

# Physiological adaptations to low-volume, high-intensity interval training in health and disease

Martin J. Gibala<sup>1</sup>, Jonathan P. Little<sup>2</sup>, Maureen J. MacDonald<sup>1</sup> and John A. Hawley<sup>3</sup>

<sup>1</sup>Department of Kinesiology, McMaster University, Hamilton, Ontario L8S 4K1, Canada

<sup>2</sup>School of Arts and Sciences, University of British Columbia Okanagan, Kelowna, British Columbia V1V 1V7, Canada

<sup>3</sup>Exercise Metabolism Group, RMIT University, Bundoora, Victoria 3083, Australia

**Abstract** Exercise training is a clinically proven, cost-effective, primary intervention that delays and in many cases prevents the health burdens associated with many chronic diseases. However, the precise type and dose of exercise needed to accrue health benefits is a contentious issue with no clear consensus recommendations for the prevention of inactivity-related disorders and chronic diseases. A growing body of evidence demonstrates that high-intensity interval training (HIT) can serve as an effective alternate to traditional endurance-based training, inducing similar or even superior physiological adaptations in healthy individuals and diseased populations, at least when compared on a matched-work basis. While less well studied, low-volume HIT can also stimulate physiological remodelling comparable to moderate-intensity continuous training despite a substantially lower time commitment and reduced total exercise volume. Such findings are important given that ‘lack of time’ remains the most commonly cited barrier to regular exercise participation. Here we review some of the mechanisms responsible for improved skeletal muscle metabolic control and changes in cardiovascular function in response to low-volume HIT. We also consider the limited evidence regarding the potential application of HIT to people with, or at risk for, cardiometabolic disorders including type 2 diabetes. Finally, we provide insight on the utility of low-volume HIT for improving performance in athletes and highlight suggestions for future research.

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**Corresponding author** M. J. Gibala: Department of Kinesiology, McMaster University, 1280 Main Street West, Hamilton, Ontario, L8S 4K1 Canada. Email: gibalam@mcmaster.ca

**Abbreviations** HIT, high-intensity interval training; PGC-1 $\alpha$ , peroxisome-proliferator activated receptor  $\gamma$  coactivator; PPO, peak aerobic power output.

## Introduction

High-intensity interval training (HIT) describes physical exercise that is characterized by brief, intermittent bursts

of vigorous activity, interspersed by periods of rest or low-intensity exercise. HIT is infinitely variable with the specific physiological adaptations induced by this form of

**Martin Gibala** (pictured) is Professor and Chair of the Department of Kinesiology at McMaster University. He studies the regulation of skeletal muscle energy metabolism including the impact of nutrition and training on exercise performance. **Maureen MacDonald** is also a Professor of Kinesiology at McMaster, where she studies the effect of exercise on cardiovascular regulation. **Jonathan Little** completed doctoral studies at McMaster and is currently a postdoctoral fellow at the University of British Columbia. **John Hawley** is Professor and Head of the Exercise Metabolism Group at RMIT University, whose focus is skeletal muscle energy metabolism related to exercise and diabetes.



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**Table 1. Summary of protocols in studies from our laboratory that directly compared 6 weeks of either high-intensity interval training (HIT) or traditional endurance training**

Variable	HIT group	Endurance group
Protocol	30 s × 4–6 repeats, 4.5 min rest (3 sessions per week)	40–60 min cycling (5 sessions per week)
Training intensity (workload)	'All out' maximal effort (~500 W)	65% of $\dot{V}_{O_{2peak}}$ (~150 W)
Weekly training time commitment	~10 min (~1.5 h including rest)	~4.5 h
Weekly training volume	~225 kJ	~2250 kJ

From Burgomaster *et al.* (2008).  $\dot{V}_{O_{2peak}}$ , peak oxygen uptake.

