Reduced-Exertion, High-Intensity Interval Training: The Effects of a Shortened-Sprint Protocol on Affective Response and $\dot{V}O_{2max}$, with Perspective on Application to HbA_{1c} Defined Non-Diabetic Hyperglycaemia

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“And is not the bodily habit spoiled by rest and idleness, but preserved for a long time by motion and exercise?”

–Plato, from *Theaetetus*, date unknown

For Sebastien and Mia

In loving memory of my father, Edmund Sidney Haines

Abstract

Background

Physical inactivity is an endemic health problem. Despite evidence to suggest regular physical activity and exercise improve health, the challenge of encouraging individuals and populations to be more active remains. Frequently, 'lack of time' is cited as the main barrier. Proponents of high-intensity interval training (HIT) emphasise time-efficiency as a practical benefit and contend that the health outcomes associated with this type of exercise are relevant to public health strategy. This includes increased cardiovascular fitness and improved blood glucose control. However, many iterations of HIT are not appreciably more time-efficient than traditional exercise guidelines, and the high-intensity nature of HIT may result in negative affective states (increasing displeasure) that could lead to poor exercise adherence. Reduced-exertion HIT (REHIT) has been developed as a genuinely time-efficient and more tolerable approach to exercise.

Aims

The principal aims of the thesis focus on two related areas of exercise science: approaches to time-efficient exercise to improve health outcomes; and the affective response to such exercise. The contribution to knowledge is predicated on critical appraisal of current literature, and based on data collected via three studies distinct in their focus and application, but connected by the theme of exploring a novel approach to REHIT that, despite including maximal capacity exercise, does not overly compromise affective response.

Methods

Study 1 used a randomised crossover design to consider differences between responses to three low-volume, high-intensity exercise protocols. Shortened-sprint REHIT (8 × 5 s sprints) was compared to traditional REHIT (2 × 20 s sprints) and sprint continuous training (SCT, one sustained maximal effort sprint). The primary outcome measure was affect (pleasure-displeasure) measured using the Feeling Scale (FS). Study 2 used a randomised controlled design to compare the effects of shortened-sprint and traditional REHIT on peak oxygen uptake ($\dot{V}O_{2peak}$), to determine if shorter sprints attenuate increases in this important health outcome. Finally, study 3 was a feasibility study to report data relevant to the acceptability of a REHIT intervention with non-diabetic hyperglycaemia (NDH) patients delivered in a National Health Service (NHS) practice setting.

Results

For study 1, peak affective valence was more positive for shortened-sprint REHIT (1.4 ± 1.7 FS units) compared to traditional REHIT (-0.1 ± 1.9) and SCT (-0.8 ± 1.6), where 1 is 'fairly good', 0 is 'neutral', and -1 is 'fairly bad' (both p = 0.001). Greater pleasure was also observed for traditional REHIT compared to SCT (p = 0.005). Likewise, lower ratings of perceived exertion (RPE) and higher enjoyment were associated with shortened-sprint REHIT (all p < 0.01). Both iterations of REHIT avoided large negative peaks in affective response and may therefore be genuinely time-efficient, yet tolerable approaches to exercise. Shorter sprints may be additionally beneficial in circumventing negative affective responses. In study 2, compared to baseline, $\dot{V}O_{2peak}$ increased following both conditions (6% for shortened-sprint REHIT [d = -0.36] and 9% for traditional REHIT [d = -0.53], both p = 0.01). However, there was substantial heterogeneity in training response within each condition (range -2% to 20%). Affective valence was again more favourable for shortened-sprint REHIT compared to traditional REHIT (1.6 ± 0.6 vs 0.2 ± 1 FS units, respectively, p = 0.001, d = 1.62). Similarly, peak RPE values were lower for shortened-sprint REHIT (14.4 ± 0.9 vs 16.2 ± 1.1, p = 0.001, d = -1.71). Despite this, there was no significant difference in enjoyment between the two protocols. For study 3 (feasibility study), the findings of this preparatory stage of trial design pre-empted problems with the intervention that could be changed to optimise the design and conduct of a larger-scale pragmatic trial to improve transferability into real-world practice. Challenges included eligibility, recruitment, patient consent, and poor clinician engagement leading to the recommendation that the study was not feasible in its current form. These findings form the basis for important learning in relation to the potential for transfer of exercise interventions into real-life scenarios with specific populations. Future interventions need to be sensitive to features of the local context such as the built environment, socioeconomic status, and the specific needs of individuals with chronic disease.

Conclusion

The original contribution to knowledge in this thesis is that a novel REHIT protocol using shortened-sprints can improve $\dot{V}O_{2peak}$ whilst minimising large negative peaks in affective response. Thus, the three studies provide preliminary evidence to suggest that REHIT is both time-efficient, yet at the same time does not overly compromise affective response. Although there is no claim to invalidate the efficacy of higher volume exercise, the practicalities of building REHIT into everyday life could improve exercise adherence. Translating current evidence into effective exercise strategies in real-world settings remains a key challenge to further research on REHIT. To counter the deleterious effects on health that modern environments create, we need to engineer physical activity into our lives in a way that is socially and culturally acceptable. REHIT could form part of a solution to achieve this.

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Copyright statement

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ACSM	American College of Sports Medicine
AMP/ATP	Adenosine monophosphate /Adenosine triphosphate
AMPK	5’ adenosine monophosphate protein kinase
BASES	British Association of Sport and Exercise Sciences
BMI	Body mass index
COX	Cytochrome c oxidase
CS	Citrate synthase
d	Cohen’s *d*
DMT	Dual-mode theory
DPP	Diabetes prevention programme
EES	Exercise Enjoyment Scale
ES	Effect size
FFA	Free fatty acid
FS	Feeling Scale
GLUT-4	Glucose transporter-4
HbA_{1c}	Glycated haemoglobin A_{1c}
HIT	High-intensity interval training
IFG	Impaired fasting glucose
IGT	Impaired glucose tolerance
NDH	Non-diabetic hyperglycaemia
NHS	National Health Service
PGC-1α	Peroxisome proliferator-activated receptor-γ coactivator-1α
REHIT	Reduced-exertion, high-intensity interval training
RMANOVA	Repeated-measures analysis of variance
RPE	Rating of perceived exertion
SCT	Sprint continuous training
SSREHIT	Shortened-sprint, reduced-exertion, high-intensity interval training
$\dot{V}O_{2max}$	Maximal oxygen uptake (per minute)
$\dot{V}O_{2peak}$	Peak oxygen uptake (per minute)
η^2	Partial eta squared

Plain language synopsis of each chapter

Part 1 – Introduction

The first two chapters broadly outline the problem of physical inactivity. **Chapter 1** introduces two important concepts: first, that increasing levels of type 2 diabetes are of concern; and second, the notion that an alternative form of exercise known as high-intensity interval training (HIT) could be used to treat or prevent this. The aims and objectives of the thesis are also stated. **Chapter 2** covers the personal and economic burdens associated with physical inactivity focussing on diabesity – a term used to describe the coexistence of the obesity and diabetes pandemics characteristic of modern environments. This chapter also considers the importance of fitness and the challenge of encouraging people to be more active, before concluding by discussing issues of using HIT to encourage increased levels of physical activity.

Part 2 – Theoretical framework

Part 2 discusses several assumptions that underpin this thesis. **Chapter 3** outlines much of the underlying theory. First, it is argued that the problem of physical inactivity must be considered from an evolutionary perspective to appreciate the causes of modern diseases. It is proposed that humans have evolved many physiological adaptations that suggest we need to be physically active to maintain good health. Second, feelings of pleasure and displeasure felt during exercise may be related to the likelihood that individuals will adhere to exercise programmes. Therefore, hedonistic (pleasure-displeasure) theories of motivation, including the dual-mode theory, are discussed. Third, the physiological mechanisms, by which HIT increases fitness and improves control of blood glucose are described. **Chapter 4** is a critical appraisal of the philosophical assumptions about the scientific methods used in this thesis, and why they are the best methods for achieving the stated aims and objectives. Finally, **Chapter 5** is a systematic review of the scientific literature concerned with the efficacy (the ability to produce a desired or intended result) and the effectiveness (the likely success under real-world conditions) of HIT.

Part 3 – Research studies

Following the systematic review in Chapter 5, Chapters 6 to 9 detail the research studies used to collect new data in this thesis. **Chapter 6** overviews this programme of research and details pilot work which assisted with choice of methods for later stages of the thesis. Principally, this involved trialling a REHIT protocol. A general methods section is also included here and outlines several procedures and measures that are common to the methods of the subsequent studies. **Chapter 7** outlines study 1 comparing three approaches to low-volume exercise, including a novel iteration of REHIT using shortened-sprints. Study 2 is described in **Chapter 8**. Shortened-sprint REHIT was compared against traditional REHIT to determine if improvements in cardiovascular fitness were similar following a 5 to 7-week exercise intervention. Finally, **Chapter 9** describes a feasibility study in which a REHIT intervention was used with patients with non-diabetic hyperglycaemia, commonly known as pre-diabetes, in an NHS practice setting.

Part 4 – Synthesis

The single chapter in Part 4 amalgamates the findings from Part 3. **Chapter 10** includes a general conclusion based on these results, with interpretation of the scope, significance, and limitations of what was found. An elaboration of suggested future research related to HIT and REHIT is included before a general summary of the whole thesis is presented.

PART ONE: INTRODUCTION

Chapter 1 Introduction, aims and objectives

1.1 Introduction

The prognosis for many chronic diseases is improved by regular physical activity or exercise. Indeed, there exists an incontrovertible relationship between many diseases and physical inactivity, including obesity, cardiovascular disease, and type 2 diabetes. Level of cardiovascular fitness, irrespective of other health outcomes, is a strong predictor of all-cause mortality and morbidity. A series of large-scale observational epidemiological studies demonstrate a protective effect of fitness on cardiovascular disease, diabetes, obesity and hypertension (Blair *et al*., 1995; Blair *et al*. 1996; Church, LaMonte, Barlow & Blair, 2005; Sui, Laditka, Hardin & Blair, 2007a; Sui, LaMonte & Blair, 2007b, Sui *et al*., 2007c). Furthermore, when considering the prevalence of physical inactivity, estimates suggest that low cardiorespiratory fitness accounts for substantially more deaths than obesity, diabetes and dyslipidaemia combined (Blair, 2009). Addressing the negative consequences associated with the high prevalence of physical inactivity in the general population is a foremost public health challenge (Vollard & Metcalfe, 2017).

Of concern is the increased prevalence and growing incidence of type 2 diabetes, including various ‘pre-diabetic’ hyperglycaemic states which precede overt diabetes. The number of people expected to die from diabetic complications is predicted to double between 2005 and 2030 (World Health Organisation, 2016). In the United Kingdom, this places considerable financial burden on the National Health Service (NHS), with the current healthcare cost of diabetes estimated to be £23.7 billion and expected to rise to £39.8 billion by 2035 (Diabetes UK, 2015a). The importance of recognising individuals whose blood glucose levels do not meet the diagnostic criteria for diabetes, but are higher than normal, lies in their higher risk of developing type 2 diabetes in the future, as well as the effectiveness of lifestyle interventions in lowering this risk (Knowler *et al*., 2002; Goh, Koh & Wackerhage, 2014). Furthermore, blood glucose excursions in pre-diabetic states contribute to the development of cardiovascular disease risk (Ceriello, 2005). The underlying defect for these metabolic abnormalities is insulin resistance. Accordingly, scientific evidence supports a protective effect of physical activity because exercise targets this primary defect, thus preventing or delaying the progression to type 2 diabetes. At a molecular level, exercise is a form of energy consumption, and depletion of cellular chemical energy within skeletal muscle causes a cascade of signalling mechanisms that promote increased glucose transport, insulin sensitivity, and glucose uptake.

However, adherence to exercise is a pre-requisite for the success of lifestyle interventions, and this is often poor. Compared to traditional exercise recommendations, which are based around relatively high-volume, continuous, moderate-intensity exercise; high-intensity interval training (HIT) is frequently considered to be more time-efficient (e.g. Gaesser & Angadi, 2011). Thus, HIT may circumvent the most commonly identified barrier preventing individuals leading a more active lifestyle – that is, internally perceived 'lack of time'. HIT is characterised by brief periods of repeated high-intensity, or 'all-out', intervals of exercise interspersed with longer periods of low-intensity recovery. Nevertheless, the time-efficiency claim is disputed since the total session duration is not appreciably different to current exercise recommendations for promoting health, necessitated by the inclusion of a warm-up, periods of rest in-between high-intensity intervals, and a cool down (e.g. Whyte *et al*., 2013). Again, others have highlighted that the high-intensity nature of HIT may present an alternative barrier to exercise, by evoking a negative affective response (i.e. displeasure), which may in-turn lead to avoidance of future exercise sessions (Hardcastle, Ray, Beale & Hagger, 2014).

For HIT to have any role in public health, the focus should be on refining protocols to make them effective and safe, yet at the same time appealing, tolerable, and sustainable. Fundamentally, protocols must be genuinely time-efficient, and appropriate to those for whom they are intended, without overly compromising cognitive and affective responses. Hence, the growing trend in HIT research is to explore the minimal amount of exercise that is required to improve health (Songsorn *et al*., 2016; Ruffino *et al*., 2016; Vollard & Metcalfe, 2017). The minimum amount of exercise that has so far been shown to improve cardiovascular fitness (measured as maximal oxygen uptake or $\dot{V}O_{2max}$) is known as reduced-exertion HIT (REHIT) and uses 2 × 20 s cycle sprints within a 10-minute session inclusive of a warm-up and cool down. Furthering research on REHIT requires investigation into similar protocols with an emphasis on isolating the dose-response relationship. A recent meta-analysis concluded that the improvement in $\dot{V}O_{2max}$ after HIT is not attenuated with fewer sprint repetitions (Vollard, Metcalfe & Williams, 2017). Therefore, traditional approaches to HIT may be unnecessarily strenuous. A focus on novel iterations of REHIT with shorter sprints is warranted, as is a clearer depiction of affective responses to such protocols which could influence long-term exercise behaviour. Transfer of this knowledge into real-world environments remains a key challenge as this will be decisive in terms of whether REHIT can contribute to a viable exercise strategy to improve public health.

This thesis principally focuses on two areas of exercise science: approaches to time-efficient exercise to improve both $\dot{V}O_{2max}$ and blood glucose control; and the affective response to such exercise. The original contribution to knowledge will relate to use of shortened-sprint REHIT as an exercise choice to oppose physical inactivity. This is appropriate since, as discussed, both $\dot{V}O_{2max}$ and insulin sensitivity are important health outcomes. The former can only be improved by exercise, while the latter is sensitive to exercise demands because blood glucose disposal primarily occurs in exercising skeletal muscle, which is the principal insulin-sensitive tissue in the body. The various sections and chapters of this thesis are subsequently united by a common theme – the use of HIT or REHIT to combat physical inactivity and improve health outcomes. The thesis culminates in three related studies which investigate these issues, whilst being distinct in their focus and application.

1.2 Aims and objectives

Aims

The aim of this thesis is to investigate the effects of a novel and time-efficient REHIT protocol on affective response, cardiovascular fitness ($\dot{V}O_{2peak}$), and blood glucose control. In comparison to traditional REHIT, the protocol will use shortened sprints. More broadly, the project aims to consider the potential of shortened-sprint REHIT as an exercise intervention for promoting health.

