a trend) to 10 (most likely to be a trend). Number 1 (since 2016) was wearable technology and number 2 (in the top 5 between 2014 and 2020) was HIIT. Despite warnings by some fitness professionals of increased injury rates during HIIT, this form of exercise has been popular in gyms all over the world. As in the past, the results of this annual survey will help the health and fitness industry to make some important decisions regarding future growth and development. The media also present HIIT as an alternative means by which individuals achieve health benefits similar to those of moderate-intensity continuous training (MICT)13. The popularity of HIIT in the community and industry might be related to its development in academic societies.

HIIT was introduced in the first half of the 20th century and often used during military training. In addition, it was credited for impressive performances at the Olympic Games by athletes. Paavo Nurmi, a Finnish middle- and long-distance runner, used fartlek training as a prototype of HIIT and won nine gold and three silver medals for his 12 events in the Olympic Games. One of the most renowned Olympic medallists is Emil Zatopek, a Czechoslovak long-distance runner who adopted interval training and won 3 gold medals (5,000 m, 10,000 m, and mara-
thon) in the Helsinki Olympic Games of 1952. Since then, HIIT has been used in many events of athletic sports, followed by applications of HIIT in health development and disease treatment. It is notable that HIIT can be applied to universal individuals in two extreme polar fields: in top athletic performance and in advanced cardiac disease management. In this narrative review, I give an overview of the current global trends and highlight issues regarding the rationale and optimisation of HIIT for health and disease.

**Latest adaptation of HIIT exercise to wider medical/social fields**

People with lifestyle-related and chronic diseases and/or older people are often physically unfit and may have cardiovascular risks. Thus, some effective techniques and attention to an individual’s condition are required when encouraging exercise training with adequate safety and high adherence, considering the existing limitations. Physical exercise offers preventive treatment effects, as well as numerous health-related benefits, for individuals with cancer. Epidemiological research has primarily been concerned with conventional exercise training that aligns with the recommendation of 150 min of moderate to vigorous physical activity per week. This recommendation is safe and effective at improving physical and psychosocial outcomes. Recently, researchers have begun to explore HIIT as a novel training regimen that may provide additional health benefits and/or improved adherence even for cancer. Specifically, exercise at higher intensities may offer more or different benefits than conventional training approaches, with potentially profound effects on the tumour microenvironment. The increasing body of research can be divided into 3 groups: preoperative care, during chemotherapy, and primary and secondary prevention. The main target cancers that have been reported so far include lung (non-small cell), breast, prostate, and colorectal cancers. In preoperative care, HIIT was used to improve cancer-related fatigue during a short period (as short as 3 weeks) of permitted time frame for preparation of operation. During chemotherapy, a randomised control trial (RCT) showed the beneficial effects of HIIT in cancer-related fatigue and quality of life compared to control (usual care), but similar to the MICT group. Therefore, future research should consider a standardised approach, implementation in cancer types across different delivery timings, and safety and feasibility in unsupervised settings.

**Terminology of HIIT: its wide utilisation**

A wide range of terms have been used in fitness and health research fields to describe various interval training protocols, which have led to many acronyms without general standardisation in the scientific literature to date. Interval training can be broadly categorised into two main types: aerobic-based and resistance-based. Aerobic-based interval training generally involves exercises that engage a large mass of muscles (e.g. cycling, running, swimming), performed with variable intensity, which improve cardio-respiratory fitness (CRF) and cardiometabolic parameters. This type of interval training includes the following: (1) HIIT involving vigorous but submaximal effort, in which the relative intensity during the intervals usually elicits ≥ 80–90% of maximal heart rate (HRmax) or > 70–80% of maximal oxygen uptake (VO2max) (2) sprint interval training (SIT) involving “all out” or “supra-maximal” (at least > 100% VO2max) effort, in which the absolute workload or speed exceeds that which would elicit VO2max; and (3) less demanding types of intermittent exercise, typically characterised by alternating periods of light and moderate exercise (e.g. interval walking). Common examples of HIIT and SIT are gym-based ergometers or treadmills and Wingate test or Tabata-style intervals, respectively. During the acute and chronic phases of cardiac rehabilitation (CR), some patients with very low capacity need to split the low- to moderate-intensity continuous training to perform physical training according to their physical capacity. This is also called HIIT in patients with advanced heart failure.