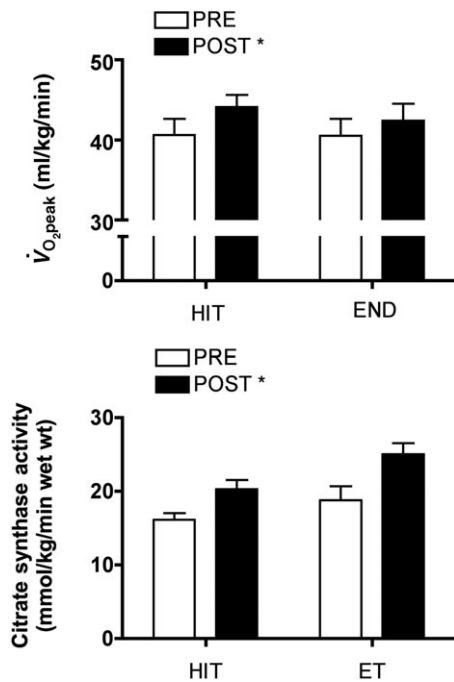
training determined by a myriad of factors including the precise nature of the exercise stimulus (i.e. the intensity, duration and number of intervals performed, as well as the duration and activity patterns during recovery). When compared on a *matched-work* basis or when estimated energy expenditure is equivalent, HIT can serve as an effective alternate to traditional endurance training, inducing similar or even superior changes in a range of physiological, performance and health-related markers in both healthy individuals and diseased populations (Wisloff *et al.* 2007; Tjonna *et al.* 2009; Hwang *et al.* 2011). Less is known regarding the effects of *low-volume* HIT, but growing evidence suggests this type of training stimulates physiological remodelling comparable with moderate-intensity continuous training despite a substantially lower time commitment and reduced total exercise volume (Gibala & McGee 2008). These findings are important from a public health perspective, given that 'lack of time' remains one of the most commonly cited barriers to regular exercise participation (Stutts 2002; Trost *et al.* 2002; Kimm *et al.* 2006). Moreover, recent evidence suggests that HIT is perceived to be more enjoyable than moderate-intensity continuous exercise (Bartlett *et al.* 2011). Here we review some of the mechanisms responsible for improved skeletal muscle metabolic control and changes in cardiovascular function in response to low-volume HIT, as well as the potential health-related implications for patients with chronic diseases including type 2 diabetes and cardiovascular disease. We also speculate on the practical application of low-volume HIT for elite performance. Although it is recognized that the underlying mechanisms are probably different compared with less-trained subjects (Iaia & Bangsbo 2010), responses in elite athletes may help our understanding of why low-volume HIT is such a potent exercise stimulus.

### Physiological remodelling after low-volume HIT

The most common model employed in low-volume HIT studies has been the Wingate test, which consists of a 30 s 'all out' cycling effort against a supra-maximal workload. Subjects typically perform four to six work bouts separated by ~4 min of recovery, for a total of 2–3 min of intense

exercise during a training session that lasts ~20 min. As little as six sessions of this type of training, totalling ~15 min of all out cycle exercise over 2 weeks, increased skeletal muscle oxidative capacity as reflected by the maximal activity and/or protein content of mitochondrial enzymes (Burgomaster *et al.* 2005; Gibala *et al.* 2006). We have also directly compared 6 weeks of Wingate-based HIT with traditional endurance training that was designed according to current public health guidelines (Table 1) (Burgomaster *et al.* 2008; Rakobowchuk *et al.* 2008). We found similar training-induced improvements in various markers of skeletal muscle and cardiovascular adaptation despite large differences in weekly training volume (~90% lower in the HIT group) and time commitment (~67% lower in the HIT group). In addition to an increased skeletal muscle oxidative capacity (Fig. 1), other endurance-like adaptations have been documented after several weeks of low-volume HIT including an increased resting glycogen content, a reduced rate of glycogen utilization and lactate production during matched-work exercise, an increased capacity for whole-body and skeletal muscle lipid oxidation, enhanced peripheral vascular structure and function, improved exercise performance as measured by time-to-exhaustion tests or time trials and increased maximal oxygen uptake (Burgomaster *et al.* 2005, 2008; Gibala *et al.* 2006; Rakobowchuk *et al.* 2008).

Wingate-based HIT is, however, extremely demanding and may not be safe, tolerable or appealing for some individuals. We therefore sought to design a more practical model of low-volume HIT that is time efficient while also having wider application to different populations including people at risk for chronic metabolic diseases. To accomplish this goal we decreased the absolute intensity of the work bouts, but increased their duration and shortened the rest intervals. Our new practical HIT model consists of 10 × 60 s work bouts at a constant-load intensity that elicits ~90% of maximal heart rate, interspersed with 60 s of recovery. The protocol is still time efficient in that only 10 min of exercise is performed over a 20 min training session. Importantly, this practical, time-efficient HIT model is still effective at inducing rapid skeletal muscle remodelling towards a more oxidative phenotype, similar to our previous Wingate-based HIT studies and



**Figure 1.** Peak oxygen uptake (top panel) and the maximal activity of the mitochondrial enzyme citrate synthase measured in biopsy samples (bottom panel) obtained before (PRE) and after (POST) 6 weeks of Wingate-based high-intensity interval training (HIT) or traditional moderate-intensity endurance training (ET)

Total exercise volume was 90% lower in the HIT group. Redrawn from Burgomaster *et al.* (2008) with permission. \*P < 0.05 vs Pre; main effect for time.