Objectives

1. Justify the evolutionary basis for the relationship between physical inactivity, obesity and type 2 diabetes.
2. Outline hedonistic theories of motivation and their basis for predicting exercise adherence.
3. Explore the potential for HIT as an exercise choice to promote public health.
4. Systematically review evidence for improving a range of health outcomes using low-volume, HIT.
5. Gain institutional ethical approval and NHS ethical approval for empirical research.
6. Carry out pilot work to trial REHIT protocols.
7. Investigate the effects of a novel, shortened-sprint REHIT protocol on:
    a. Perceptual responses (i.e. affect, exertion, and enjoyment)

b. Cardiovascular fitness (i.e. $\dot{V}O_{2peak}$)
c. Body composition

8. Using the Medical Research Council (MRC) complex intervention framework, conduct a feasibility study to describe and report data relevant to the viability of using a REHIT intervention in NDH patients in an NHS practice setting.

Intended original contribution to knowledge

This thesis will contribute to new knowledge by:

- Investigating adaptations (including $\dot{V}O_{2peak}$) to HIT using a novel, shortened-sprint REHIT protocol. This will elaborate on the dose-response relationship to intermittent exercise.
- Comparing affective responses for various low-volume approaches to HIT, including shortened-sprint REHIT. Response to a single bout of exercise, and responses throughout a longitudinal intervention will be recorded.
- Implementing a shortened-sprint REHIT protocol in individuals with NDH.
- Using a time-efficient HIT exercise prescription within in an NHS practice setting.
- Exploring the effects of REHIT on HbA_{1c}, which is a widely used measure in clinical practice.

Chapter 2 Rationale

2.1 Physical inactivity

Physical inactivity has been described as the greatest public health problem in developed, industrialised countries (Sallis, 2009). It is an endemic social problem in the United Kingdom, and a strong and prevalent risk factor for a wide range of non-infectious diseases. The extent of the problem was exemplified in the 2008 Health Survey for England on physical activity and fitness, which was the first-time objective measures of physical activity were used in a national general population survey (Craig, Mindell & Hirani, 2009). It was estimated subjectively that 61% of men and 71% of women measured did not meet minimum physical activity recommendations for health. However, this figure increased to 94% for men and 96% for women when measured objectively using accelerometry. Although direct comparison between objective and self-reported measures is not possible, the consequences of such levels of physical inactivity are harmful for a range of health outcomes. *Homo sapiens* may be, because of evolution, an exercise-dependent species and many polygenic diseases are triggered by a divergence between our genomes, which have been selected for high physical activity, and our sedentary lifestyles (Goh, Koh & Wackerhage, 2014). As such, chronic diseases such as obesity and type 2 diabetes are a natural consequence of modern lifestyle.

Undoubtedly there are other factors in the modern environment, besides physical inactivity, that are associated with disease. For example, modern diets characterised by a reduced intake of fruit and vegetables, and increased consumption of energy dense foods high in fat and sugar, are drastically different to the diets of ancestral humans (Lindeberg, Cordain & Eaton, 2003). However, although focussing on one aspect of health can be misleading, it is nevertheless defensible to single-out physical inactivity as particularly damaging to our health because normal phenotypic gene expression is threatened in the absence of sufficient activity, and manifests pathologically (Booth, Chakravarthy & Spagenburg, 2002a). Evidence to suggest that humans evolved to ‘expect’ physical activity comes from several lines of reasoning, such as: comparative anatomy, especially to that of other apes; anatomical, biomechanical and biochemical study of fossils and human remains; and more recently genome-molecular signalling studies (Booth *et al*., 2002; Lieberman, 2013). Furthermore, studies of populations minimally affected by modern habits, or still living hunter-gather lifestyles, demonstrate superior health markers and physical fitness compared to industrialised populations (Cordain, 2007). Other studies of recently acculturated groups consistently show deleterious effects on health and susceptibility to lifestyle-mediated disease after forgoing traditional lifestyles for a more industrialised one.

Skeletal muscles rapidly change in response to inactivity and, as the largest tissue mass of the body, have an important and direct role in disease prevention and management – most notably for type 2 diabetes, since blood glucose disposal occurs primarily in skeletal muscle. A fundamental property of muscle is its ability to adapt; it is one of the most malleable tissues of the human body, capable of extensive remodelling if systematically challenged (Green, 2012). Although the function of skeletal muscle is to shorten and generate force, they also release myokines which are small proteins that are produced and released by muscle cells in response to muscle actions and can have systemic effects. They have autocrine, paracrine and endocrine effects which can modulate function in other tissues and organs that are potentially important in the prevention and management of certain diseases (Green, 2012). Molecular signalling studies demonstrate that the intracellular mechanisms leading to the exercise-induced stimulation of glucose uptake in skeletal muscle are mediated in response to the metabolic status of the muscle caused specifically by muscle action: that is, physical activity (Hawley & Lessard, 2008). Furthermore, regulation of energy balance and by association adiposity, is to a significant degree managed by exercise-induced increases in caloric expenditure, mediated by muscle action. In short, to function optimally skeletal muscle must be active regularly. As such the effects of physical inactivity on obesity and disease are incontrovertible (Hambrecht & Gielen, 2005).

2.2 Obesity and type 2 diabetes

Obesity has increased rapidly and is now so prevalent in the UK that it is described as an epidemic (Mitchell, Catenacci, Wyatt, & Hill, 2011). Together with this is an epidemic of type 2 diabetes. The expression 'diabesity' describes the co-existence of both epidemics, and was originally used in the 1970's to describe studies of human obesity and impaired glycaemic control (Sims *et al*., 1973). An historical perspective of the term and the coexistence of obesity and type 2 diabetes is provided by Haslam (2012, 2013). Insulin resistance appears to be the primary defect in the pathogenesis of type 2 diabetes (Hardman & Stensel, 2009) and an obesity-induced, high lipid concentration in the principal insulin-sensitive tissues – that is skeletal muscle, adipose tissue and liver – can cause this. Transgenic lipodystrophic mice with no white adipose tissue, develop insulin resistance and type 2 diabetes due to an accumulation of triglycerides in skeletal muscle and liver, instead of the absent adipose tissue (Kim, Gavrilova, Chen, Reitman & Shulman, 2000). Upon transplantation of adipose tissue into these mice, triglyceride content in muscle and liver returns to normal, as does insulin signalling and action. This study demonstrates the importance of alterations in the partitioning of fat between adipocytes, skeletal muscles and liver, and association with insulin resistance.

Traditional views of adipocytes as a simple energy reserve – storing and releasing triacylglycerol – have been replaced by the view that they are an endocrine cell, which releases many signalling molecules that have local as well as systemic effects (Kershaw & Flier, 2004; Carey, 2005). For example, increasing fat mass (i.e. overweight and obesity) results in increased plasma free fatty acid (FFA) concentration, which causes insulin resistance (Boden, 2008). Indeed, obesity is closely associated with peripheral and hepatic insulin resistance, in addition to low grade inflammation caused by pro-inflammatory cytokines (Boden, 1997; Tataranni & Oretega, 2005) both of which contribute to type 2 diabetes, in addition to hypertension and disorders of blood coagulation and fibrinolysis (Bray, 2004). Once plasma FFA levels are elevated, they may compete with glucose for uptake and oxidation reducing insulin stimulated glucose uptake (Randle, Garland, Hales & Newsholme, 1963; Boden, Chen, Ruiz, White & Rossetti, 1994; Boden & Chen, 1995) and inhibiting the anti-lipolytic action of insulin, which further increases the rate of FFA release into circulation (Jensen, Haymond, Rizza, Cryer & Miles, 1989). Other fat related metabolites such as ceramides inhibit the insulin-signalling cascade, further reducing insulin-stimulated glucose uptake (Kahn, Hull & Utzschneider, 2006). Defective adipokine (adipose tissue hormone) release, as a result of obesity, may further contribute to insulin resistance in skeletal muscle and liver by activating adenosine monophosphate-activated protein kinase (AMPK) (Kahn *et al*., 2006; Muoio & Newgard, 2008).

The deposition of adipose tissue is also an important determinant of the health consequences associated with obesity. In particular, the two abdominal fat depots – abdominal subcutaneous fat and intra-abdominal, or visceral, fat – are associated with increased pathogenesis of numerous cardiovascular and diabetes risk factors (Ross & Janssen, 2012). Anatomically, visceral fat consists of adipocytes contained within the visceral peritoneum, which is a membrane that covers the abdominal organs of the gastrointestinal tract, and extends from approximately the eleventh thoracic vertebrae to the fifth lumbar vertebrae. Compounds released from visceral fat drain into hepatic portal circulation directly to the liver, and this sustained exposure of the liver to an increased flux of FFAs, is the antecedent to many disturbances in glucose and lipid metabolism (Björntorp, 1990). As discussed, hyper-adiposity also increases the release of cytokines that may link to metabolic health risk, and visceral fat produces more of these than subcutaneous fat (Matsuzawa, 2002). These studies demonstrate the link between adiposity and insulin resistance, and may represent a feedback mechanism to prevent further weight gain above a certain level (Ross and Janssen, 2012). Considering the prevalence of obesity in developed nations, these biological systems seem insufficiently powerful to prevent or regress weight gain. It is possible that our current environment is too overwhelmingly obesogenic, and that our physiology has always relied on an external event, such as famine or high levels of physical activity, to control this (Haines, 2015).

Type 2 diabetes is an endocrine condition characterised by insulin resistance, whereby skeletal muscle, adipose tissue and liver become desensitised to insulin, leading to a disturbance of glucose regulation (Williams & Williams, 2005). The result is hyperglycaemia. Initially the pancreatic β-cells compensate by secreting up to 4–5 times more insulin than usual (Kahn *et al*., 2006), known as compensatory hyperinsulinaemia, which maintains fasting and post-prandial blood glucose within the normal range. However, this state increases the likelihood of hypertension and dyslipidaemia, in addition to disturbances in haemodynamic function, inflammation, coagulation and fibrinolysis (Reaven, 2005), all of which increase the risk of cardiovascular disease (Lakka *et al*., 2002; Kip *et al*., 2004). In 1988, this cluster of related abnormalities was designated syndrome X (Reaven, 1988) and subsequently diagnostically referred to as the ‘metabolic syndrome’ by the World Health Organisation (Alberti & Zimmet, 1998). With insulin resistance as the defining feature of the cluster, the term ‘insulin resistance syndrome’ is also used. Compensatory hyperinsulinaemia cannot be maintained indefinitely so, if left untreated, the insulin-releasing β-cells in the pancreas become impaired and secrete less insulin than is required to maintain normal blood glucose. This results in progressive hyperglycaemia and eventual β-cell failure, leading blood glucose concentration to rise above a diagnostic threshold defined as type 2 diabetes. The natural history of insulin resistance and diabetes should be viewed as a continuum, rather than distinct disease processes.

The pathophysiological association between obesity, insulin resistance and type 2 diabetes has been documented for some time (Kylin, 1923). Later studies demonstrated a link specifically between intra-abdominal obesity and metabolic abnormalities (Vague, 1947) and this has more recently been implicated as the most powerful risk factor for insulin resistance and type 2 diabetes (Colditz, Willet, Rotnitzky & Manson, 1995; Hu *et al*., 2001). Physical inactivity, insulin resistance, adiposity, and type 2 diabetes are inextricably linked, and present together in an individual more frequently than might be expected by chance. Given the potential for physical activity and exercise to regulate energy balance, and by association adiposity, in addition to the beneficial effects on insulin sensitivity in both normal and insulin resistant populations, it is an essential component of treating the metabolic syndrome (Borghouts & Keizer, 2000; Albright, 2013). Indeed, exercise has long been recognised as an important component of diabetes care (Lawrence, 1926). However, the challenge of encouraging individuals and populations to lead a more active lifestyle remains. The ubiquitous coexistence of obesity and type 2 diabetes represent a subset of the metabolic syndrome. It has been shown that 60–90% of all people with type 2 diabetes are, or have been, obese (Halpern & Mancini, 2005; Stumvoll, Goldstein & van Haeften, 2005), and the relative risk of developing type 2 diabetes has been shown to increase by 4.5–9% for every additional kilogram of weight gain (Ford, Williamson & Liu, 1997). Diabesity is now one of the biggest threats to health and healthcare economies in the UK, and worldwide (Rajeswaran, 2012).

2.3 Non-diabetic hyperglycaemia (NDH)

The transition from early metabolic abnormalities to clinically diagnosed type 2 diabetes may take many years. There also exists an intermediary stage where patients' blood glucose levels are higher than normal but not high enough to be diagnosed as diabetes. This population are often referred to as having 'pre-diabetes', or non-diabetic hyperglycaemia (NDH), which are umbrella terms to describe intermediate hyperglycaemic states (Yudkin & Montori, 2014). Specifically, impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) represent distinct pre-diabetic states and have a heterogeneous pathogenesis, with different rates of progression to diabetes (Nathan *et al*., 2007). They can present in isolation or together and differ in their site of insulin resistance. Individuals with IFG predominantly have hepatic insulin resistance, whereas those with IGT have skeletal muscle insulin resistance (Qiao, Jousilahti, Eriksson & Tuomilehto, 2003; Abdul-Ghani, Tripathy & DeFronzo, 2006). The natural history of both IFG and IGT is variable, with ~25% progressing to diabetes, ~50% remaining in an abnormal glycaemic state, and ~25% reverting to normal glucose control over an observational period of 3–5 years (Gabir *et al*., 2000; Stern, Williams & Haffner, 2002). However, with longer observation most individuals with these states appear to develop type 2 diabetes (Nathan *et al*., 2007). NDH invariably precedes type 2 diabetes and is diagnostically defined as blood glucose concentrations of 7.8–11.0 mmol·L two hours after a 75-g oral glucose tolerance test (for IGT); or a fasting plasma glucose value of 5.6–6.9 mmol·L (for

IFG); or a glycated haemoglobin A_{1c} (HbA_{1c}) value of 5.7–6.4% (American Diabetes Association, 2013). Diagnostic criteria for NDH in the UK differ somewhat from the United States, aligning with recommendations from the World Health Organisation (John, 2012): that is, an HbA_{1c} value of 6.0–6.4% (or 42–46 mmol·mol).

A recent report on the prevalence of NDH in England indicated that there has been an extremely rapid rise in the proportion of adults who meet the criteria for this state (Mainous III, Tanner, Baker, Zayas & Harke, 2014). The prevalence increased from 11.6% to 35.3% between 2003 and 2011. Furthermore, the prevalence was 50.6% of the population for those who were overweight (Body Mass Index [BMI] > 25) and ≥ 40 years of age. This is of concern when considering that data on overweight and obesity among adults (defined as people aged 16 and over) from the Health Survey for England 2013 (Craig & Mindell, 2014) showed that 62.1% of adults are overweight or obese. It has been suggested that hyperglycaemic blood glucose excursions in pre-diabetic states contribute to the development of macro- and micro-vascular disease risk (Baron, 2001; Ceriello, 2005). Without intervention, it is estimated that up to 70% of those with pre-diabetic states will eventually develop type 2 diabetes (DeVegt *et al*., 2001; Vendrame & Gottlieb, 2004), and that 5–12% of the 7 million people in the UK with IGT will progress to type 2 diabetes every year (Santaguida *et al*., 2006; Diabetes UK, 2009). Therefore, interventions – such as behaviour change and exercise – for individuals who are diagnostically considered to have NDH are high priority, as they provide a substantial opportunity for preventing future burden of diabetes on the NHS, the UK economy, and patients and their families (Diabetes UK, 2009).