**Rationale of HIIT as a training protocol**

Recently, due to the effectiveness and “superiority” of HIIT, it has been purported as a time-saving alternative to “traditional” MICT in CR and other target fields described previously. However, the rationale for HIIT adoption is not fully substantiated in the scientific literature. In this section, potential protocols with explanation of the rationale for adopting HIIT are explored.

**Peak oxygen uptake (VO2peak) and long-term prognosis.**

Accumulated evidence suggests that VO2peak is the strongest predictor of future health, all-cause/cardiovascular mortality, and cardiovascular risks. Moreover, previous studies have suggested that even people with established cardiovascular disease (CVD) risk factors or chronic diseases can attenuate the risk of CVD and premature mortality if they obtain high VO2peak. Thus, it has become a major goal in fitness and medical fields to improve VO2peak in patients with lifestyle-related diseases with or without cardiac disorders, as a primary or secondary prevention strategy. The main benefits of HIIT that have been reported are higher or at least similar levels of VO2peak improvement within a shorter period compared to MICT, as shown by many studies that targeted a variety of participants including sedentary and older individuals and those with obesity, metabolic syndrome, diabetes, and cardiac diseases. Therefore, HIIT could be a first-line choice of exercise that is used as therapy and not merely as a training regimen.

Furthermore, HIIT improves cardiac performance, met-
abolic and vascular function such as insulin resistance, and endothelial function in clinical conditions\textsuperscript{5}. SIT has also been reported to have effects similar to those of MICT\textsuperscript{49}).

**Promising way to maintain high VO\textsubscript{2peak} in less time, but with comparable health benefits.** Considering the prognostic value of changes in VO\textsubscript{2peak}, it is important to know how to effectively improve VO\textsubscript{2peak}\textsuperscript{44}). Traditionally, endurance exercise training (ET) that improves health-related outcomes has consisted of low- to moderate-intensity training. MICT remains the gold standard recommendation in several guidelines\textsuperscript{55-57}. However, a growing body of evidence suggests that HIIT has been recognised as an alternative, which is more time-efficient and a more enjoyable protocol than MICT\textsuperscript{48}). The ACSM also assessed HIIT for cardio-metabolic disease prevention\textsuperscript{1}.

**High intensity in HIIT is “relatively” high intensity.**

HIIT should not be easily excluded in individuals who are sedentary or older or have a chronic disease or complications with cardiovascular diseases due to reasons that they are unfit and have risks. Although HIIT intrinsically includes “high”-intensity intervals, this “high” level is a relative one calculated based on the individual baseline fitness level (estimated by VO\textsubscript{2peak} and HR\textsubscript{peak}) in each participant (Fig. 2). That is, HIIT should not be operated as a one size fits all protocol but as a finely tailored one. As an extreme case, critically ill cardiac patients with a left ventricular assistance device could undergo HIIT in CR with inotropic agents\textsuperscript{20}. Thus, two subjects exercising next to each other may look very different, one running very fast and the other walking, even when they both are exercising at the same relative intensity\textsuperscript{44}) (Fig. 2). The differences stem from different CRF levels, but they would be experiencing the same relative exercise stress. From a practical point of view, it has been pointed out that in severely deconditioned patients, as in those with heart failure, the normal PA of daily living actually corresponds to high-intensity ET. Hence, using the same intensity during structured ET may, in a short period of time, increase these patients’ CRF level, making daily tasks less strenuous\textsuperscript{44}). Thus, HIIT can be adapted to a wide range of clinical conditions after appropriate clearance.

**Enjoyable protocol.** An increase in enjoyment during exercise has also been suggested as a rationale of adopting HIIT as a training protocol\textsuperscript{48}). By contrast, MICT has been rendered as a monotonous and boring protocol\textsuperscript{48}). However, there are controversies regarding this matter. The level of “enjoyment” of all of the 3 protocols (MICT, HIIT and SIT) declined over the duration of the study\textsuperscript{49}). The insufficiently active group displayed lower affective responses over time (sessions 4 to 10) than the active group to the low-dose HIIT protocol\textsuperscript{45,50}). Sagelv et al. examined exercise enjoyment following one session of 4 × 4 min HIIT and 45 min MICT. The participants reported a higher rating of perceived exertion (RPE) in the HIIT session compared to the continuous endurance session, yet also reported equal enjoyment\textsuperscript{49}). A systematic review showed that although HIIT exercise may be recommended for obtaining positive psychological responses in the acute phase, chronic studies should clarify the applicability of HIIT for exercise adherence\textsuperscript{52}). SIT, an all-out and more strenuous exercise than HIIT, might be inappropriate for a largely sedentary population due to the generation of aversive feelings\textsuperscript{53}).