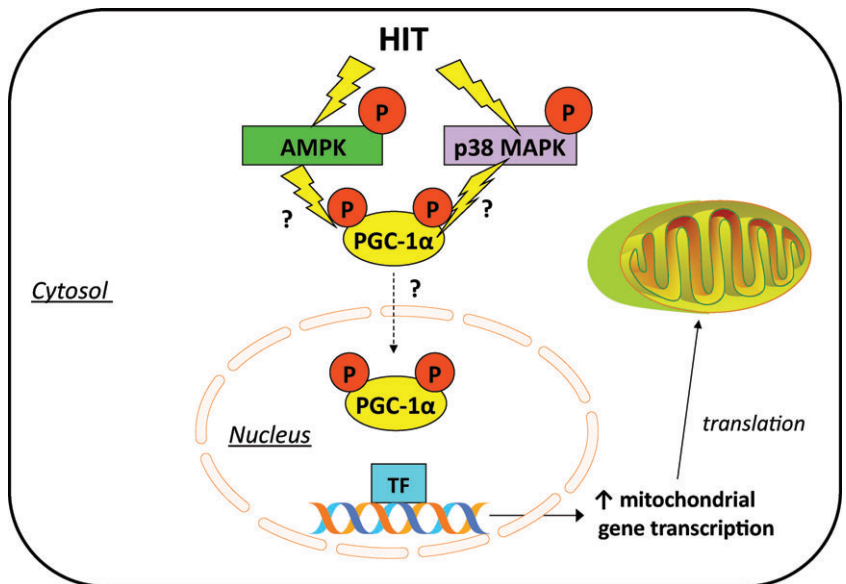
high-volume endurance training (Little *et al.* 2010b). Both types of low-volume HIT protocols are also effective for improving functional performance, as shown by cycling time trials that resemble normal athletic competition (Gibala *et al.* 2006; Little *et al.* 2010b).

The molecular mechanisms underlying skeletal muscle metabolic adaptations to low-volume HIT have recently been investigated. Given the potency of HIT to increase mitochondrial capacity, it is perhaps not surprising that investigations have examined the influence of low-volume HIT on the activation of peroxisome-proliferator activated receptor  $\gamma$  coactivator (PGC)-1 $\alpha$ , which is regarded as the ‘master regulator’ of mitochondrial biogenesis in muscle (Wu *et al.* 1999). Evidence suggests that exercise intensity is the key factor influencing PGC-1 $\alpha$  activation in human skeletal muscle (Egan *et al.* 2010). In this respect, acute low-volume Wingate-based HIT increases PGC-1 $\alpha$  mRNA by several-fold when measured 3 h post-exercise (Gibala *et al.* 2009; Little *et al.* 2011b). This is comparable with the acute increase in PGC-1 $\alpha$  mRNA expression observed after a bout of continuous endurance-type exercise (Norrbom *et al.* 2004; Egan *et al.* 2010). Similar to endurance exercise (Wright *et al.* 2007; Little *et al.* 2010a), acute Wingate-based HIT may activate PGC-1 by increasing its nuclear translocation (Little *et al.* 2011b). The increase in nuclear PGC-1 following low-volume HIT coincides with increased mRNA expression of several mitochondrial genes (Little *et al.* 2011b), suggesting that a program of mitochondrial adaptation is engaged with these short bursts of intensity exercise (Fig. 2).