2.4 The burden of diabesity

The burden of obesity and type 2 diabetes is well known and is a significant economic challenge to the NHS since both diseases are associated with significant treatment and personal morbidity (World Health Organisation, 2006). In 2015, the prevalence of diabetes in the UK was 3.5 million adults (Health and Social Care Information Centre, 2015). It is estimated that a further 549,000 people remained undiagnosed and the prevalence is expected to reach 5 million by 2025 (Diabetes UK, 2015b). Ninety percent of diabetic cases are type 2 diabetes (Health and Social Care Information Centre, 2014), caused by lifestyle choices superimposed over the interplay between genetic susceptibility and environment. Research suggests that people from South Asian and African-Caribbean communities are two to four times more likely to develop type 2 diabetes than those from Caucasian backgrounds (Tillin *et al*., 2012; Ntuk, Gill, Mackay, Sattar, Pell, 2014), and that obesity is considered the most potent risk factor, accounting for 80–85% of the overall risk of developing type 2 diabetes (Hauner, 2010). In the UK, it is estimated that 59% of women and 68% of men are overweight or obese (Ng *et al*., 2014). This underlies the national, and global, spread of the disease. Cardiovascular disease accounts for 52% of mortality in people with type 2 diabetes (UK Prospective Diabetes Study, 1998), and those with diabetes have a two-fold risk of developing cardiovascular disease compared with those without diabetes (Emerging Risk Factors Collaboration, 2010).

Economically, the current estimation is that 10% of the NHS budget is spent on diabetes (£10 billion). The total cost (direct care and indirect costs) associated with diabetes in the UK is £23.7 billion and is predicted to rise to £39.8 billion by 2035 (Hex, Bartlett, Wright, Taylor & Varley, 2012). The economic burden associated with obesity is similarly stark. The 2007 report from Foresight (Tackling Obesities: Future Choices Project Report) provided an overview of obesity in the UK which included modelled estimates of future trends in levels of obesity and obesity-related diseases, and associated costs in terms of both the health service and of wider society (Butland *et al*., 2007). Estimates of the direct costs to the NHS for treating overweight and obesity and related morbidity in England were £4.2 billion. Estimates of the indirect costs (costs arising from the impact of obesity on the wider economy such as loss of productivity) were £15.8 billion (*ibid*.). Although it is difficult to define costs, interpret trends and compare estimates (National Obesity Observatory, 2011), what is clear is that obesity and diabetes are a burgeoning public health problem. NHS costs attributable to overweight and obesity are projected to reach £9.7 billion by 2050, with wider costs to society estimated to reach £49.9 billion per year (Butland *et al*., 2007). Whether diabetes and obesity have a distinct pathogenesis or whether they have a common underlying mechanism is still a topic of debate (Eckel *et al.*, 2011); however, at the healthcare coalface, we should address both conditions in a unified manner and not as two conditions in isolation (Rajeswaran, 2012).

2.5 Exercise in the treatment and management of obesity and type 2 diabetes

Since physical inactivity, obesity and insulin resistance are inextricably linked, exercise needs to be considered an essential part of preventing, delaying or treating type 2 diabetes. The benefits of regular exercise in the prevention and treatment of disease is strongly evidenced with preventative and therapeutic effects against cardiovascular disease, type 2 diabetes, metabolic syndrome, obesity, osteoporosis, colon cancer, breast cancer and depression (Booth, Chakravarthy, Gordon & Spangenburg, 2002b; Department of Health, 2011; Jones *et al*., 2011). This is particularly important for diabetes because exercise improves the primary defect – insulin resistance – and directly targets some of the most serious comorbidities associated with the disease, such as cardiovascular disease and depression (Barbour, Edenfield & Blumenthal, 2007; Colberg *et al*., 2010; Hu *et al*., 2011). Therefore, lifestyle interventions that include exercise, should be considered a cornerstone of diabetes prevention and management. It has been suggested that if exercise were a drug it would be the most powerful poly-pill in the world, with a unique and unusually extensive beneficial side-effect profile (Anstiss & Bromley, 2010).

The perceived benefit of exercise and physical activity in healthcare and public discourse seems to reside in the association with weight loss. Whilst this is unequivocally important, especially for type 2 diabetes, it is equally important to realise that exercise provides benefits irrespective of weight loss. Evidence from mechanistic studies demonstrate clear improvements in metabolic health and glycaemic control, via 'adiposity independent' mechanisms (Telford, 2007; Yates, Davies, Sehmi, Gorely & Khunti, 2011). Furthermore, exercise can alter the deposition of adipose tissue. For example, exercise has been shown to reduce intra-abdominal and hepatic adipose tissue without impacting overall mass (Johnson *et al*., 2009). This is important because intra-abdominal fat is associated with increased pathogenesis of numerous cardiovascular and diabetes risk factors. Therefore, an assertion by Yates (2012) – that the historic preoccupation of judging lifestyle interventions solely by their effects on body weight might be damaging, and that emphasising healthy lifestyles for their own sake will allow exercise to be used to its full potential – is particularly apt.

Yates (2012) also states there is unequivocal evidence that physical activity is directly involved in the processes governing glucose regulation. Evidence for a causal link between physical activity and the prevention and treatment of type 2 diabetes is supported by the full spectrum of methodology needed to infer causality, from observational research, to experimental mechanistic investigation to randomised controlled trials (RCTs). Gill and Cooper (2008) reviewed data from 20 longitudinal cohort studies and found that regular physical activity substantially reduced risk of type 2 diabetes. Even after adjustment for differences in BMI between active and inactive groups, a high level of physical activity was associated with a 20–30% risk reduction. This reduction was greatest in those at increased baseline risk of the disease (e.g. those with obesity or NDH). Additionally, meta-analyses have consistently demonstrated the benefit of physical activity in benefiting those with type 2 diabetes. For example, Boulé, Kenny, Haddad, Wells & Sigal (2003) summarised the effect of structured exercise training on cardiorespiratory fitness ($\dot{V}O_{2max}$). Data from nine randomised trials comparing exercise and control groups (overall n = 266) found an 11.8% increase in $\dot{V}O_{2max}$ in the exercise group and a 1.0% decrease in the control group. Studies using higher exercise intensities tended to produce greater improvements in $\dot{V}O_{2max}$ and HbA_{1c}. Similarly, in a Cochrane review, Thomas, Elliot & Naughton (2006) found that exercise significantly improved glycaemic control compared to non-exercising populations. Data were taken from 14 RCTs (n = 377) with exercise interventions ranging from 8 weeks to 12 months. Decrease in HbA_{1c} was 0.6% (6.6 mmol·mol) which is in line with other meta-analyses (e.g. Boulé *et al*., 2001; Umpierre *et al*., 2011). Furthermore, this improvement in glycaemic control occurred without change in total body mass, but importantly, exercise did result in a reduction of intra-abdominal adipose tissue (- 45.5 cm^2 cross sectional area) which, as discussed, is an important risk factor for metabolic disease. Other meta-analyses (43 studies including 3476 participants) have supported the use of exercise as a weight loss intervention, particularly when combined with dietary change (Shaw, Gennat, O'Rourke & Del Mar, 2006).

Several international long-term intervention trials have demonstrated that a structured lifestyle intervention, including encouragement to be more physically active, has beneficial effects on reducing the incidence of type 2 diabetes in at risk populations (e.g. those with IGT). Collectively these studies are referred to as 'diabetes prevention trials' and the findings are held in high esteem and have been well publicised. These studies were conducted across a range of countries including: Sweden (Eriksson & Lindgärde, 1991), China (Pan *et al*., 1997), Finland (Tuomilehto *et al*., 2001), USA (Knowler *et al*., 2002), Japan (Kosaka, Noda & Kuzuya, 2005) and India (Ramachandran *et al*., 2006). Currently the NHS Diabetes Prevention Programme (NHS DPP) is being implemented across England and will cover the whole country by 2020, with the aim of identifying those at high risk to refer them onto an evidence-based behaviour change programme to help reduce their risk (NHS England, 2016). It is unknown if the results of the diabetes prevention trials can be replicated in other populations, or if such individual behaviour change strategies, rather than population based strategies, are sustainable and affordable in the context of demographic, cultural and socio-economic factors (Zimmet, Shaw & Alberti, 2003; Barry, Roberts, Finer, Vijayaraghavan & Greenhalgh, 2015). They nevertheless demonstrate the efficacy of physical activity to reduce the burden of diabetes. For example, in the USA DPP, individuals with IGT randomised to the lifestyle arm of the trial, experienced a greater reduction in incidence of type 2 diabetes than those randomised to drug therapy (metformin) (58% vs 31%, respectively) (Knowler *et al*., 2002).

To promote health, the American College of Sports Medicine (ACSM) and American Diabetes Association (ADA) (Colberg *et al*., 2010) recommend aerobic exercise training for a total of 150 minutes per week at a moderate intensity (40%–60% $\dot{V}O_{2max}$). Exercise should be performed at least three times per week with no more than two consecutive days between bouts of activity due to the transient nature of exercise-induced improvements in insulin action (King *et al*., 1995; Boulé *et al*., 2005). Although most clinical trials have used an exercise frequency of three times per week (e.g. Boulé *et al*., 2001; Thomas *et al*., 2006), current guidelines recommend five sessions of moderate activity per week (e.g. Haskell *et al*., 2007; O'Donovan *et al*., 2010). Exercising at higher intensities (> 60% $\dot{V}O_{2max}$) might confer additional benefit, since a meta-analysis demonstrated that exercise intensity predicts improvements in overall blood glucose control more than exercise volume (Boulé *et al*., 2003). Additionally, resistance exercise should be undertaken two or three times per week on non-consecutive days, and of a sufficient intensity to maintain muscle mass and strength (i.e. 5 – 10 exercises involving the major muscle groups, progressing to a resistance of ~75%–80% of one repetition maximum) (Albright *et al*., 2000; Sigal, Kenny, Wasserman & Castaneda-Sceppa, 2004). For improving blood glucose control, combining aerobic and resistance exercise in a single session may be of greater benefit than either activity alone (Sigal *et al*., 2007), although whether this is simply due to the increased volume of exercise and associated caloric expenditure is not clear.

2.6 The importance of cardiovascular fitness

Reducing adiposity should not be the singular or even primary aim of physical activity interventions. The historic preoccupation of judging interventions solely by the effects on body weight needs to be challenged among healthcare and fitness professionals, in addition to altering broader public misconception (Yates, 2012). The seminal research of Blair and colleagues, almost 30 years ago, highlighted the importance of cardiovascular fitness in reducing mortality (Blair *et al*., 1989). Since then, a plethora of epidemiological evidence supports the independent role of fitness in managing disease risk. In a prospective study of 9,777 men, those with higher fitness had a lower incidence of all-cause-mortality and cardiovascular disease after adjusting for other risk factors of premature mortality including age and health status (Blair *et al*., 1995). Low fitness is an important independent precursor of mortality with adjusted relative risks of 1.5 and 2.1 for men and women, respectively (Blair *et al*., 1996). Furthermore, improving baseline fitness reduced mortality risk by 44% at subsequent testing (4.9-year follow-up) (Blair *et al*., 1995). Moderate cardiovascular fitness also seems to protect against other predictors of mortality such as smoking, dyslipidaemia, adiposity, and hypertension (Blair *et al*., 1996; Sui *et al*., 2007b, c). Other prospective cohort studies have highlighted that moderate cardiovascular fitness is more strongly associated with all-cause mortality than the overall volume of self-reported leisure-time physical activity (Lee *et al*., 2011). Consequently, a recent statement from the American Heart Association recommended that fitness should be considered in clinical practice with a focus on individuals who are habitually sedentary, because most risk reduction occurs when moving from the least fit group to the next least fit group (Ross *et al*., 2016).

These arguments should not be taken to imply that weight loss is not an important health outcome. Rather, a fixation with weight loss is misdirected, and potentially harmful if it interferes with the positive message of embracing a healthy lifestyle for its own sake (Yates, 2012). There are also several methodological issues with large-sale, purely observational studies. They use relatively weak measurement instruments to measure very complex behavioural attributes such as physical activity, and primary end-points (usually mortality or presence of a disease) are evaluated against a behavioural, biochemical or physiological predictor measured several years previously – which may have changed in the intervening period (Willaims & Williams, 2005). It is also difficult to infer change from non-experimental data since change in risk associated with movement between quantiles is partly attributed to measurement error (Williams, 2003). Nevertheless, there is unequivocal evidence that adequate cardiorespiratory fitness is protective independent of other risk factors, and as such needs to be considered a fundamental aim of physical activity interventions to improve public health.

2.7 The challenge of prescribing exercise as medicine

Although evidence for the *efficacy* (the ability to produce a desired or intended result) of exercise interventions in treating disease is strong, some have argued there is an apparent dearth of evidence for its *effectiveness* (the likely success under real-world conditions) (Beedie *et al*., 2015). Many studies intending to examine exercise effectiveness use laboratory-style methods and controls that would be impractical and uneconomical in real-world interventions (Beedie, Mann & Jimenez, 2014). As such, as a medicine – exercise has been shown to treat patients and bring about its intended effect under ideal circumstances, but it remains equivocal whether it can be similarly beneficial in the usual or clinical setting. These concerns were reflected in recent reports from the UK Government (All-Party Commission on Physical Activity, 2014) and Public Health England (2014), and are potentially decisive because effectiveness is what matters to commissioners and patients (Beedie *et al*., 2015). A common criticism of the use of exercise as a treatment is poor adherence, which can be defined as 'the extent to which a person's behaviour corresponds with agreed recommendations from a healthcare provider' (Sabaté, 2003). Adhering to an exercise programme enhances its effectiveness, and is clearly an important pre-requisite for the success of any intervention. Adherence to exercise is reported at between 40% and 50% (Hallal *et al*., 2012) in the general population, but is lower in patients with type 2 diabetes (Qiu, Sun, Cai, Liu & Yang, 2012). However, similarly poor adherence is reported for commonly prescribed drugs, yet – as argued by Church & Blair (2010) – the medical establishment seems to require a higher adherence standard for exercise prescription than for medication prescription. Considering the wide-reaching benefits caused by and associated with exercise, this could be damaging to the aims of health promotion.

At the root of poor adherence to exercise is perceived lack of time (Reichart, Barros, Dominigues & Hallal, 2007). In a systematic review of 13 studies on the reported barriers to regular exercise among adults either at high risk or already diagnosed with type 2 diabetes, 'lack of time' was the most commonly cited internal barrier to exercise (Korkiakangas, Alahuhta & Laitinen, 2009). Simultaneously, current exercise guidelines for health focus on relatively high volumes of moderate-intensity exercise on most or all days of the week. Current guidelines from the ACSM (Haskell *et al*., 2007), British Association of Sport and Exercise Sciences (BASES; O'Donovan *et al*., 2010) and the Department of Health (2011) recommend 150 minutes per week of moderate-intensity aerobic exercise, or 75 minutes of vigorous-intensity aerobic exercise. For adults at risk of metabolic disease it is recommended to effectively double these durations of exercise (O'Donovan *et al*., 2010). Therefore, the use of exercise as a preventative or therapeutic treatment is problematic and the challenge of encouraging individuals and populations to lead a more active lifestyle remains. We must nevertheless ensure the healthcare service is as committed to getting patients active as to getting them to take medications or submit to various procedures that have less scientific evidence supporting their benefit (Sallis, 2009). The challenge of tackling the cause of physical inactivity is of course extremely complex and multifactorial, and part of the problem lies in the disparity between public health policy, clinical guidelines and the delivery of physical activity promotion within the NHS in the UK (Weiler, Chew, Coombs, Hamer & Stamatakis, 2012). However, despite attempts to more closely align healthcare with the fitness industry, such as exercise referral schemes (e.g. Dugdill, Graham & McNair, 2005), the reality is that engineering large volumes of physical activity into everyday life for the general population is likely to prove very difficult indeed.