**Optimising outcomes in HIIT**

There are large inter-individual differences among exercise training responses\textsuperscript{44}). One method for optimising the exercise benefit is to decrease the ratio of non-responders in the corresponding exercise programs. Several factors that affect the response to exercise could be considered.

**Responder/non-responder to the exercise: genetic matter.**

Genetic factors have been proposed from various points of basic and clinical research\textsuperscript{55-57}) regarding the response to exercise. In the HERITAGE (HEalth, RIsk factors, exercise Training And GEnetics) Family Study revealed that the trainability of VO\textsubscript{2max} is highly familial and includes a significant genetic component\textsuperscript{49}). By contrast, Bonafiglia et al. revealed in a randomised crossover study design that the individual response to exercise training is highly variable following different training protocols and that the incidence of non-response to exercise training may be reduced by changing the training stimulus for non-responders to three weeks of endurance training\textsuperscript{50}). This study suggested that the existence of true non-responders to exercise training is unlikely and that different training protocols should be considered when optimising individual exercise prescriptions. Treating genetic disadvantages is not realistic; therefore, the most efficient exercise mode should be explored for each participant.

**Importance of high intensity in the HIIT protocol to decrease non-responders.** One in five adults, following physical activity (PA) guidelines, are reported to not demonstrate any improvement in CRF\textsuperscript{50}). Seventy-eight healthy adults were divided into five groups comprising one, two, three, four, and five 60-min exercise sessions per week, respectively, but otherwise following an identical 6-week endurance training programme. The prevalence of CRF non-response gradually declined exercising by 60, 120, 180, 240, or 300 min (1–5 times of 60-min workouts a week) for 6 weeks. In participants exercising for 240 or 300 min, there were no non-responders. However, with 60, 120, or 180 min, there were non-responders. Following a successive identical 6-week training period but comprising 120 min of additional exercise per week in these groups, CRF non-response was universally
abolished. The potential for CRF improvement may be present and unveiled with appropriate exercise training stimuli in healthy individuals without exception\(^{(40)}\). This study showed that total exercise amount per week might be related to increased response in endurance training. On the contrary, a high intensity was important in the following studies. In a study by Ross et al., abdominally obese participants were randomly assigned to (1) low-amount, low-intensity exercise (LALI), (2) high-amount, low-intensity exercise (HALI), or (3) high-amount, high-intensity exercise (HAHI)\(^{(41)}\). At 24 weeks, 38.5\%, 17.6\%, and 0\% of the participants within the LALI, HALI, and HAHI groups, respectively, were CRF non-responders. At a fixed exercise intensity, increasing exercise amount reduced the rate of non-response by 50\%. At a fixed amount of exercise, increasing the exercise intensity eliminated non-response. Low-intensity exercise may not be sufficient to improve CRF for a substantial proportion of sedentary obese adults. In this context, HIIT could be more beneficial than MICT to optimise the outcome. However, even in HIIT, the actual intensity during intervals should be higher to obtain more benefits. Moholdt et al. assessed the impact of exercise intensity during HIIT on the increase in VO\(_{2\text{peak}}\) among patients with coronary artery disease (CAD) for 12 weeks\(^{(42)}\). The increase in VO\(_{2\text{peak}}\) for the three intensity categories were 3.1, 3.6, and 5.2 mL/kg/min for the <88\%, the 88–92\%, and the >92\% of HR\(_{\text{max}}\) categories, respectively. Thus, even within the high-intensity training zone, exercise intensity was an important determinant for improving VO\(_{2\text{peak}}\).