The upstream signals that activate PGC-1 $\alpha$  and mitochondrial biogenesis in response to low-volume HIT have not been clearly elucidated but probably relate to robust changes in intramuscular ATP:ADP/AMP ratio following exercise (Chen *et al.* 2000) and the concomitant activation of 5'-adenosine monophosphate-activated protein kinase (AMPK) (Gibala *et al.* 2009; Little *et al.* 2011b). Activation of p38 mitogen-activated protein kinase (MAPK), possibly via increased generation of reactive oxygen species (ROS) (Kang *et al.* 2009), may

**Figure 2.** Potential intracellular signalling mechanisms involved in HIT-induced mitochondrial biogenesis

Low-volume HIT has been shown to activate 5'-AMP-activated protein kinase (AMPK) and p38 mitogen-activated protein kinase (MAPK). Both of these exercise-responsive signalling kinases are implicated in direct phosphorylation and activation of PGC-1 $\alpha$ . Increased nuclear abundance of PGC-1 $\alpha$  following HIT is hypothesized to co-activate transcription factors (TF) to increase mitochondrial gene transcription, ultimately resulting in accumulation of more mitochondrial proteins to drive mitochondrial biogenesis.



also be involved (Gibala *et al.* 2009; Little *et al.* 2011b). Elevated levels of PGC-1 protein also accompany increased markers of mitochondrial content following a period of low-volume HIT. Six weeks of Wingate-based HIT increased the protein content of PGC-1 by  $\sim 100\%$  in young, healthy individuals (Burgomaster *et al.* 2008) and 2 weeks of  $10 \times 1$  min HIT resulted in a  $\sim 25\%$  increase in nuclear PGC-1 protein (Little *et al.* 2010b). Collectively, these results indicate that PGC-1 $\alpha$  is probably involved in regulating some of the metabolic adaptations to low-volume HIT. Given the positive effects that a modest increase in muscle PGC-1 $\alpha$  appears to have on oxidative capacity, anti-oxidant defence, glucose uptake, resistance to age-related sarcopenia and anti-inflammatory pathways (Sandri *et al.* 2006; Benton *et al.* 2008; Wenz *et al.* 2009), the increase in PGC-1 $\alpha$  following low-volume HIT may highlight potential widespread health benefits for this type of exercise.

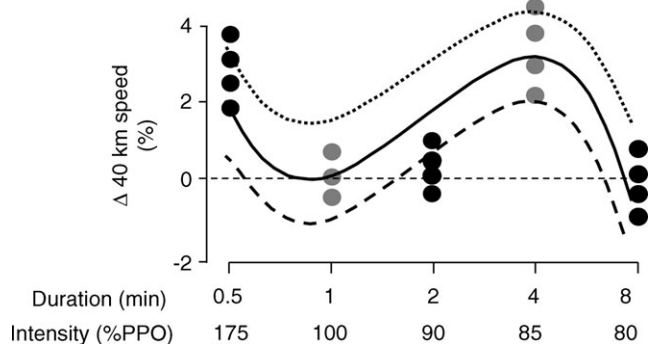
The impact of interval types of training programs on cardiovascular structure and function has also been investigated (Wisloff *et al.* 2009), but few studies have utilized low-volume HIT models. However, as little as 2 weeks of Wingate-based HIT has been reported to increase cardiorespiratory capacity as reflected by changes in peak oxygen uptake ( $\dot{V}_{O_{2peak}}$ ) (Whyte *et al.* 2010) although this is not a universal finding (Burgomaster *et al.* 2005). Another study showed that 6 weeks of Wingate-based HIT increased  $\dot{V}_{O_{2peak}}$  to the same extent as traditional endurance training despite a markedly reduced time commitment and total training volume (Burgomaster *et al.* 2008). We have also shown in young healthy men and women that low-volume HIT increases compliance in peripheral but not central arteries (Rakobowchuk *et al.* 2008). The protocol also

increased endothelial function in the trained legs to an extent that is comparable to changes observed after a much higher volume of continuous moderate-intensity training (Rakobowchuk *et al.* 2008). The mechanisms regulating cardiovascular adaptations to various forms of low-volume HIT have yet to be comprehensively examined.

### Potential application of HIT in people with or at risk for cardiometabolic disorders

While much of the work conducted to date has involved relatively high-volume protocols that are comparable in volume to traditional endurance training, HIT has been shown to improve cardiorespiratory fitness in a range of populations including those with coronary artery disease, congestive heart failure, middle age adults with metabolic syndrome and obese individuals (Warburton *et al.* 2005; Wisloff *et al.* 2007; Moholdt *et al.* 2009; Munk *et al.* 2009). In many cases, the increase in cardiorespiratory fitness after HIT was superior to after continuous moderate-intensity training (Wisloff *et al.* 2007; Tjonna *et al.* 2008, 2009; Moholdt *et al.* 2009). Endothelial function, assessed using flow-mediated dilatation of the brachial artery, is improved to a greater extent following HIT compared with continuous moderate-intensity training (Wisloff *et al.* 2007; Tjonna *et al.* 2008, 2009; Moholdt *et al.* 2009). Other studies have documented beneficial changes in various components of resting blood pressure (Rognmo *et al.* 2004; Schjerve *et al.* 2008; Whyte *et al.* 2010) and left ventricular morphology (Wisloff *et al.* 2007). It appears that this type of cardiac remodelling requires a longer duration of training and greater exercise volume than the load required to alter cardiorespiratory fitness or peripheral vascular structure and function. It could be that the short intense bursts of activity with low-volume HIT induce large-magnitude increases in cellular and peripheral vascular stress, while effectively 'insulating' the heart from those stresses due to the brief duration of the exercise bouts. This relative central insulation permits individuals to train at much higher intensities than they would otherwise, but may also result in different timelines and effective stimulus loads between the central and peripheral components of the cardiovascular system.