2.8 An alternative approach to exercise prescription: HIT

The optimal dose of exercise is not without ambiguity. Church and Blair (2009) highlight that the commonly prescribed dose of 150 minutes per week of moderate-intensity physical activity is the result of a self-fulfilling prophecy whereby, based primarily on epidemiological data, 150 minutes was identified as a good recommendation. Subsequent research has used this threshold to define intervention goals resulting in research examining 150 minutes per week rather than research examining different doses, intensities, types, or frequencies of exercise. Although 150 minutes may be efficacious, it should not preclude alternative approaches to exercise, which could be more time-efficient and eminently achievable for more of the population.

The advent, and current popularity (Thompson, 2013), of high-intensity interval training (HIT) could offer some solution. HIT is characterised by an alternating low-intensity, high-intensity interval based approach to exercise. Total duration of exercise is usually less than traditional aerobic exercise and most of the exercise time is spent at a low-intensity, with the caveat that a series of high-intensity (described as ‘maximal’ or ‘all-out’) periods of exercise are included. Proponents of HIT highlight the physiological benefits this type of exercise offers (e.g. Gibala, Little, MacDonald & Hawley, 2012). Reduced expression of peroxisome proliferator-activated receptor-γ coactivator (PGC)-1α, which is involved in transcription of mitochondrial biogenesis and metabolism, is lower in people with insulin resistance, NDH, and type 2 diabetes (Patti *et al*., 2003). Several studies have confirmed the potency of HIT in increasing the expression of and nuclear mitochondrial content of PGC-1α (Burgomaster *et al*., 2008; Gibala *et al*., 2009). This suggests HIT might have the potential not just to reduce the time burden of exercise, and therefore appeal to people who otherwise would not engage with it (e.g. Gaesser & Angadi, 2011), but also to increase the ability of the cell to oxidise glucose benefitting insulin resistance (Lowell & Shuman, 2005). This has clear relevance to clinical practice because the acceptability and accessibility of the activity to those for whom the intervention is intended, and the practicalities of building the activity into everyday life, need to be considered (Haines, Gillibrand & Garbutt, 2012) – in addition to physiological efficacy.

2.9 Redefining HIT

Research has repeatedly demonstrated the efficacy of HIT in improving a range of physiological parameters relevant to health (e.g. Gibala & McGee, 2008). However, studies have mostly relied on protocols that can generally be assumed to be too intense for use by the general population and clinical patients. By doing so, this approach to exercise only serves to exchange one barrier (time) for another (intensity of exercise). More recent research on HIT has started to focus on affective states, such as pleasure and displeasure associated with this type of exercise (e.g. Jung *et al*., 2014). Furthermore, in many studies the time commitment to carry out HIT on a per session basis is only minimally less than traditional exercise recommendations. For these reasons, it is not clear whether HIT could be used as a time-efficient or practicable approach to exercise with the aim of reducing the burden of physical inactivity. What is clear, however, is that further studies using HIT protocols that are less intense and genuinely time-efficient, and therefore have the potential to be adopted by the general population, are needed. Research with individuals at high risk of, or already diagnosed with, metabolic disease is particularly important. In healthcare, this is important because honesty and clear and effective communication between the healthcare provider, or exercise professional, and patient is important in the nurturance of trust as part of the therapeutic relationship, which can in-turn improve adherence to interventions and patients' healthcare outcomes (Martin, Williams, Haskard & DiMatteo, 2005). If we wish to laud HIT as time-efficient and promote it as a physical activity and exercise option to promote public health, we need to refine protocols to provide evidence for their efficacy *and* effectiveness. As such, this thesis will explore a shortened-sprint REHIT protocol with the aim of being a genuinely time-efficient yet tolerable approach to exercise. This is predicated on a theoretical framework that proposes exercise is required for optimal health, and that hedonistic (pleasure-displeasure) theories of motivation, based on an intensity-affect-adherence series of events, might be an important predictor of future exercise behaviour.

Further critical discussion of the evidence for HIT as an exercise therapy for a range of populations is included in appendix 2. Moreover, Chapter 5 of this thesis provides detail of a systematic review of literature comparing the effects of time-efficient HIT against control or exercise comparison groups.

PART TWO: THEORETICAL FRAMEWORK

Chapter 3 Background Information

3.1 Perspectives based on evolutionary theory

3.1.1 Introduction

As a result of Darwinian evolution, *Homo sapiens* are an exercise-dependent species (Goh, Koh & Wackerhage, 2014). Polygenic diseases such as diabetes are in part triggered by a divergence between our genomes, which have been selected for high physical activity, and our current lifestyles which are marked by inactivity (*ibid*.). Therefore, chronic diseases such as type 2 diabetes are a natural consequence of modern lifestyle. An awareness of the ancestral human lifestyle and the discordance between our genes and modern environment can further our understanding of pathophysiology for diseases such as obesity and diabetes.

Human, chimpanzee (*Pan troglodytes*), and bonobo (*Pan paniscus*) ancestral lines split ≈7 million years ago, with modern humans evolving in Africa ≈300,000 to 200,000 years ago (Soares *et al*., 2008; Hublin *et al*., 2017). Throughout this time, human ancestors, like all other organisms, responded to environmental change through biological evolution (Eaton, Cordain & Sebastian, 2007). It is thought that most of the modern human genome comprises genes selected during the Palaeolithic Era in Africa (Pritchard, 2010), from 2.5 million to 11,000 years ago (Cordain, 2007). Since this time and up to the modern day, due to the slow rate of evolutionary change, our genome has changed little – yet through social organisation and technological innovation lifestyle has changed dramatically. Most of our ancestral past was spent as a hunter-gatherer or forager, subsisting on hunted wild animals and gathered wild plant foods. Following the Neolithic Revolution (≈10,000 years ago) humans have lived as agriculturalists, horticulturists and pastoralists. More recently, the Industrial Revolution (from 1800 to 1945) and the Modern Age have further transformed the lifestyle and activity profile of humans. We have all but engineered physically activity out of our lives creating what is often referred to as an ‘obesogenic environment’.

It is important to emphasise that the period over which these dramatic environmental changes have occurred is very short. On an evolutionary scale, they have happened ‘in the blink of an eye’ and are too recent for the human genome to have fully adapted (Carrera-Bastos, Fontes-Villalba, O’Keefe, Lindeberg & Cordain, 2011). It has been estimated that time since the

Neolithic Revolution represents only 0.5% of the history of the genus *Homo*, and that the Industrial Revolution and Modern Age – which represent the beginning of 'Western lifestyle' – represent just 0.009–0.005% of this time respectively (Carrera-Bastos *et al*., 2011). It is with this perspective that we should view the twin epidemics of obesity and diabetes for the mismatch between our ancient physiology and our current lifestyle underlies much modern disease.

3.1.2 Evolutionary perspectives of physical activity behaviour

Affective responses, that is sensations of pleasure and displeasure, in response to physical activity may be manifestations of evolved psychological mechanisms, selected for their ability to promote beneficial behaviours and to avoid risk (Nesse, 1990). It is reasonable to assume that pleasure associated with moderate-intensity exercise is a psychological mechanism that evolved to reward, and thus promote, this behaviour (Eikelboom, 1999). This would have been advantageous because many obligatory physical activity tasks required for survival fall within this range of intensity. Indeed, genetic polymorphisms have been associated with pleasure-based dopamine receptor mechanisms that reward and promote physical activity in humans, and attests this point (Simonen *et al*., 2003). Yet, the idea that we may have evolved to gain pleasure from exercise seems contradictory when considering the prevalence of physical inactivity in modern populations. However, modern humans have changed in ways that could make exercise unpleasant. For example, we now have an undesirable amalgamation of low fitness, reduced muscle mass, and high body mass (Ekkekakis, Hall & Petruzzello, 2005). Furthermore, it is also possible that the level of maximal exercise capacity has been subject to similar evolutionary pressures. Severely strenuous exercise, including HIT, results in a potentially critical perturbation of homeostasis. What prevents harm, is activation of protective mechanisms mediated by interoceptive (internal stimuli) sensations and conscious awareness of physiological responses, manifested as an overwhelming perception of fatigue and displeasure (Cabanac, 1979). These evolutionary perspectives should be considered when developing exercise strategies to combat physical inactivity.

Despite strong evidence supporting the myriad benefits of regular physical activity for health, the challenge of encouraging individuals and populations living in an obesogenic environment to do more exercise remains. If we have evolved to manage energy balance, it would be sensible to suggest that selection pressures acted on our propensity to avoid unproductive activity, as well as our ability to be physically active when needed. This perspective, could explain the innate human tendency to avoid voluntary exercise, and why long-term lifestyle behaviour change including more regular activity is difficult. Therefore, most people will only maintain optimal health and a healthy body weight by exerting substantial cognitive effort. We should recognise that genetic differences in susceptibility to obesity will make this harder for some than for others (Peters, Wyatt, Donahoo & Hill, 2002).

It is unlikely that we could build the political will to change the environment back to one that requires high levels of physical activity to subsist in daily life (Peters *et al*., 2002). The challenge is not to 'go back in time' but to engineer physical activity (and healthy eating) back into our lives in a way that is compatible with our current socio-cultural values (*ibid*.). Since the biological evolutionary mechanisms that determine how we regulate adiposity and glucose control developed under conditions in which obligatory physical activity was required to manage energy balance, exercise should be a central component of any public health strategy to improve health outcomes. Considering evidence from molecular signalling studies demonstrating that the mechanisms leading to the insulin- and exercise-induced stimulation of glucose uptake in skeletal muscle are specifically triggered by muscle action (i.e. physical activity), it seems regular movement is an integral requirement for normal genotypic expression and good health. Arguably, exercise is the essence of the machine (Booth *et al*., 2002a).

Parrying physical inactivity induced disease could conceivably be achieved in two ways. First, by focussing on realistic strategies to cognitively manage levels of exercise. It seems practically infeasible to attempt to engineer a significant volume of physical activity into modern lifestyle, so we should consider focussing on modifying physical activity guidelines that unrealistically promote high-volumes of activity. Second, by acceptable alterations to the obesogenic environment including land use, transport opportunities, and the way in which foods are manufactured and marketed. We can no longer rely on our instinct to regulate health – we must now rely on our intellect (Haines, 2015). Further critical appraisal of evolutionary perspectives of exercise, obesity, and diabetes is included in appendix 1.

3.2 Hedonicity, exercise and behaviour change: Psychological affective valence

3.2.1 Introduction

Despite the health benefits of regular exercise, the challenge of encouraging individuals and populations to lead a more active lifestyle remains. A common issue is poor adherence to exercise programmes. The problem is a complex interaction of psychobiological and environmental mediators, which are inherently resistant to research efforts to determine the most important predictors of physical activity behaviour (Ekkekakis, Parfitt & Petruzzello, 2011). Several broad-spectrum social or health psychology theories including the health belief model (Becker *et al*., 1977), the theory of planned behaviour (Ajzen, 1991), and the transtheoretical model (Marshall & Biddle, 2001) have been used to investigate and explain the challenges associated with maintaining exercise behaviour. These models are more suited to increasing the initial adoption of physical activity, rather than understanding and improving maintenance of participation (Dishman, 2001). However, approximately half of individuals who start an exercise programme stop within the first six months (Robinson & Rogers, 1994; Dishman & Buckworth, 1997) and it is important to remember that the decisions people make about physical activity behaviour are subject to environmental influence, and occur at several levels of consciousness. Other theories including social cognitive theory (Bandura, 1977), achievement motivation theory (Weiner, 1985), and self-determination theory (Deci & Ryan, 1985; Chatzisarantis, Hagger & Smith, 2007) hold that a high level of motivation and competence are needed to participate in regular physical activity. More recent notions contend that causal events link exercise adherence to feelings of pleasure versus displeasure – known as affective valence – associated specifically with exercise intensity. Indeed, sensations and perceptions during and after exercise, and their influence on adherence, has long been suspected as a contributor to the public health problem of physical inactivity (Ekkekakis, Hall & Petruzzello, 2008).

3.2.2 Hedonic theory of motivation

An alternative approach to predicting physical activity and exercise behaviour targets the motivational properties of the exercise stimulus itself, and the implications of the components of the exercise 'dose', including the intensity and frequency of exercise (Ekkekakis *et al*., 2008). Hedonic theories of motivation are predicated on an intensity-affect-adherence chain of events, with the degree of *pleasure* that exercisers experience a likely candidate for mediating the relationship. Although the relationship is probably complex the central tenet, proposed some time ago (Pollock, 1978), is that people are more likely to participate in exercise programmes that they enjoy. Studies have shown that decision making is a neuro-anatomical and cognitive process that is influenced by emotions and feelings operating consciously and sub-consciously (Bechara, Damasio & Damasio, 2000). It has also been suggested from an evolutionary perspective that hedonicity (i.e. pleasure and displeasure) is the signal for behaviour optimisation, and that minimising displeasure could be the key to achieving optimal behaviour (Cabanac, 2006). This is clearly relevant to the intended aims of high-intensity interval training (HIT) because the exercise dose is being manipulated with the intention of making exercise as convenient, efficient, and tolerable as possible.

Within this theoretical framework, dual-mode theory (DMT) explains the apparent decline in pleasure that accompanies increasing exercise intensities (Ekkekakis, 2003; Ekkekakis, Hall & Petruzzello, 2005). Specifically, affect experienced during exercise is influenced by the metabolic cost associated with the intensity at which exercise is performed. A reliance on anaerobic substrate phosphorylation increases by-products which decrease skeletal muscle force via central and peripheral responses. The ventilatory threshold, defined as a nonlinear increase in expired carbon dioxide relative to consumed oxygen, or a rise in blood lactate concentration because of the rate of production exceeding the rate of clearance, has been used to standardise definitions of exercise intensity in relation to affect – that is, exercise is either below, at, or above this point. These intensities are integrated into the DMT (Ekkekakis *et al*., 2005) in-line with the three-domain typology of exercise intensity (i.e. moderate, heavy and severe) as outlined by Gaesser & Poole (1996). Intensities above the ventilatory threshold are usually accompanied by a cascade of biochemical, neuroendocrine, autonomic, cardiovascular, and respiratory changes that dramatically transform the internal environment and challenge maintenance of homeostasis with perturbations closely linked to affect (Cabanac, 2006; Ekkekakis *et al*., 2008). Furthermore, people typically choose not to engage in behaviours they find aversive. This in-turn may predict future engagement in that activity (Emmons & Diener, 1986; Williams, Dunsinger, Jennings & Marcus, 2012) and longer-term exercise adherence (Williams *et al*., 2008). As such HIT may only be a viable alternative to traditional exercise guidelines if perceptive responses relating to displeasure are minimised.