**Learning from multicentre RCTs comparing HIIT and MICT with negative results in CR.** Less workout time with identical total energy expenditure for more gain has been the main rationale of HIIT protocol compared to MICT even in patients with cardiac disease and cardiometabolic risk factors. This has been proven to be true in multiple single-centre RCTs\(^{(43-45,63-67)}\) and meta-analyses\(^{(48,49)}\). However, two multicentre RCT studies\(^{(50,71)}\) that compared an increase in VO\(_{2\text{peak}}\) between HIIT and MICT in patients with CAD (multicentre study on aerobic interval exercise training in CAD: SANITEX-CAD)\(^{(50)}\) and CHF (study of myocardial recovery after exercise training in heart failure: SMARTEX-HF study)\(^{(71)}\) showed negative results in the superiority of HIIT in VO\(_{2\text{peak}}\) improvement. These studies have highlighted the challenges of the practical feasibility of HIIT in CR\(^{(40)}\). In particular, adherence to ET intensity and continuously increasing ET workload throughout the ET period may seem challenging in multicentre studies\(^{(40)}\). Analyses of these results clarified the issues of adherence to exercise intensity in both HIIT and MICT groups. In these studies\(^{(50,71)}\), it is unknown if there were peripheral limitations to ET, such as a high degree of muscle wasting, and limitations in patients’ ability to exercise at a high intensity; however, a large overlap in ET intensity between HIIT and MICT groups was seen in both studies and could be a key factor explaining no difference between the groups\(^{(40)}\). That is, the intensity was lower than expected in the HIIT group, and by contrast, higher in the MICT group. There might have been a variance in practical techniques (tips) to yield optimal gain by pursuing intensity among the participating institutions. The low feasibility to ET intensity prescription in HIIT could also be due to the patients’ ability and/or motivation to exercise at a high intensity or the challenges of implementing the ET program in a multicentre setting.

Another indispensable factor for exercise response to occur over time is the principle of increasing exercise workload as training adaptation progresses\(^{(48,63)}\). The increased workload seems to be greater in single-centre studies than in RCTs. The increased workload per session was 0.83 and 2.6 W in MICT and HIIT, respectively, in a single-centre study\(^{(4)}\). Similarly, in another single-centre study, it was 1.2 and 1.7 W in MICT and HIIT, respectively\(^{(72)}\). Meanwhile, it was 0.28 and 0.42 W in MICT and HIIT, respectively, in the SMARTEX-HF study\(^{(51)}\) and 0.97 and 1.05 W in MICT and HIIT, respectively, in the SAINTEX-CAD study\(^{(70)}\). These might have affected the extent of increase in VO\(_{2\text{peak}}\) and the difference in VO\(_{2\text{peak}}\) increase between HIIT and MICT protocols. The practical implications of the findings may be to keep a combined focus on both target ET intensity\(^{(40)}\) and continuous progress in ET workload to secure sufficient relative exercise intensity as VO\(_{2\text{peak}}\) improves throughout the exercise period\(^{(40)}\).

In patients with CAD, coaching in combination with use of heart rate (HR) monitors is necessary to achieve exercise within a target HIIT intensity zone. Without active coaching, patients tend to exercise below the lower limit of target HR (85\% of HR\(_{\text{peak}}\)), despite the use of HR monitors and a knowledge of target intensity. This may indicate that the implementation of HIIT might be more difficult than previously predicted. In addition, several of the previous single-centre studies have been performed using treadmill exercise\(^{(2,41,63,67)}\), while a majority of the patients in multicentre studies\(^{(50,71)}\) used cycling as the mode of ET. The effect of cycling versus walking or running during HIIT thus needs to be further addressed, with potential differences in societies with a population more familiar with cycling, as opposed to those less trained with cycling exercises\(^{(50)}\).

Although there was no significant difference in improvement in VO\(_{2\text{max}}\) and left ventricular remodelling, Karlsen et al. evaluated the predictors of good response in the SMARTEX-HF study\(^{(51)}\). Their analyses suggested that age, left ventricular ejection fraction, New York Heart Association classification, and the ability to improve VO\(_{2\text{peak}}\) might be considered when giving exercise training advice and evaluating exercise response in heart failure with reduced ejection fraction (HFrEF) as a data point to a gradient toward a poor exercise response in the oldest and most symptomatic HFrEF patients\(^{(51)}\).
Practical issues in improvement of adherence to HIIT

Karlsen et al. proposed the key practical considerations for successful clinical and home-based HIIT. Based on their clinical experience, they emphasised the importance of appropriate warm-up, adjustment of exercise workload, and use of both the Borg scale and correct measurement of HRpeak. Furthermore, guidelines for the delivery and monitoring of HIIT in a clinical population would be beneficial for health personnel who are inexperienced in HIIT prescription.