Low-volume HIT studies in persons who might be at risk for cardiometabolic disorders or patients with chronic disease are very limited. However, recent work has shown that as few as six sessions of either Wingate-based HIT and the more practical constant-load model over 2 weeks improve estimated insulin sensitivity in previously sedentary, overweight individuals (Whyte *et al.* 2010; Hood *et al.* 2011). Insulin sensitivity in these studies was calculated based on either single fasting glucose and insulin measurements (Hood *et al.* 2011) or the



**Figure 3. The effect of varying the intensity of interval training on changes in 40 km time-trial performance**

Well-trained male cyclists were randomly assigned to one of five different doses of high-intensity interval training (HIT):  $12 \times 30$  s at 175% of peak sustained power output (PPO),  $12 \times 1$  min s at 100% PPO,  $12 \times 2$  min at 90% PPO,  $8 \times 4$  min at 85% PPO, or  $4 \times 8$  min at 80% PPO. Cyclists completed six HIT sessions over a 3 week period in addition to their habitual aerobic base training. Redrawn from Stepto *et al.* (1999) with permission.

response to an oral glucose tolerance test (Whyte *et al.* 2010) and therefore primarily reflects hepatic as opposed to peripheral (skeletal muscle) insulin sensitivity. Peripheral insulin sensitivity following exercise training may be improved by increased skeletal muscle glucose transport capacity, mediated in part by the protein GLUT4. Skeletal muscle GLUT4 content after short-term HIT is increased by a comparable magnitude ( $\sim 2$ -fold) to that observed after high-volume endurance training (Hood *et al.* 2011). We also recently demonstrated that low-volume HIT was well tolerated and rapidly improved skeletal muscle GLUT4 content in eight patients with type 2 diabetes (Little *et al.* 2011a). This small pilot study also showed that six sessions of HIT over 2 weeks reduced average 24 h blood glucose concentration and post-prandial glucose excursions, measured via continuous glucose monitoring under standardized diet but otherwise free-living conditions (Little *et al.* 2011a). These beneficial adaptations were realized even though the weekly training time commitment was much lower than common public health guidelines that generally call for at least 150 min of moderate to vigorous exercise per week to promote health. While the preliminary evidence from these small, proof-of-principle studies are intriguing, large-scale studies are clearly needed to resolve whether low-volume HIT is a realistic, time-efficient exercise alternative to reduce the risk of cardiometabolic disease or improve health and wellbeing in patients with chronic disease.

### HIT and athletic performance

HIT has been an integral part of training programs for the enhancement of athletic performance since the beginning of the 19th century. Yet despite being a core component of competition preparation, the unique effect of specific training interventions on the performances of well-trained individuals is sparse. This, perhaps, is understandable for several practical reasons. First, exercise physiologists have found it difficult to convince elite athletes that it could be worthwhile to experiment with their normal training programs. Second, even if athletes (and their coaches) were willing to modify their training practices, conventional approaches to investigate the response to different doses of a treatment (i.e. interval training) using repeated-measures design in which each athlete receives all the different doses is totally impractical for studies of physical training; the long-lasting effects of any given dose of training prevent athletes from receiving more than one dose of the treatment.