3.2.3 Hedonicity and HIT

Hedonistic views and dual-mode theory have been used to question the likely adoption of HIT in public health settings and sedentary populations. Hardcastle, Ray, Beale & Hagger (2014) contend that high-intensity exercise might evoke a high degree of negative affect that may lead to an avoidant response with the prospect of future exercise sessions. It may also evoke anticipated perceived incompetence, lower self-esteem and potential failure (Hein & Hagger, 2007; Lindwall, Larsmann & Hagger, 2011). The generally accepted view is that lower-intensity effort makes exercise programmes more enjoyable (Pollock, 1978; Parfitt & Hughes,

2009) and that the intensity of exercise, more so than frequency, is related to non-adherence (Lee *et al*., 1996; Perri *et al*., 2002). In a study using 30 young adults participating in 15 minutes of treadmill exercise below, at, and above ventilatory threshold, affective valence did not decline when the intensity was below or at threshold, but did show a significant, quadratic and relatively homogenous decline when the intensity was 10% above the threshold (Ekkekakis *et al*., 2008). This supports the notion of a negative relationship between exercise intensity and affect, and specifically the use of ventilatory threshold as a physiological landmark beyond which affective valence starts to decline.

Based on DMT, one of the primary reasons for the advocacy of HIT – that it might appeal to individuals who otherwise would not engage with more time-consuming exercise – is juxtaposed with the conclusion that the intensity of exercise is likely to pose a significant barrier for many. Therefore, in replacing one barrier (time) with another (intensity) HIT is likely to suffer similarly poor adherence compared with current exercise guidelines, if the intensity of the activity is intolerable. However, critiques based on hedonicity have mostly relied on *continuous* exercise above the ventilatory threshold, which may be wholly inappropriate for understanding intensity-affect relationships associated with HIT, because the intermittent nature fundamentally alters the exercise experience. Indeed, as pointed out by Del Vecchio, Gentil, Coswig & Fukuda (2015) most critiques of the likely affective responses to HIT do not specifically involve HIT studies. Therefore, the findings from research based on DMT and exercise intensities associated with ventilatory threshold, cannot be assumed to generalise to studies of HIT.

The sensation of exertion and affective response depends on the type of work performed by skeletal muscle (Cabanac, 2006). Different types of work perturb homeostasis in various ways altering perceptual response. When work is extended overtime however, the sensation of the exertion becomes a function of duration (Cafarelli, Cain & Stevens, 1977). When standardised for duration and total external work output, continuous predominantly aerobic cycling and weightlifting have been shown to modify ventilatory flow, heart rate, and level of lactate, cortisol, insulin and blood glucose less than intermittent anaerobic cycling (VanHelder, Radomski, Goode & Casey, 1985). However, in this instance the exercise protocol used during intermittent cycling is not reflective of modern interpretations of HIT. At the start of exercise, sensation is a function of the muscle's resistance to external force (Cafarelli, 1982). These considerations highlight the importance of dose-response for approaches to HIT that aim to maximise physiological benefit without overly compromising perceptual response. Many approaches to HIT are likely to induce affective and physiological responses that render the activity intolerable for many people. However, it is possible that some iterations of HIT could be genuinely time-efficient and tolerable, without incurring the penalties of extended duration anaerobic metabolism. Whether such approaches could elicit the same physiological benefits as more intense HIT is not known.

Bartlett *et al*. (2011) compared high-intensity interval running with moderate-intensity continuous running and found that, despite higher perceived exertion, ratings of perceived enjoyment after exercise were significantly higher following interval running. This finding contradicts the view that lower-intensity effort makes exercise programmes more enjoyable (Pollock, 1978). Greater enjoyment may be relevant for improving exercise adherence and could be due to the varied activity profile of interval approaches to exercise. However, this research is based on a small sample of eight healthy and active males, thus it is difficult to extrapolate the findings to wider public health settings. Furthermore, the protocol used was dissimilar to most interpretations of modern HIT, and despite the increased perceived exertion, did not differ to continuous exercise in terms of heart rate response, oxygen requirement or energy expenditure. Therefore, the metabolic and substrate requirements for the two approaches to exercise included in this study were perhaps more similar than would be expected for HIT.

Furthermore, in the study of Bartlett *et al*. (2011) it is also an important consideration that enjoyment was measured after the exercise bout had finished because perceptual response *during* the exercise bout could be very different. A review of the dose-response literature, both within single studies and across meta-analyses, examining the effects of exercise intensity on affective changes measured from pre- to various time points post-exercise failed to show a reliable dose-response relationship (Ekkekakis & Petruzzello, 1999). Indeed, after the cessation of exercise there is a general unanimous shift in affective valence toward pleasure compared to pre-exercise, regardless of intensity (Ekkekakis, 2008). It is likely that dose-response effects may occur during exercise and then dissipate before post-exercise measurements of affect are recorded. Therefore, to capture a more complete depiction of affective responses, measurements should be taken during exercise. This is pertinent for measuring affective responses to HIT because the intensity of exercise changes dramatically between periods of recovery and ‘maximal’ or ‘all-out’ activity.

Affective associations with exercise might explain variance in physical activity behaviour and may also be mediated by cognitive variables such as anticipated benefits, barriers, cognitive attitudes, and perceived behavioural control (Kiviniemi, Voss-Humke & Seifert, 2007). The *peak-end rule* contests that memory associated with the pleasure or displeasure of exercise is influenced by two specific episodes; the moment a distinct 'peak' affective response is experienced, and the 'end' of activity – with the duration having little effect (Redelmeirer & Kahneman, 1996; Kahneman, 1999; Fredrickson, 2000). During exercise, the peak moment could relate to pleasure or displeasure and could influence retrospective evaluations of that activity. As such, this is an important consideration for affective responses associated with HIT, because even if most exercise time is spent at a low-intensity; the high-intensity sprints could produce a negative affective peak which in-turn could impact motivational factors related to individual attraction to exercise and future adherence. It is not clear whether the peak or end affective state is most important in predicting retrospective evaluations of events, but applying the DMT to the peak-end rule would suggest that individuals who exercise above the ventilatory threshold would record a more negative affective peak compared to those who exercise below the threshold (Parfitt & Hughes, 2009). This could have implications for the design of HIT protocols. Efforts should be directed to minimise the perceptual displeasure associated with the high-intensity portions of HIT. For example, it seems likely that the supra-maximal intensity prescribed in Wingate-based approaches to HIT (e.g. Burgomaster *et al*., 2008; Rakobowchuk *et al*., 2008; Whyte *et al*., 2013) would result in a high negative peak affective valence response and would therefore create a reluctance to repeat the exercise. Although the peak-end rule has received some experimental support in studies that have manipulated discomfort or pain (Stone, Schwartz, Broderick & Shiffman, 2005; Kemp, Burt & Furneaux, 2008) very little research has applied the rule to experiences during exercise, and no research has considered this with HIT. Indeed, the motivational significance of the exercise stimulus during HIT might be important – and has been an underexplored factor underlying physical activity behaviour in general (Ekkekakis, 2009).

3.2.4 Studies that have measured affective response to HIT

More recent research has started to consider the intensity-affect relationship of HIT. Oliveira *et al*. (2013) compared psychological responses between HIT and vigorous-intensity continuous training. Both approaches to exercise were adjusted to allow the same total duration and average intensity, set at the boundary between the heavy and severe exercise domains (85%

of the respiratory compensation point). Affective valence was measured throughout exercise using the Feeling Scale (FS) (Hardy & Rejeski, 1989) and values were lower (less pleasurable) during HIT than for continuous training. Furthermore, scores decreased more over time during HIT and coincided with increased perception of effort and arousal. Despite the lower FS values (greater negative affect) observed during HIT, the overall activity enjoyment measured 10 min post-exercise was not significantly different compared to continuous training. This contradicts the findings of Bartlett *et al*. (2011) who reported greater enjoyment after interval training. Most recently, Decker & Ekkekakis (2017) observed lower pleasure and enjoyment associated with HIT compared to moderate-intensity continuous exercise, measured throughout each exercise bout. This raises questions relating to the sustainability and tolerability of HIT, which is less likely to be adopted by the general population if it is associated with greater displeasure, despite a reduced time commitment. However, the protocol in this study used relatively long intervals (4 × 3 min intervals at 115% of power at the ventilatory threshold) and as such the results of other approaches to HIT using differing interval and recovery patterns may yield different results.

Differences in training protocols are likely to have a significant impact on perceptual responses irrespective of the average intensity of exercise. The protocol used by Oliveira *et al*. (2014) was very intense requiring participants to maintain an intensity of 100% of $\dot{V}O_{2peak}$ for 2 min, and is not representative of the recent emphasis on refining HIT to make it as tolerable as possible. Although measures of acid-base balance were not taken, this protocol results in extreme physiological responses and feelings of fatigue, a fact reflected by the inability of eight of the 15 participants to complete the HIT protocol. The predominance of anaerobic metabolic pathways during exercise, determined by the magnitude of the intensity stimulus, is likely to be a key factor in the psychological response to HIT. Although the opponent process theory (Solomon, 1980) proposes that a feeling of pleasure can occur after an aversive stimulus – which can activate reward and encourage repetition of that stimulus – it is not clear if people adhere to exercise based on perceptions experienced during or after exercise. Furthermore, the FS is related to basic affect, whereas rating of enjoyment is related to emotional state for which the time of data collection post event is an important consideration.

In contrast to the study of Oliveira and colleagues, Jung *et al*. (2014) assessed a more practical lower-volume approach to HIT using a 1:1 work-to-rest ratio lasting 1 min each (20 min total duration eliciting a heart rate ~90% HR_{max}), and compared this to both moderate and vigorous-intensity continuous exercise. HIT resulted in more pleasant affective responses than vigorous continuous exercise but not moderate exercise. Nevertheless, despite more negative affective states for HIT compared to moderate continuous exercise, participants reported greater enjoyment of HIT in-line with the findings of Bartlett *et al*. (2011), in addition to a greater preference and improved confidence to engage with HIT compared to continuous exercise. There was also a large magnitude effect (effect size of 1.4) for more pleasant in-task affect nearing the end of the training bout in HIT (92.5% completed), compared to vigorous exercise. The difference in responses compared to Oliveira *et al*. (2013) are likely a result of the lower intensity. A further equivocal unique aspect of HIT was an apparent positive rebound effect 20 min post-exercise not associated with vigorous continuous exercise. This suggests that the intermittent nature of HIT might afford a unique perceptual and emotional response, associated with the successive positive accomplishments of completing each high-intensity bout (Jung *et al*., 2014).

Other researchers have suggested that HIT may be a viable alternative to continuous exercise in the promotion of health and fitness. Kilpatrick, Greeley & Collins (2015) found that HIT protocols, described as 'heavy' and 'severe', produced affective and enjoyment responses that were more like moderate continuous exercise, and more positive than heavy continuous exercise, in healthy and recreationally active participants. The same research group (Martinez, Kilpatrick, Salomon, Jung & Little, 2015) also studied insufficiently active overweight and obese participants, and found that affect and enjoyment were higher for shorter interval trials compared to longer intervals, and continuous exercise. Others have used low-volume HIT and reported improved perception of health without inducing the mood disturbances associated with higher-volume HIT (Freese *et al*., 2014). Collectively these studies demonstrate that the DMT, whereby negative affective responses to exercise are consistently a result of the intensity and associated metabolic cost of exercise, might not fully explain affective states during and following discontinuous exercise characterised by discrete periods of high- and low-intensity exercise. Specifically, it seems that interval exercise above the ventilatory threshold can be pleasurable, although the duration of the high-intensity period of exercise is a determining factor. Thus, hedonic theories of exercise behaviour such as the DMT may need elaboration to consider the full spectrum of intermittent exercise.

3.2.5 Conclusion

Minimising displeasure is likely to be an important signal for optimising exercise behaviour. Hedonistic theories of motivation, such as DMT, are predicated on a relationship between intensity, affect and adherence, and have been used to question the likely success of HIT because high-intensity exercise may present a significant barrier for many. Since adherence is a prerequisite for the effectiveness of any exercise intervention this is a challenge for the furtherance of the research agenda on HIT. Furthermore, it is not clear if affective response during or after exercise is the most important consideration in predicting future exercise behaviour. So far, research findings on affective response to HIT have been inconsistent because of the different protocols used in terms of intensity, frequency and duration of the high-intensity bouts, in addition to recovery in-between bouts. What is clear is that differing HIT protocols, particularly those which place a high reliance on anaerobic energy pathways, can have significantly different effects on the perceptual and emotional response to exercise. Therefore, the challenge remains to maximise physiological benefit without overly compromising perceptual response.

3.3 Physiological and molecular mechanisms by which HIT improves glucose control and cardiovascular fitness

3.3.1 Introduction

Exercise can be precisely defined as a potential disruption to homeostasis by muscle activity that is either exclusively or in combination, concentric, isometric or eccentric (Winter & Fowler, 2009). The associated disruption to homeostasis (i.e. stability of physiological processes) causes adaptations to occur at the biochemical, cellular, and whole-body levels of organisation. Hence exercise-induced perturbation to metabolism is an important mediator of health outcomes, and the intensity, frequency, and duration of exercise should be such that metabolic energy expenditure is usually substantially above that at rest (Bouchard & Shepard, 1994). In general, there are several mechanisms by which exercise increases glucose uptake, both acutely and via insulin-stimulated glucose uptake in the days after exercise. More specifically, increased energy turnover in response to HIT may lead to the activation of several muscle proteins which then, via various transcriptional co-factors, regulates the expression of mitochondrial genes to increase oxidative capacity and cardiovascular fitness (Barr & Wackerhage, 2014). Given that the modern human genome was selected for an environment where physical activity was obligatory, it should not be surprising that regular exercise is fundamental for optimal phenotypic expression and good health.

3.3.2 Glucose transport and uptake

Principally, regulation of muscle glucose transport in response to exercise can be considered via two separate pathways. Firstly, intracellular changes in the metabolic status of the muscle mediate molecular signalling mechanisms that increase glucose uptake. These are in direct response to muscle activity and are thought of as 'insulin-independent', bypassing the typical insulin signalling defects associated with insulin resistance conditions (Hawley & Lessard, 2008). For example, release of calcium from the sarcoplasmic reticulum changes ion balance activating the Ca^{2+}/calmodulin-dependent protein kinase pathway, which stimulates glucose transport (Wright, Geiger, Holloszy & Han, 2005). Calcium-binding proteins may play an important role in metabolism including lipid breakdown and catalysing rate-limiting steps in glycogenolysis (Nishizawa *et al*., 1988). Furthermore, at a molecular level exercise is a form of energy consumption, and decreases in cellular chemical energy (ATP and creatine phosphate) in response to exercise increase adenosine monophosphate (AMP) levels, evoking AMP-activated protein kinase (AMPK) mechanisms which improves insulin sensitivity (Jessen & Goodyear, 2005). As such, these feedback mechanisms serve to ensure increased glucose uptake into skeletal muscle during exercise. Additionally, feed-forward control mechanisms such as the stimulation frequency of motor nerves, which increases during exercise, might further regulate glucose transport (Richter, Nielsen, Jørgensen, Frøsig & Wojtaszewski, 2003). Due to these mechanisms, exercise can be considered an insulin mimetic, and is responsible for the acute increase in glucose transport during and 2–4 hours after exercise (Holloszy, 2005). Higher-intensity exercise is likely to activate these responses more than moderate-intensity exercise resulting in greater skeletal muscle glucose uptake (Rose & Richter, 2005).