Protocol development to overcome barriers to exercise.

A 4 × 4-min HIIT is a globally well-known protocol that has been utilised for health and disease treatment and is adaptable to older people and to people with cardiovascular diseases. This protocol was adopted in two randomised multicentre studies in Europe to evaluate the efficacy of HIIT compared to MICT for CHF in CR based on accumulated evidence. However, a 4 × 4-min HIIT takes at least 35 min including warm-up and cool-down and might need a pre-training period before adopting a 4 × 4-min protocol in sedentary participants.

The most common external barrier among the middle-aged and elderly respondents was “not enough time” (46.7% and 48.4%, respectively); meanwhile, the most common internal barrier among middle-aged and elderly respondents was “too tired” (48.3% and 51.7%, respectively in a cross-sectional study. Thus, the reasons for nonparticipation in exercise could be multi-factorial.

More sophisticated exercise protocols would be expected to spread HIIT and SIT in wide target populations. In this regard, somewhat complicated, but participant-friendly, HIIT training regimens have been developed for targets with specific clinical/social subsets. To overcome the feeling of difficulty experienced during the 4 × 4-min protocol by sedentary or older individuals, a finely-tuned HIIT protocol, in which the frequency, workload, and work duration are initially set at low levels and altered during the training course, has been reported. The Japanese version of the High-intensity Interval Aerobic Training (J-HIAT) program is composed of 3 sets of 2–3 min cycling at vigorous intensity (first and second sets: 3 min at 85%–90% VO2peak; third set: 3 min at 80%–85% VO2peak) with 2-min active rest at 50% VO2peak between each set (healthy, but sedentary young 20–30-year-old adults). This protocol was originally developed to control energy expenditure for astronauts participating in long-term space missions and showed more VO2max increase than MICT when applied for 8 weeks, 3 days a week, as a supervised exercise intervention with even lower energy expenditure. The J-HIAT protocol has been successfully modified for older adults (aged 60–69 years) by the same group as EJ-HIAT (The elderly Japanese male version of High-intensity Interval Aerobic Training) with 3 sets of a little lower intensity (0–10% VO2max) and shorter duration (0–1 min) depending on the 1st–3rd bout, than those of J-HIAT. A significant aerobic and metabolic response was attained by the shorter protocol than by the 4 × 4-min protocol, with a completion rate of 100%.

Growing evidence suggests that low-volume HIIT stimulates physiological remodelling comparable to MICT despite a substantially lower time commitment and reduced total exercise volume, suggesting its importance from a public health perspective, when considering that “lack of time” remains one of the most commonly cited barriers to regular exercise participation.

SIT, which takes less training time, has been reported to be as efficient as MICT in improving VO2peak. On the contrary, SIT might be inappropriate for a largely sedentary population because SIT is a strenuous “all-out” protocol. High RPE of SIT, even with a very short time bout, might cause disinclination (dislike) due to fatigue and discomfort, leading to low long-term adherence. SIT could be more time-efficient than 4 × 4-min HIIT; however, the total time commitment would still be long due to the longer rest time of SIT than that of HIIT, with a total time commitment of 30 min including rests between bouts, warm-up, and cool-down. Considering this background, the concept of low-volume SIT was developed recently. One possible alternative strategy could be to define the minimum volume of exercise required to improve health indices with the aim of increasing exercise adherence. Vollaard et al. reviewed SIT protocols with the shortest duration and least amount of work. They also constructed a modified SIT aiming for the most time efficient and effective protocol with high adherence for sedentary subjects and diabetic patients. To date, this training protocol, named reduced-exertion HIIT (REHIT) (10-min SIT sessions, 3 sessions a week for 6 weeks, involving only two 20-s Wingate sprints), represents the smallest volume of exercise (per session) that has been shown to induce positive effects on health. This protocol was sufficient to improve VO2max by 10%–13%,