Over a decade ago we embarked on a series of investigations into the effects of interval training in competitive endurance athletes using a standardized training protocol, namely, replacing a portion ( $\sim 15$ – $20\%$ ) of an athletes' aerobic base training with six to eight sessions of continuous (5 min) high-intensity (90% of

$\dot{V}_{O_{2peak}}$ ) work bouts undertaken twice a week throughout a 3 week intervention period (see Hawley *et al.* 1997 for review). We systematically examined the effect of this interval training protocol on a variety of outcome measures including performance (Lindsay *et al.* 1996; Stepto *et al.* 1999), skeletal muscle metabolism (Westgarth-Taylor *et al.* 1997; Stepto *et al.* 2001), cell signalling (Yu *et al.* 2003; Clark *et al.* 2004) and the interaction of HIT with various diet manipulations (Stepto *et al.* 2002; Yeo *et al.* 2008). Stepto *et al.* (1999) employed a novel approach to determine the effects of divergent interval training protocols on performance lasting  $\sim 1$  h by fitting polynomial or other curves to the responses for each interval training dose for individual athletes. As we originally hypothesized, training sessions that employed work bouts that were closely matched to race-pace ( $8 \times 4$  min at 85% of peak aerobic power output (PPO)) significantly enhanced performance (2.8%, 95% CI = 4.3–1.3%). Yet, somewhat surprisingly, short-duration, supra-maximal work bouts ( $12 \times 30$  s at 175% of PPO) were just as effective in improving performance (2.4%, 95% CI = 4.0–0.7%). Consistent with this observation, Psilander *et al.* (2010) recently reported that a single bout of low-volume HIT ( $7 \times 30$  s 'all out' efforts) stimulated increases in mitochondrial gene expression that were comparable to or greater than the changes after more prolonged ( $3 \times 20$  min bouts at  $\sim 87\%$  of  $\dot{V}_{O_{2peak}}$ ) endurance exercise in well-trained cyclists. Given the lower volume of work and the fact that mitochondrial transcription factor A, the downstream target of PGC-1 $\alpha$ , was only increased after the 30 s protocol, the authors concluded that brief intense interval training might be a time-efficient strategy for highly trained individuals.

Guellich and colleagues (2009) have recently extended our early findings (Stepto *et al.* 1999, Fig. 3) that 'polarized training' enhanced endurance performance. These workers reported that elite endurance athletes from a range of sports including rowing, running, cycling and cross-country skiing perform only a small portion of their training at competition/race-pace intensities, with the bulk of their workload comprising low-intensity, high-volume workouts, and exposure to extreme HIT sessions. In a recent review Laursen (2010) proposed that a polarized approach to training, in which  $\sim 75\%$  of total training volume be performed at low intensities, with 10–15% performed at supra-maximal intensities may be the optimal training intensity distribution for elite athletes who compete in intense endurance events. We suggest that the unique genetic and/or molecular signature resulting from polarized training is a fertile area for future research. Indeed, directly linking exercise-induced signalling cascades in skeletal muscle to defined metabolic responses and specific changes in gene and protein expression that occur after diverse interval training

regimens may provide clues as to why HIT is such a potent intervention for promoting both health outcomes and enhancing athletic performance and exercise capacity.

### Conclusion and directions for future research

Considerable evidence currently exists to support a role for low-volume HIT as a potent and time-efficient training method for inducing both central (cardiovascular) and peripheral (skeletal muscle) adaptations that are linked to improved health outcomes. Limited work has examined the application of low-volume HIT in people with, or at risk for, cardiometabolic disorders, and at present the potential benefits of this type of training are unclear. Regardless of the group studied, the majority of low-volume studies have utilized relatively short intervention periods (i.e. lasting up to several weeks). Future work involving long-term (i.e. months to years) interventions in a variety of clinical cohorts (i.e. individuals with insulin resistance, obesity, type 2 diabetes and cardiovascular disease) are urgently needed to better understand how manipulating the exercise stimulus impacts on cardiovascular and musculoskeletal remodelling in these populations. One aspect that is unclear from the present literature is the precise intensity and minimal volume of training that is needed to potentiate the effect of the stimulus-adaptation on outcomes such as mitochondrial biogenesis and relevant health markers. To answer such questions, a complex series of studies needs to be undertaken that systematically 'titrate' levels of the 'training impulse' and determine subsequent cellular, performance and clinical responses after divergent training interventions. In this regard, the perspectives gained from the use of supra-maximal interval-based training in well-trained athletes may aid in understanding why and how low-volume HIT improves health and functional performance in the general population and in many chronic disease states. Information derived from future studies will need to provide practical, evidence-based recommendations for novel exercise prescription that can be incorporated into daily living and form an integral component in the development of future combinatorial therapies for the prevention and treatment of chronic inactivity-related diseases. If achieved, these goals will simultaneously reduce the economic burden associated with an inactive lifestyle.

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