Secondly, as the acute increase in glucose transport diminishes, depletion of muscle glycogen associated with exercise increases muscle insulin sensitivity. This is caused by up-regulation of the enzyme glycogen synthase and glucose transporter (GLUT)-4 protein. GLUT-4 allows facilitated diffusion of glucose into the muscle cells where it can be polymerised and stored as glycogen. Since exercise depletes this stored glycogen, muscle cells must recover during the post-exercise period and often overcompensate in a process known as muscle glycogen supercompensation (Wojtaszewski *et al*, 2003). This is achieved by an increase in glucose transport mediated by translocation of more GLUT-4 to the muscle sarcolemma (cell surface) from intracellular storage sites followed by an increase in the intrinsic activity of the transporters (Furtado, Poon & Klip, 2003). In this way, exercise enhances insulin-stimulated glucose transport post-exercise because of an enhanced recruitment and activity of GLUT-4 in response to glycogen depletion. This may last for up to 48 hours (Perseghin *et al*, 1996).

3.3.3 Physiological and molecular responses to HIT

The molecular mechanisms underlying skeletal muscle metabolic adaptations to HIT have been reviewed elsewhere (e.g. Gibala & McGee, 2008; Gibala, Little, MacDonlad & Hawley, 2012). Although such adaptations to training are undoubtedly complex and determined by many physiological and psychological factors, research has focussed primarily on several specific ‘peripheral’ adaptations. For example, the origin of improvements in cardiovascular fitness (or $\dot{V}O_{2max}$) are thought to be signalling mechanisms involved in skeletal muscle remodelling towards a more oxidative phenotype, resulting in improved skeletal muscle oxygen extraction due to increased mitochondrial density (Jacobs *et al*., 2013; Sloth *et al*., 2013). However, recent research has suggested that improvements in $\dot{V}O_{2max}$ are due to improvements in ‘central’ oxygen delivery, such as increases in maximal stroke volume and cardiac output, rather than peripheral adaptations (Astorino *et al*., 2016). Other research contradicts this, reporting improvements in aerobic performance without accompanying increase in cardiac output (Macpherson, Hazell, Olver, Paterson & Lemon, 2011). Similarly, evidence as to whether HIT increases blood volume is also conflicting (Warburton *et al*., 2004; Jacobs *et al*., 2013). Therefore, it remains unclear whether improvement in $\dot{V}O_{2max}$ is attributable to central or peripheral adaptations. Nevertheless, Vollard, Metcalfe & Williams (2017) recently speculated that improvement in $\dot{V}O_{2max}$ after HIT could be explained by both peripheral *and* central adaptations with rapid glycogen depletion, which is characteristic of HIT, as the mediator.

Skeletal muscle glycogen is the main storage form of glucose in the body, and acts as an acute regulator of skeletal muscle metabolism. It also determines signalling events that occur in response to exercise and affects skeletal muscle adaptation to exercise (Philp, Hargreaves & Baar, 2012). During HIT, the rapid rate of glycogenolysis significantly perturbs homeostasis via change in intramuscular ATP:ADP/AMP ratio (Chen *et al*., 2000; Xiao *et al*., 2011), which is followed by an attendant activation of glycogen-bound 5’ AMPK. Essentially, AMPK functions as an energy-deficit sensor, and is increased as muscle glycogen diminishes (Hudson *et al*., 2003; Goh *et al*., 2014). Activation of p38 mitogen-activated protein kinase (MAPK) is also thought to be activated in response to the metabolic status of skeletal muscle (Gibala *et al*., 2012). These upstream signals in-turn activate peroxisome proliferator-activated receptor-γ coactivator (PGC)-1α which is the ‘master regulator’ of mitochondrial biogenesis in skeletal muscle (Wu *et al*., 1999). The role of these peripheral mechanisms is well established after HIT. Furthermore, the high rates of glycogenolysis during HIT are associated with accumulation of metabolic by-products and a hypertonic intramyocellular environment, and a transient ~15–20% drop in plasma volume which could act as a stimulus for central adaptations including increased blood volume (Metcalfe *et al*., 2015). Therefore, via glycogen depletion, HIT may improve cardiovascular fitness via both peripheral (increased mitochondria density) and central (increased blood volume) mechanisms. These mechanisms were once considered to be exclusive to higher volume, continuous, moderate-intensity exercise. Whereas this type of exercise lowers the absolute *amount* of energy stored in skeletal muscle more dramatically than HIT, it is the *rate* at which energy is depleted during HIT that signals similar mechanisms that lead to improvements in both $\dot{V}O_{2max}$ and glucose uptake.

3.3.4 Other physiological considerations

In overweight and obese individuals, several fat related metabolites such as free fatty acids and ceramides inhibit the insulin-signalling cascade, reducing insulin-stimulated glucose uptake (Boden & Chen, 1995; Kahn *et al*., 2006). High intramuscular triglyceride concentrations are also associated with insulin resistance in those with obesity and type 2 diabetes (Goodpaster, He, Watkins & Kelly, 2001). Paradoxically, endurance based exercise can also result in elevated intramuscular triglyceride storage, although this adaptation seems to be related to an increased propensity to oxidise triglyceride as fuel during exercise (Schrauwen *et al*., 2002). The ability to do this is likely to be important in preserving insulin sensitivity. Shepherd *et al*. (2013) demonstrated increased intramuscular content and enhanced net breakdown of triglyceride following six-weeks of high-volume HIT, suggesting that this type of activity can also contribute to mechanisms that may improve insulin sensitivity. This change was found to be related to upregulated expression of perilipin 2 and 5 proteins, which function to form lipid droplets in adipose tissue and are thought to be important in mediating the hydrolysis of intramuscular triglyceride as a fuel during exercise (Shepherd *et al*., 2012).

Regulation of energy balance and by association adiposity, is to a significant degree managed by exercise-induced increases in caloric expenditure, mediated by muscle action. However, it is not known how effective HIT is in reducing fat mass since most studies are of insufficient duration to consider the long-term effects on subcutaneous or abdominal adipose tissue. Nevertheless, several studies have reported reductions in fat mass which suggests that HIT might play a role in exercise-mediated control of energy balance (e.g. Tremblay, Simoneau & Bouchard, 1994; Boudou, Sobngwi, Mauvais-Jarvis, Vexiau & Gautier, 2003; Trapp, Chisholm, Freund & Boutcher, 2008). More generally, there is a clear inverse relationship between physical activity and all-cause mortality, with a ~30% risk reduction when comparing the most active with the least active individuals (US Department of Health and Human Services, 2008). The strength of evidence for benefit is strong for cardiovascular disease and stroke (20–35%), metabolic syndrome (20%), type 2 diabetes (40%), colon and breast cancer (30% and 20%, respectively), and mental health (20–30%) (US Department of Health and Human Services, 2008). The physiological mechanisms by which exercise effects these health outcomes are numerous, and although the specific impact of HIT is not known, HIT nonetheless contributes to meeting physical activity recommendations (e.g. Department of Health, 2011).

Chapter 4 Philosophical Underpinning

4.1 Introduction

As discussed throughout Chapter 3, an underlying assumption of this thesis is that regular exercise or physical activity is essential for optimal health outcomes. The premise for this is based on observations of evolved adaptations in *Homo sapiens*, in addition to biochemical, cellular, and physiological adaptations that occur in response to regular physical activity. The implication is that many diseases, including obesity and diabetes, are caused by deficient exercise stimulus. Accordingly, if we remain physically inactive, we fail to deal with the cause of such diseases. Awareness of this discordance between genome and environment exemplifies the need to engineer physical activity into modern lifestyle to maintain adequate fitness and reduce the burden of evolutionary mismatch diseases. Likewise, the hedonistic nature of human behaviour has been emphasised. In relation to exercise adherence, motivation to exercise may be explained by psychological theories such as dual-mode theory and the peak end rule which suggest that pleasure and displeasure responses experienced during activity influence future behaviour. Together, these exhortations form the foundation for considering how to address the endemic levels of physical inactivity among the general population. A fundamental assumption is that most people do not meet physical activity recommendations, and are insufficiently active or sedentary resulting in deleterious effects on health. The most commonly cited reason for this behaviour is perceived lack of time and as such, recommendations to partake in high-volumes of activity may be unsuitable. This thesis contributes to strategies that could help counter the problem of physical inactivity.

To tackle this problem in part, the research studies in this thesis advocate an alternative type of exercise known as high-intensity interval training or HIT, predicated on two assumptions. First, that HIT produces rapid physiological adaptations which are reliably quantifiable and beneficial for health; and second, that hedonistic theories of motivation predict the degree of pleasure that exercisers experience and strongly influences behaviour change. As such, these assumptions frame the way in which knowledge is generated to address the problem of promoting physical activity behaviour change, included in this thesis. Underscoring these assumptions, the methods used to accomplish the aims and objectives of this research were selected based on fundamental views about the most appropriate way to acquire knowledge within exercise science. How such knowledge is produced reflects greatly on underlying epistemological assumptions and beliefs, accepted research traditions, socio-cultural perspectives, and the shared beliefs and values of researchers (Brustad, 2002). These epistemological decisions are in-turn, predicated on several underpinning ontological beliefs about what can be known. Therefore, the aim of this chapter is to provide a critical discussion on the principles and practices of science – and by association the philosophical aspects that underlie research methods and methodologies within the field – to provide a conceptual clarification and justification for the data, methods, and theories used within this thesis.

Exercise science uses the principles of the mainstream sciences, and applies them to exercise and physical activity to improve health. The philosophy of science is concerned with the foundations, methods, and implications underlying this endeavour. Philosophically, we might ask whether broad or narrow conceptions of health should be used, or if the benefits of exercise and physical activity should be measured in an objective or subjective manner (McNamee, 2005). Further questions relate to the application of the scientific method (or methods) to the study of exercise and health since this is not straightforward – because exercise science covers both the natural and social science domains, and therefore does not form a single disciplinary context. Although an obvious simplification, these questions could be debated from two dialectical views: on one hand 'realists' (usually interested in the natural sciences), uphold the objectivity and progressive nature of scientific knowledge; and on the other 'relativists' (usually in the social sciences and humanities), who recognise the culturally embedded status of claims for universal factuality and regard science as just one system of belief among many alternatives, all worthy of equal weight because the very concept of 'scientific truth' represents a social construction. Although this is an intentionally misrepresented proposition – because few working scientists and critical thinkers would endorse the claim that all systems of belief are equal – it does exemplify an opinion that knowledge about exercise and health should progress using a range of methods and methodologies, and not simply procedures associated with traditional or 'normal science'.

Given the multi-disciplined nature of exercise science, I will contend that the appropriateness of scientific methodologies depends on the best way to approach the problem at hand. Indeed, the reason for adopting a scientific methodology at all, rather than a non-scientific one, is not necessarily clear. The question as to whether it is appropriate to use scientific methods in the study of humans is fundamental (Ryall, 2009), and it may be wholly inappropriate to assume that it is possible to uncover laws governing human behaviour in the same way that causes can be reduced to generalisations in the physical sciences (Winch, 2008). I will also contend that the human propensity to dichotomise and demarcate between science and non-science, can be an unhelpful way of thinking. Approaches using mixed methodologies may make good sense, as they allow for collection, analysis, and application of a variety of data. However, if we adopt several approaches to acquisition of knowledge we must recognise that not all these methods are strictly scientific. As such, the veracity of claims we make using them, and by association the reliability of predictions we can make about the world around us, must be considered with this in mind. I will also argue that exercise science researchers who align themselves with positivism perhaps do so uncritically, when in fact the interface between the natural and social sciences is more appropriately described by the post-positivist philosophical approach known as *critical realism*. However, if the main aim of scientific research is to make an inference about an effect in a population based on the study of a sample; approaches based on positivistic ideals, such as *scientific realism*, might be more appropriate. Fundamentally, how we define science is important, but whether our research questions fall within the natural or social sciences should drive the epistemological decisions that we make, which in turn determines whether we can predict or simply explain the future behaviour of phenomena that we can observe.

4.2 What is science?

Any definition of science will generate a criterion of demarcation between what is and is not science. This is necessary because it is a widely-held belief that there is something special about science and its methods (Chalmers, 1999). A suitable description of science outlined by Winter (2003), proposed that science – simply defined as 'a way of working' – is characterised by procedures that allow the term to be used and that if these procedures are not followed work cannot be regarded as science. This contrasts with Sharp (2003) who suggested that science can be of varying qualities, from bad to excellent; and Maguire (1991) who rejected the idea that there is only a single universal logic of scientific method that distinguishes between science and non-science. Although using a practical continuum of methods, or a 'what works' approach to science, is useful in real-world settings – since problems faced by exercise scientists are unlikely to present themselves as well formed structures that fit easily within a purely positivistic framework (Schön, 1987) – I agree with Winter (2003) and uphold that at some point along this continuum, methods become non-scientific – at least in so far as the term is normally used. Using the term 'science' to cover everything from string theory to psychoanalysis is not appropriate, because doing so elides the difficult fact that the ways in which we try to understand and deal with the physical world and those in which we try to understand and deal with the social one, are not the same (Gould, 2003). Within the context of this thesis, exploring the efficacy and effectiveness of HIT as a strategy to improve health is an attempt to predict cellular and physiological adaptations, but is also an attempt to gain an understanding of human behaviour in relation to a specific environment. Thus, understanding both phenomena requires differing approaches in which the methods of research, the aims of inquiry, and the standards of judgement differ. Whether both approaches are scientific is less clear.

Almost thirty years ago, Raven and Squires (1989) raised the question, ‘What is science?’ and stated that if exercise [science] is indeed a science, it should uphold scientific rigour by obeying the basic tenets of scientific inquiry. They adopted Karl Popper’s axioms of scientific inquiry (from his text *Conjectures and Refutations*) to judge the credibility of scientific thought and theory. Popper's basic tenets stipulate that the criterion of the scientific status of a theory is its falsifiability, refutability, or testability (Popper, 1970). Hale (2001) argued that there is a *prima facie* case for suggesting that not all [sport and exercise] human movement scientists follow Popper’s criteria of scientific method, citing both physiology and psychology examples where a strict application of Popper's refutability axiom should have resulted in the rejection of well-established ideas via falsification. For example, the value of the oxygen plateau as the defining measure of cardiorespiratory fitness has been questioned, since this is not always evident upon cessation of exercise. Indeed, the use of peak oxygen uptake ($\dot{V}O_{2peak}$) as opposed to maximal oxygen uptake ($\dot{V}O_{2max}$) attests this point and suggests a strict application of the refutability axiom should have resulted in the rejection of the ‘plateau phenomenon’. However, the historical basis for this physiological model originates in the research of the Nobel Laureate and founding father of exercise science, Archibald Vivian Hill (Hill and Lupton, 1923), and consequently it has been suggested that this ‘Foundation Myth’ has escaped modern intellectual scrutiny (Noakes, 2005). Similarly, exercise psychologists use a range of constructs which are measured using notoriously biased and unreliable methods such as self-report for which, despite applied support, there is a lack of empirical evidence for a causal link between construct and outcome. In these instances, exercise scientists are guilty of the practice described in Popper’s seventh axiom of introducing *ad hoc* secondary assumptions to avoid the refutation of a theory. In Popperian terms this “... conventionalist stratagem... rescues theory from refutation only at the price of destroying, or at least lowering its scientific status” (Popper, 1970, p. 37).