Vollaard et al. also found that after performing only two maximal sprint intervals, each additional sprint in a training session reduced the overall improvement in fitness by around 5%. This result might raise questions about the previously held “common sense” idea that performing more repetitions of high-intensity exercise would produce greater improvements in CRF. The effects of the REHIT protocol were confirmed by other groups of patients with type 2 diabetes mellitus and metabolic risks. The main finding of this study was that 8 weeks of REHIT elicited more potent and time-efficient improvements in CRF and cardiometabolic health compared to traditional MICT in work place settings. REHIT was also effective with two sessions/week in improving health in the workplace under unsupervised conditions, showing the most effectiveness in a dose-response relationship. It was shown that one session of REHIT elicits positive affective
valence and similar pleasure: displeasure and enjoyment responses in adults having diverse CRF in an untrained population\(^{48}\). The exercise intervention was delivered on a commercially available cycle ergometer (CAR.O.L., Integrated Health Partners Ltd, London, UK) which can be delivered unsupervised. The exercise VO\(\text{max}\) significantly improved in the exercise group (+7.4%) compared to the control group (−2.3%). Participants considered the REHIT intervention acceptable and enjoyable and were confident in their ability to continue to perform REHIT. REHIT could be a promising low-dose SIT even for an untrained and unfit population with potential long-term adherence.

Two groups developed the SIT protocols for sedentary older individuals\(^{99,100}\). Although the number of participants was small, these protocols were well tolerated and showed no adverse events. These studies might show the potential of SIT for older adults in the future.

It might be beneficial to listen to music during SIT. Stork et al. determined whether listening to self-selected music can reduce the potential aversion to an acute session of SIT by improving affect, motivation, and enjoyment, and to examine the effects of music on performance\(^{101}\). Peak and mean power output, RPE, affect, task motivation, and perceived enjoyment of the exercise were measured during four 30-s “all-out” Wingate Anaerobic Test bouts. Music enhanced in-task performance and enjoyment of an acute bout of SIT.

**Improved adherence to non-supervised high-intensity session participation after lab-/gym-based HIIT.** One of the important aspects of HIIT/SIT is the long-term maintenance of protocols in a non-supervised way. Although lab-/gym-based training would be desirable in terms of efficacy and safety, future studies should explore long-term adherence\(^{102}\). Some feedback on long-term adherence has already been accumulated from recent studies.

**Long-term follow-up after CR.** For home-based training (following a supervised period), HIIT, compared to MICT, has resulted in greater exercise adherence in the long-term (30 months) following CR\(^{103}\). Aamot et al.\(^{104}\) showed long-term adherence (1 year), which was evaluated by estimating change in VO\(\text{peak}\) and self-reported objectively measured physical activity in a multicentre randomised study. There was no significant difference between home-based and lab-based (treadmill or group exercise) 12-week HIIT CR. This result implies that the 12-week HIIT protocol experience has the potential to improve long-term adherence to PA regardless of whether it is home-based or lab-based.

**The Generation 100 study: 1-year follow-up\(^{17}\).** Understanding how exercise participants prefer to exercise may help in developing tailored exercise programs and increase sustained exercise participation in populations without an exercise habit. In the Generation 100 study, which was an epidemiological study, frequency, intensity (HIIT or MICT), type (running or cycling), location (indoor or outdoor), and social setting (alone vs. together with others) of exercise were assessed using exercise logs recorded after each exercise session from 618 older adults (aged 70–77 years) randomised to MCT or HIIT over a one-year period\(^{17}\). Approximately 300 healthy older adults, with some initial instruction and a few sessions of supervised training, showed good adherence to unsupervised HIIT over the course of one year, meeting the goal of averaging two sessions per week. Exercise logs were kept to evaluate adherence to the protocol, the level on an RPE scale, and location and mode of performance based on personal preferences (Fig. 3). This novel information may help researchers and clinicians to develop tailored exercise programs in an ageing population.