This view of science is perhaps obsolete, arising from discordance between early schools of scientific thought and the way modern scientists use the scientific method to develop knowledge. Historically, empiricism was influential in determining what counts as scientific inquiry and upholds that knowledge should be derived from ideas developed in the mind by way of sense perception. Traditional definitions of science favour a positivistic, inductivist model whereby systematic testing is undertaken to produce a general conclusion about the phenomena being studied (Ryall, 2009). This understanding led to the positivistic notion that science is objective and simply led by observation of natural phenomenon. A strict application of Popper's refutability axiom, means that theories that disagree with observation should be abandoned, and fits in with this view of traditional scientific empiricism. However, in practice scientists generally do not abandon theories because of experimental falsifications (Lakatos and Musgrave, 1974). Rather, theories are modified to consider the new data, and by seeking explanations for falsifications, these new theories improve and expand on the original theory. This perspective of science challenges traditional views on the interaction between observation and theory, and opposes Hale's reference to Raven and Squires (1989) original recommendation of Popperian falsificationism as a good model of scientific practice in exercise science.

The discordance between observation and theory possibly resides in the notion that science should be a dispassionate and objective endeavour striving for truth. More honestly, science is a human cultural activity, and as such scientists adopt procedures and attitudes which are derived, consciously or not, from some basic beliefs about the scientific enterprise (Parry, 2005). Although we may strive for objectivity, it is natural to hold on to theories and models that provide evidence for a phenomenon. Science is therefore led by theory rather than pure observation; the observations reside within the theory (Gould, 2003). This view supports much older ideas as to how science operates. In a letter to Henry Fawcett in 1861, Charles Darwin wrote: "How odd it is that anyone should not see that all observation must be for or against some view if it is to be of any service" (Darwin Correspondence Database, 2013). In other words, most scientific observation must be done within a theoretical context to be useful, and in this regard all observation is to some extent 'theory-laden'. The influential empiricist David Hume exemplified this line of thought as long ago as 1777 by expressing that, ideas never arise independently but rather are derived either from outward or inward sentiment (Hume, 1777). Similarly, Medawar (1982) claimed that pure inductivism, that scientific knowledge comes from recording of unbiased sense data, is simply unattainable and is an inadequate scientific methodology. Some recent accounts of science oppose positivist views where observation is considered to be an approach for objectively discriminating between possibilities. Opposition to this view is classically outlined by Kuhn (1962), whereby scientific observation is influenced by prior beliefs and experiences and is used to generate information.

Science has traditionally been positivistic, and the typical model of how 'true science' *should* operate is derived from physics which may be inappropriate for many disciplines of exercise science. Positivism asserts that the natural world follows systematic, orderly, and predictable laws caused by underlying causative mechanisms. Whilst this may be appropriate for natural sciences, such as physiology and biomechanics, it might not be appropriate for social science disciplines of exercise science that aim to explain human behaviour. Although the social world may be grounded in a non-negotiable physical world, the indelible fact remains that the methodologies associated with positivistic approaches are not necessarily appropriate for understanding the complex interaction between psychobiology and the environment. In its strongest form positivism upholds that unity of scientific knowledge is possible. In his text *Consilience*, a term coined to describe the 'jumping together' of disparate facts into a unitary explanation, Wilson (1999) asserts that unification is possible via reductionism; through physics, chemistry, biology, the behavioural and social sciences, and even through the bigger divide between science and humanities into art and ethics. More moderate positivistic thinking asserts that only a certain type of knowledge counts as scientific; that is experiment supporting careful observation and verification to develop generalisations, hypotheses, and theories. Most sciences train their experts to think linearly, to identify the problem and to find the correct solution (Reid *et al*., 2004). However, given the inherent complex interaction of psychobiological and environmental mediators which influence physical activity behaviour, this classic philosophy of science may be inadequate for the study of exercise and health. Indeed, the most important predictors of physical activity behaviour are difficult to determine and seem inherently resistant to research efforts. In principle, this is not because science cannot generate the appropriate range in ways of knowing the empirical world, but rather because the history of science has favoured quantitative and experimental techniques not always suited to a subject's phenomenology (Maguire, 1991). Nevertheless, positivism does include many ideals that natural *and* social science researchers are comfortable with – such as belief in an objective reality (however imperfect our ability to know this might be) – so to dismiss it would be wholly inappropriate.

The belief in the possibility of objectivity is a core component of positivist philosophy and indeed the Western scientific tradition (Brustad, 2002). However, within exercise science, the term 'positivistic' is often abused or at least not thought about, and is used to denote little more than a predilection for statistics, experimental method or dependence on hypothesis testing (McNamee, 2005). Historically, positivism gave rise to the stricter and more radical doctrine of logical positivism, which was famed for vigorous scientific anti-realism and aimed to abolish science of unobservable things including causality, mechanism, and principles. More broadly positivism contends that the logic of inquiry is the same across all sciences, both social and natural. These positions are likely to be different from what many scientists mean when they uncritically align themselves with positivism. Alternatively, *scientific realism* represents a philosophical position that many exercise scientists might feel to be more suitable than strict orthodox positivism. Scientific realism contends that the world described by science is the real world, and centres on the notion that scientific knowledge is progressive in nature, and that it can predict phenomena successfully (Boyd, 1983). Philosophical views of science aligned with scientific realism, should promote observation, constancy with which events of one kind are followed by others (i.e. cause-and-effect), and verification (or some variant such as falsification). A variation of realism, known as *critical realism*, may also be appropriate when discussing the interaction of the physical and social sciences in exercise science. Critical realist approaches take human agency into consideration, accept that some knowledge is socially constructed, make use of qualitative methods, and suggest that theory delivers causal-explanatory accounts rather than predictions (Lipscomb, 2014). This approach is more applicable to exercise scientists trying to explain human behaviour. These assumptions contrast with scientific realism which considers phenomena to be atomistic, views causality as Humean event regularity, makes use of quantitative methods, and considers science a vehicle for delivering predictions (Lipscomb, 2014). However, both approaches are ontologically (or metaphysically) and semantically similar. Realism is committed to literal interpretation of scientific claims about the world, and the notion that the reality we observe is the real world (independent of mind) of which we can establish fundamental truths (Chakravartty, 2016).

4.3 Philosophical framework used in this thesis

More than one philosophical position on the generation of knowledge is required to fully understand how HIT could improve population health. These approaches use different epistemic and methodological approaches, and differ in the extent to which it is possible to reduce causes to generalisations. Investigating the physiological effects of HIT, in terms of discrete outcomes such as maximal oxygen uptake, is possible using a scientific realist (or even positivist) approach to predict future outcomes. This is appropriate because quantitative and experimental techniques are well suited to the resolution of relatively simple systems, causally set by a few determining variables subject to experimental manipulation, and operating under invariant laws of nature that minimally impact participant phenomenology (subjective experience and consciousness) (Gould, 2003). However, problems arise when using this approach to develop knowledge when investigating the way in which HIT influences exercise adherence and general physical activity behaviour. The complex interaction of psychobiological and environmental factors makes it difficult to discern the most important predictors of physical activity behaviour change. In this instance, a critical realist approach is more suitable whereby human agency and social construction of knowledge are considered. Under these circumstances, we may attempt to explain rather than predict the future behaviour choices in relation to exercise. Both approaches are based on very similar ontological assumptions however. Simply, it is the epistemological assumptions that differ which in turn determines the choice of methodology most suited to answering the research question at hand.

A specific epistemological issue relates to whether one form of inquiry deserves epistemic dominance over the other. Approaches to science appropriately underpinned by scientific realism, or positivism, can emphasise verification, observation, and constancy to establish cause-and-effect to provide true, or probable, descriptions of phenomena. The methods associated with these methodologies could be considered superior because of their potential to control error and confounding variables, and thus more reliably establish cause-and-effect and make predictions about future phenomena. Within exercise science this is to be expected more often for some disciplines (e.g. those more closely aligned to physics, chemistry, and biology) than for others (e.g. psychology and sociology). Therefore, methodologies that fall within the natural sciences, and which adopt a realist ontology and experimental epistemology making use of quantitative methods, questionably deserve an epistemological dominance. The foundation to this statement is that these methods are rigorous and repeatable with successful prediction regarded the primary aim of knowledge generation. However, in claiming that non-positivistic or critical realist views of knowledge – often making use of subjective and qualitative methods – are epistemologically inferior, is not to suggest they have no value. Rather it is to point out that they are not strictly scientific ways of working and lack generalisability, and therefore predictive power. The main aim of scientific research is to make an inference about an effect in a population based on the study of a sample; and ethnographic, phenomenological, and other qualitative, interpretivist methodologies cannot do this. Indeed, they do not and should not aim to do so. Simply: the scientific method – a way of working – is not well suited to studying all phenomena. We should acknowledge that many research questions relating to exercise science and health are best answered using multiple paradigms where differing epistemological assumptions are valuable. That some of the methods included in this recommendation are not-scientific remains true. The knowledge we acquire from science is not sacrosanct. It is fallible, partial and approximate. Nevertheless, it is the most reliable means we have for predicting phenomena in the world around us (Ladyman, 2002) – particularly the physical world of cause-and-effect and our interaction with it – and therefore we might legitimately favour it.

Although many historians of science may refute positivism (e.g. Kuhn, 1962), it still shares many ideas that natural *and* social scientists feel comfortable with. Most scientists are still anti-metaphysical; many consider verification appropriate in certain circumstances; and among those committed to falsificationism there is still a positivistic element in the idea of a single criterion to demarcate science from non-science (McNamee, 2005). However different verification and falsification are, they are both an attempt to provide a criterion of demarcation between science and non-science and Popper shares many positivistic ideals such as the distinction between observation and theory, the movement toward the one true theory of the universe, the structure of reasoning, and the unity of science (McNamee, 2005). However, to reassert the view held by Hale (2001, p. 213) made fifteen years ago:

> "If a belief in the Popperian model [of science] is misplaced… current [sport and exercise science] researchers may feel the need to describe and defend alternative methodologies on which the scientific nature of their research is based. Alternatively, they could perhaps mount a case for saying that a scientific method *per se* does not exist… and rid itself of an outmoded, irrelevant, and unhelpful way of thinking about the subject.

If this is deemed appropriate, exercise scientists might adopt the term '*scientia*', from the literal Latin meaning 'any legitimate form or body of knowledge' (Gould, 2003), to direct research and practice decisions. However, to add my own caveat to this piece of advice: The emphasis should not be whether we adopt a traditional approach to science or a new one. Instead, it is imperative to understand that the research question drives the process and that under different circumstances adopting one approach over another may be preferable. Even if one of these approaches cannot legitimately be labelled as scientific, it still might be the *best* approach to use. A misappropriated desire to be categorised as science, perhaps to generate respect and credibility by emulating the methods and tangible results of the 'hard sciences', is intellectually dishonest.

This way of working reflects four sets of assumptions related to ontology, epistemology, human nature, and methodology proposed by Burrell and Morgan (1979). 'Positivism' and 'idealism' present extreme positions representative of these four assumptions. Per Burrell and Morgan (1979, p. 7), positivism "... reflects the attempt to apply models and methods derived from the natural sciences to the study of human affairs". This approach adopts a realist approach to ontology, a positivist epistemology, deterministic views of human nature, and the use of nomothetic methodologies. Such scientific methods may lend themselves well to the natural sciences; specifically, physiology and biomechanics within exercise science. Alternatively, idealism opposes positivistic ideals. In contrast to the natural sciences, it is nominalist, stressing the subjective nature of human affairs, anti-positivist in epistemology, voluntarist with regard human nature, and favours ideographic methods (Burrell and Morgan, 1979). Using different nomenclature, this continuum may be described as positivist at one end, and interpretivist at the other. To place emphasis on this dichotomy, knowledge gained using idealism or interpretivism which does not follow the scientific method cannot be labelled scientific. However, this does not invalidate claims to knowledge that such approaches generate. For example, the relationship between the intensity of HIT and affective responses might not be amenable to conventional dose-response models. Indeed, the search for a global or nomothetic model to explain this relationship may be misguided (Ekkekakis, Hall & Petruzzello, 2005). Fundamentally, this is due to the complex interaction of many biological sub-components, both physiological and psychological, that make it inherently difficult to generate hypotheses about abstruse emergent behaviours – such as the decision to exercise or not. Until we can adequately describe biological systems mathematically, rather than though experiments and verbal reasoning alone, the situation will remain (Yates, 2017). Elements of exercise science are a descriptive rather than predictive science.

Throughout this chapter I have advocated that it is important to demarcate between scientific and non-scientific methods, and that for research to be considered scientific, it must follow associated methods and procedures. Equally, I have emphasised that the scientific method is not well suited to studying all phenomena, and in these instances researchers should adopt different approaches – including ones that are not scientific. I have also suggested that scientific realism and critical realism may be appropriate positions to adopt for the study of exercise science, since the field covers both natural and social science domains. It is my view that, when used appropriately, the former is more closely aligned with positivistic standards and deserves an epistemic dominance. However, acceptance of this view of science comes with a proviso. We should not believe uncritically in the dominance of the 'normal' scientific method and we must appreciate that not all research questions can be answered using a scientific approach. Exercise scientists must recognise that humans are conscious of their behaviour and thus capable of altering it under experimental conditions contributing a layer of complexity not inherent within pure natural sciences. Furthermore, psychological and behavioural factors can alter physiological processes and as such are a challenging source of bias in human physiology research (Grossman, 2005). Challenges to and critiques of positivism have consistently emphasised the relatively poor validity of a positivistic approach in producing research with human respondents that ignores their humanness (Lincoln and Guba, 1985). Once again, these exhortations on the limitations of positivistic inquiry accentuate the recognition that multiple approaches to answering research questions exist (Harris, 1981; Martens, 1987; Hoshmand, 1989). Although I believe firmly in the demarcation problem of science, that is distinguishing between science from non-science, making use of broader methodologies offers a multi-dimensional view of phenomena and substantiates Maguire's (1991) view that exercise scientists must study people 'in the round' to understand the inherent complexities of the field.

This is not universally accepted, and problems of scientific rigour arise due to the hierarchical levels of scientific evidence prevalent in Western science, in addition to the inherent difficulties of implementing randomised controlled trials (RCT's) with people in exercise and health settings (Winter, 2002, 2004). Experimental research designs and RCT's have been labelled the 'Gold Standard' of research, although this claim has been challenged (e.g. Scriven, 2008). Nevertheless, the tendency of policy research and funding agencies to favour positivist RCT methodologies when prescribing what counts as evidence may be damaging to the pursuit of knowledge. RCT's are difficult to conduct, expensive to implement, and are not suitable for answering all research questions. Furthermore, they require stringent internal validity if results that indicate a causal relationship are to be reliable. As pointed out by others, the nature of studying humans as they interact with their environment is neither stable, free from influences or confounding variables (Grossman, 2005; Christ, 2014). Thus, the application of the RCT and positivistic experimental ways of working are simply incompatible with the complex reality that is the social world (Brady and O'Regan, 2009). Therefore, at a practical level, the tendency to demarcate between science and non-science can be unhelpful. Alternative paradigms other than positivistic ones, should be considered when guiding decisions about appropriate methodologies (Christ, 2007). Approaches using mixed methodologies make good sense, as they allow for collection and analysis of a variety of data resulting in inferences that are applicable to a broader research spectrum (Christ, 2014). Such an approach, where inferences are made using both quantitative and qualitative methodologies in a single study, is a viable means of achieving this in exercise science research. Epistemological dualism (objectivism *and* subjectivism) might blend deductive and inductive research in a complimentary manner, allowing for fuller knowledge about interventions (Teddie and Tashakkori, 2009). Such an approach is open to diverse methods where qualitative methodologies are considered on their contribution to knowledge rather than adherence to predetermined methods or approaches (Biddle, 2000).