**High-intensity stair climbing.** Allison et al. showed that all-out cycling could be substituted by the stair climbing as an alternative exercise mode\(^{105}\). This method could be a practical one as it can be applied easily in daily life anywhere, such as in the buildings and subway stations. Danford et al. adapted this type of low-dose HIIT as an unsupervised CR for patients with coronary artery disease, in comparison to MICT\(^{106}\). In this study, after 1 month of a supervised protocol (two times/week), participants performed unsupervised SIT for two months (three times/week) with no difference in exercise intensity (96 ± 8% vs. 87 ± 8% of HR\(\text{peak}\)) or number of exercise sessions/week (3.0 ± 3.2 vs. 3.2 ± 2.2) between the high-intensity stair climbing and MICT groups.

**The Norwegian Trial of Physical Exercise after Myocardial Infarction (NorEx).** Maintaining high PA or having a long-term increase in PA from before to after MI was associated with a lower post-MI risk of all-cause and CVD mortality\(^{107}\). Despite the substantial evidence for the benefits of CR, only a small percentage of patients with MI are referred to, participate, or complete CR programs in the inpatient and home health setting\(^{108}\). NorEx is a registry-based multicentre RCT across Norway, which is the largest exercise intervention ever performed for secondary prevention and rehabilitation of patients who have suffered MI\(^{109}\). The research involves ensuring exercise adherence of approximately 4,500 participants over a period of four years. The primary objective is to determine the efficacy of physical exercise using the personality activity intelligence (PAI) system\(^{110,111}\) and a two-way communication system (coach-patients-study administration) on mortality and cardiovascular morbidity in patients with MI. PAI might have the potential to contribute to improvement in adherence to home-based training in CR, shedding new light on this medical field. PAI is a personalised metric developed for PA tracking with the aim to make it easier to quantify how much PA per
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Fig. 1 Literature search for “high-intensity interval training” by PubMed globally and in Japan. The number of articles has gradually increased both globally and in Japan. The total number is 2,857 globally and 94 in Japan through June 30, 2020. The increase is dramatic, particularly in the last decade. This increase might reflect the popularity of high-intensity interval training protocols in the general population and its wide adaptation across various fields.

Fig. 2 Relatively high intensity prescribed for two individuals in high-intensity interval training. This figure shows two individuals performing high intensity interval training (HIIT). They have different absolute peak heart rates (HRpeak) and energy consumption, but exercise at identical relative intensity (% of HRpeak). Red line: HIIT performed as 4 × 4 min of roller ski training by a highly trained Olympic athlete with an HRpeak of 188. Target HR zone is 169–179 beats/min (90–95% of HRpeak). Blue line: HIIT performed as 4 × 4 min of outdoor uphill walking by patient with coronary artery disease (CAD) with an HRpeak of 130. Target HR zone is 117–124 beats/min (90–95% of HRpeak).
Adapted from Karlsen T et al. Prog Cardiovasc Dis 2017; 60: 67-77.

Fig. 3 Representative 4 × 4 min of HIIT practice sessions in cardiac rehabilitation at St. Olav’s University Hospital and The Generation 100 Study in Trondheim, Norway.
A: Phase 2 cardiac rehabilitation at St Olav’s University Hospital in Trondheim. Participants can choose modes of exercise which they prefer during high-intensity interval training.
B: The Generation 100 Study (indoors).
C: The Generation 100 Study (outdoors). Participants run uphill during interval and walk or jog downhill during active rest.
D: The Generation 100 Study (outdoors). Borg scale measurements during exercise are kept between 16 and 18.
week is needed to reduce the risk of premature mortality from non-communicable diseases\(^\text{12}\). PAI can be used by integrating the individual’s gender, age, and resting time and HR\(_{\text{max}}\). Among individuals ranging from the general population to subgroups of patients with CVD, a PAI ≥ 100 per week at baseline, maintaining ≥ 100 PAIs and then increasing the PAI score over time, was associated with multiple years of life gained\(^\text{13}\). It is expected that PAI has the potential to contribute to improved adherence to home-based training in CR, shedding new light on this medical field. Furthermore, participants will be able to self-learn which intensity is necessary for which exercise duration by spending time using PAI. The dose and intensity of PA/exercise achieving 100 PAI depend on the individual baseline data, and change according to the updated HR data. As an example, 30 minutes of vigorous exercise per week yielded scores of 100 PAI, demonstrating that it is the most time-efficient method.

**Safety and risks of HIIT and SIT**

**HIIT.** There is little risk of HIIT for young adults without any known cardiac disease. By contrast, there is an understandable concern regarding the safety of HIIT in adults with known or occult CAD and/or CHF. At present, the evaluation of the safety of HIIT among adults with varied health and disease characteristics is compromised by the limited availability of relevant data, which is due to the low proportion of studies reporting adverse events\(^\text{14}\). There are limited data on safety regarding CR under supervision. In stable and selected patients in CR, HIIT/MICT can be performed with relatively low risk\(^\text{15}\). Rognmo et al. examined the risk of cardiovascular events during organised HIIT and MICT among 4846 patients with CAD in three CR centres\(^\text{16}\). One fatal cardiac arrest during moderate-intensity exercise (129,456 exercise hours) and two non-fatal cardiac arrests during HIIT (46,364 exercise hours) were reported. No myocardial infarctions were reported. These low event rates preclude a definitive quantitative determination of the risk associated with HIIT\(^\text{17}\). More recently, a systematic review examined the cardiovascular complications associated with HIIT in CR sites for patients with CAD or CHF\(^\text{18}\). Based on 23 studies involving 547 participants completing 17,083 HIIT sessions (equivalent to 11,333 training hours), there was only one major, non-fatal cardiovascular event. Another systematic review reported no deaths or cardiac events requiring hospitalisation among 465 HIIT patients and 488 MICT patients within a medically supervised CR setting\(^\text{19}\).

Meanwhile, a recent systematic review also evaluated the safety of HIIT among 156 patients with cardiometabolic disease and found the incidence of adverse acute responses within 24 hours post exercise, to a single session of HIIT to be around 8% and “mild in nature” and only “somewhat higher compared to previously reported risk during MICT”, and concluded that “caution must be taken when prescribing HIIT to patients with cardiometabolic disease”\(^\text{20}\).

Although HIIT appears to provide a time-efficient alternative to MICT, additional long-term studies assessing the safety of HIIT are needed before it can be widely adopted in individuals with known or suspected CAD, particularly in unsupervised, nonmedical settings\(^\text{21,22}\).

Currently, guidelines by Taylor et al.\(^\text{75}\) could help judge the adoption of HIIT among participants with clinical problems. These guidelines summarised the clinical considerations for HIIT based on ACSM and AHA statements, including an initial assessment\(^\text{23,24}\), absolute contraindications to participants\(^\text{11,19}\), monitoring checklist, and indications for avoiding/ceasing HIIT\(^\text{19}\). Medical clearance should be sought for all patients with clinical conditions from medical specialists or general practitioners and for patients after surgery or percutaneous coronary intervention, from the respective surgeon or interventionalist, prior to commencing HIIT\(^\text{75}\).

**SIT and low-dose/shorter SIT.** Systematic reviews on the safety and risk of injury for SIT are very limited\(^\text{25}\). Supra maximal sprints used in protocols such as the Wingate protocol are associated with blood pressure elevation, as well as blood flow increase, which could pose the risk of dislodging unstable plaque, potentially leading to acute MI\(^\text{26,27}\). Redistribution of blood flow (increased flow in muscle followed by decreased flow in visceral organs) also might pose a risk to patients with CVD and chronic kidney disease. However, to date, SIT has been adopted in healthy young people, irrespective of their athletic or sedentary lifestyle. For these subjects, the cardiovascular risk could be low due to the low incidence of hypertension and/or atherosclerotic disease. For individuals with lifestyle-related and/or cardiovascular disease, the potential risk of the SIT protocol has not been evaluated. Thus, for the time being, it should not be adopted for individuals with clinical issues without proper clearance\(^\text{18}\). Ruffino et al. investigated REHIT among 16 patients with type 2 diabetes, and neither risk nor cardiovascular event was reported\(^\text{28}\).

**Conclusions**

For generally unfit target populations, with lifestyle-related disease and/or chronic disease, to benefit from HIIT effectively and safely, the optimisation of HIIT protocols for adherence to high intensity and high participation rates during long-term use should be considered.

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**Conflict of Interests**

The author declares no conflict of interests.
Author Contributions

SI designed the study and collected and analysed the data. He also drafted and edited the manuscript.

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