The perspectives on science outlined in this chapter underpin the theoretical framework adopted within this thesis. Whilst the ontological view remains constant – that is, literal interpretation of scientific claims about the world of which we can establish fundamental truths – diverse epistemological assumptions are made for different aspects of data collection. To be clear, the effects of HIT can be considered in two ways concomitantly. First, various physiological outcomes are minimally effected by participant subjective experience and consciousness, and therefore can be approached using a scientific realist or positivist model. Second, it is important to recognise that the likely success of any HIT intervention in the 'real-world' is related to the acceptability and accessibility of the activity to those for whom the intervention is intended, in addition to the practicality of building the activity into everyday life (Haines, Gillibrand & Garbutt, 2012). As such, psychological responses to the intervention, such as pleasure and enjoyment, provide a fuller understanding of its applicability to real-world health outcomes. To consider this adequately requires a different perspective, one which acknowledges human agency and the complex interplay between psychobiological responses and the environment. To accomplish this, a critical realist approach is necessary. More broadly the theoretical framework underlying this thesis outlines an approach which recognises minimum requirements below which work cannot be regarded as science, and a framework in which knowledge could be graded into various categories depending on the precise methodologies engaged. It is recommended that we should acknowledge that not all forms of knowledge are scientific, yet such methods should be judged based on their individual merits. At the same time, we should celebrate the reliable knowledge we gain using the scientific method because of the way it establishes probable cause-and-effect. An excellent and lucid account by Parry (2005, p. 32) summarises this position particularly well:

> "Some of our knowledge is not of the scientific variety and so does not answer to such criteria – but this in no way invalidates it. Good science is good at what science is good at. We can't ask for more than that. What we call science is valued because (and to the extent that) it delivers the goods. It, and no other forms of prescientific activity… has survived and progressed and now dominates our thinking about the physical world of cause-and-effect and our interaction with it. Quite rightly so – it is the best source of such knowledge that we have, and to the extent that we value such knowledge, so shall we value the origin of it. But that should not blind us to two things. Science is not the only source of our knowledge. Science fetishism is an invitation to ideological intrusion."

4.4 Conclusion

Exercise scientists should uphold the principles and practices of science, and by association research methods. Science is not led by conjecture and refutation of purely objective observations. Rather it is theory-laden and progressive in nature, and can predict phenomena successfully. Although it was the first philosophy of science in the twentieth century, few modern scientists strictly apply the tenets of scientific inquiry as laid down by orthodox positivism. Nevertheless, positivism still shares many ideas that natural and social scientists can associate with, and that are in-line with the scientific realism and critical realism approaches recommended in this chapter. Approaches based on scientific realism or even positivism can be applied to some disciplines within exercise science including physiological adaptations to HIT. This approach emphasises verification, observation, and constancy to establish cause-and-effect to provide true, or probable, descriptions of phenomena. Other questions in exercise science should make use of other approaches, to explain rather than predict events. These approaches may be unable to use scientific methods, and as such, to label this part of exercise science scientific is a misnomer.

Exercise science is concerned with both the natural and social science domains. As such the assumptions, socio-cultural perspectives, and traditions that form our methodologies and methods vary due to the fundamentally different questions we ask. Accordingly, a moment's thought should allow us to see that these questions also need to be answered in fundamentally different ways. Despite the human propensity to dichotomise and debate the merits of one approach, scientific or otherwise, against another; it should not blind us to the value that non-scientific methodologies can contribute. In a remarkably appropriate *bon mot*, the musician, writer and comedian Tim Minchin stated that "we tend to generate false dichotomies and argue one point by using two entirely different sets of assumptions, like two tennis players trying to win a match by hitting beautifully executed shots from either end of separate tennis courts" (Minchin, 2013). This is very fitting. Too much emphasis on the dichotomy between the value of science and non-science may be damaging, and for this reason adopting approaches that have differing epistemological and methodological assumptions is defensible. However, in doing so it is also important to recognise that not all the methods we use are scientific, and we should acknowledge that the standards and veracity of the claims we make based on the evidence available cannot be held to the same standards of judgment. To do so would be intellectually dishonest. My personal bias toward establishing cause-and-effect and the associated probability of error, is based on approaches to science that are rooted in positivistic ways of working. These are important because of the results they get, and the way in which they have transformed the world in little over 400 years.

In summary, the conceptual framework which underpins the research in this thesis adopts a philosophical position of scientific realism. That is, the world described by science is the real world, regardless of how it may be interpreted. Accordingly, a realist view of ontology is adopted throughout this thesis. Furthermore, approaches aligned with positivism are best positioned to allow probability based inferences about an effect in a population based on the study of a sample. These epistemological approaches work well for natural science based research questions which are minimally effected by human agency. Therefore, experimental methodologies are used to assess the physiological adaptations to HIT throughout this thesis. However, this approach may be problematic when investigating the ways in which HIT may impact exercise adherence, or expected effectiveness in real-world settings. This is due to the complex interaction of psychobiological and environmental factors which may influence behaviour. Consequently, a critical realist approach to epistemology is adopted to account for this complex reality. Shifting the epistemological viewpoint to critical realism allows for selection of methods which more appropriately answer the research question, where human agency and social construction of knowledge are relevant. Psychological constructs that are investigated using experimental methods, such as pleasure and perceived effort, are not directly observable. Rather, they are theoretical constructs interpreted using arbitrary scales for which considerable interpretation and subjective thought processes influence results. Whether these methods can be considered scientific depends fundamentally on how we define science. Nonetheless, they are still the appropriate methods to use.

Chapter 5 Systematic Review of Literature

The efficacy and effectiveness of genuinely time-efficient high-intensity interval training: A systematic review

5.1 Abstract

Many chronic diseases are a natural consequence of modern lifestyle characterised by physical inactivity. Although the benefits of regular exercise are strongly evidenced, the challenge of engineering high-volumes of physical activity, as recommended in current guidelines, into our lives remains. Low-volume, high-intensity interval training (HIT) has been proposed as an alternative and more 'time-efficient' approach to exercise. However, low-volume HIT protocols vary in terms of intensity and session duration. Many studies have used protocols that are too intense to be adopted by the general population. Furthermore, some of the protocols require a similar time commitment per session when compared to traditional exercise guidelines. Therefore, they do not uphold the time-efficiency claim. It is recommended in this review that the total duration of each session be the criterion for demarcating if HIT is to be considered time-efficient or not, and that as a minimum this duration, inclusive of a warm-up and cool down, should be less than current guidelines – which is 30 minutes. This review aims to: (1) consider issues of practicality by describing a low-volume approach to HIT, and (2) evaluate the current evidence specifically for *low-volume* HIT as an exercise treatment for a range of populations.

Keywords: high-intensity, interval training, affective response, PGC-1α, review

5.2 Introduction

An incontrovertible relationship exists between physical inactivity, obesity and a wide range of chronic diseases. Discordance between our genomes selected for high physical activity, and the modern environment in which we have all but made redundant the need for obligatory physical activity, might be at the root of this problem (Booth *et al*., 2002a; Eaton *et al*., 2002; Eaton & Eaton, 2002). Evidence of the benefits of regular exercise is supported by the full spectrum of methodology needed to infer causality, including observational research, experimental mechanistic investigation and randomised controlled trials (Booth *et al*., 2002b; Jones *et al*., 2011). Despite this, the challenge of encouraging individuals and populations to lead a more active lifestyle remains, with perceived ‘lack-of-time’ the most commonly cited barrier to regular activity (Reichart *et al*., 2007; Korkiakangas *et al*., 2009). As such, a common criticism of the therapeutic potential of exercise is poor adherence. It is estimated that 50% of individuals who start an aerobic exercise programme will stop within the first six months (Robinson & Rogers, 1994), and the situation is typically worse in patients with chronic disease (Qiu *et al*., 2012).

Considering these challenges, the use of exercise as a preventative or therapeutic treatment might be problematic because traditional exercise guidelines for health have focussed on relatively high-volume activities performed on most or all days of the week. Currently the American College of Sports Medicine (Haskell et al., 2007), the British Association of Sport and Exercise Sciences (O’Donovan et al., 2011) and the Department of Health (DoH, 2011) recommend 150 minutes of moderate-intensity or 75 minutes of vigorous-intensity aerobic exercise per week. For adults at risk of cardiovascular disease or type 2 diabetes, 300 minutes per week is recommended (O’Donovan *et al*., 2011). An alternative approach to exercise is high-intensity interval training (HIT) which has received recent research interest in addition to widespread media attention and popularity within the fitness industry (Thompson, 2013). HIT is characterised by alternating a series of short, high-intensity (often described as ‘maximal’ or ‘all-out’) intervals of exercise with periods of active recovery or light exercise. The potency of this exercise to induce a range of rapid beneficial adaptations is unequivocal. Several systematic reviews and meta-analyses demonstrate the beneficial effects of HIT in healthy, sedentary or active adults (Sloth, Sloth, Overgaard & Dalgas, 2013; Weston, Taylor, Batterham & Hopkins, 2014a), cardiovascular disease patients (Hwang, Wu & Chou, 2011; Guiraud *et al*., 2012; Weston, Wisløff & Coombes, 2014b), type 2 diabetes patients (Francois & Little, 2015) and on cardiometabolic disease risk (Kessler, Sisson & Short, 2012). Additionally, a plethora of experimental studies have identified some of the mechanisms underlying these beneficial changes including: skeletal muscle remodelling toward a more oxidative phenotype (Gibala *et al*., 2009; Hood *et al*., 2011; Little *et al*., 2010, 2011a; Cochran *et al*., 2014), improved blood glucose regulation (Babraj *et al*., 2009; Little *et al*., 2011b; Gillen *et al*., 2012) and improved cardiac autonomic function (Bond *et al*., 2015).

Time-efficiency is often lauded as one of the practical benefits of HIT. Proponents emphasise the potential to reduce time burden and therefore appeal to people who otherwise would not engage with exercise (Gibala & McGee, 2008). However, HIT differs in mode; interval intensity, duration and frequency; and the total duration of the exercise session. Furthermore, it is possible that HIT protocols do not require appreciably less time to complete than traditional exercise when time to complete a warm-up, recovery in-between intervals and a cool down are considered. Therefore, it is important to qualify the protocols that are genuinely time-efficient. Exercise guidelines that recommend 150 minutes of activity per week are often split into 30 minutes of activity over five days per week. To illustrate this point, in a systematic review and meta-analysis, Weston *et al*. (2014b) found the median duration of HIT exercise from 10 studies was 38 min. For example, Tjønna *et al.* (2008) and Wisløff *et al.* (2007) used 4 × 4 min intervals of uphill treadmill walking and running at an intensity of ~90% maximum heart rate in metabolic syndrome and heart failure patients. The total time commitment of the HIT exercise sessions in these studies was 38–40 min inclusive of a warm-up and cool down. Notwithstanding a range of health improvements, it is difficult to see how these exercise protocols could be labelled as 'time-efficient', since they exceed the total duration of exercise associated with traditional exercise recommendations. To claim a HIT exercise intervention is time-efficient based on the minimal time spent at high-intensity is spurious, when the total time commitment of each session is no different to the current guidelines for promoting health – necessitated by the inclusion of a warm-up, periods of rest in-between high-intensity intervals and a cool down. In short, such exercise interventions do not fulfil the 'time-efficiency' claim (Hardcastle *et al*., 2014).

What has not been considered well is whether genuinely time-efficient approaches to HIT can elicit similar physiological benefits as more time intensive approaches. Therefore, the aim of this systematic review is to compare the effects of time-efficient HIT against control or exercise comparison groups for apparently healthy participants and those with chronic disease. This first requires an operational definition of 'time-efficient HIT' to be identified. Additionally, issues of practicality and likely effectiveness of HIT, including exercise intensity, adherence and safety will be discussed.

5.3 Methods

A definition of time-efficient HIT was identified before performing the systematic literature review.

5.3.1 Operational definition of time-efficient HIT

The terms 'sprint interval training', 'high-intensity interval training' and 'low-volume, high-intensity interval training' are often used interchangeably. However, the various protocols vary in terms of their time commitment. If HIT is to have any role in public health strategy, the time-efficiency claim is paramount. Such exercise could appeal to individuals who otherwise would not adhere to the more time-consuming volumes of exercise outlined in traditional guidelines. Therefore, it is recommended in this review that the *total time commitment of each session* be the criterion for demarcating if HIT is time-efficient or not. Traditional exercise guidelines stipulate 150 minutes of exercise per week, often split into 30 min of activity on five days per week (Haskell *et al*., 2007; O'Donovan *et al*., 2010; DoH, 2011). Therefore, in order to maintain the time-efficiency claim, the maximum duration, inclusive of a warm-up and cool down, should be less than traditional guidelines – which is 30 min per session. As such, the following definition of time-efficient HIT was formulated and served as inclusion criteria:

- Total time commitment of each session: ≤ 30 min inclusive of a warm-up, recovery and cool down
- Intensity: maximal or sub-maximal (both anaerobic and aerobic emphasis acceptable)
- Number and duration of high-intensity sprints: no limitations (but must include distinct intervals of work and rest)
- Recovery: no limitations

5.3.2 Search procedure

Electronic searching of PubMed, MEDLINE and CINAHL® databases were performed from the past 20-years (to February 2016). The search was carried out using the Medical Subject Heading (MeSH) database with search results limited to English language articles, human participants and clinical trials. The MeSH terms 'exercise' and 'training' were used with the text words 'high-intensity' OR 'interval' OR 'sprint interval', making use of Boolean operators as conjunctions. Additional relevant publications were identified by using the PubMed 'related articles' link, as well as reviewing the reference lists of retrieved articles.

5.3.3 Inclusion criteria

Inclusion criteria regarding study design, the training and health status of the participants, and the HIT intervention were formulated before the search. Only experimental studies that included a comparison group were included in the review. This included randomised controlled trials where HIT was compared against no treatment or a positive control, such as another approach to exercise (e.g. moderate-intensity continuous exercise). Repeated measures designs (e.g. crossover) where participants acted as their own controls were also included. Other quasi-experimental designs, including matched sampling and non-random allocation to groups were included to ensure a wide range of literature could be considered for review. Studies that included only a single session of HIT were also included for this reason. Cross-sectional and case-control (retrospective) studies, animal studies and studies including dietary interventions alongside HIT were excluded. Reviews and meta-analyses were also excluded. There were no limitations on the participants age, sex, physical activity level or body mass index, and patients with a range of non-communicable diseases (e.g. obesity, diabetes and metabolic syndrome) were included. However, studies using patients with known cardiovascular disease were excluded since other reviews on the effects of HIT have been conducted with coronary artery disease (Cornish, Broadbent & Cheema, 2011), cardiac rehabilitation and heart failure (Guiraud *et al*., 2012), and lifestyle-induced cardiometabolic disease (Weston *et al*., 2014b). Studies using either highly-trained participants or athletes were also excluded. There were no limitations on the mode, frequency or intensity of HIT, but the total time commitment per session had to be ≤ 30 min, inclusive of a warm-up and cool down, as defined above. Resistance training programmes were excluded, since the nature of such programmes in terms of their technicality and work-to-rest ratios are very different than what is generally accepted as high-intensity interval training (Gaesser & Angadi, 2011) Finally, for inclusion studies had to achieve a Physiotherapy Evidence Base Database (PEDro) score of 3 or more.

5.3.4 Data collection and analysis

As shown in figure 5.1, the search procedure yielded 1877 articles. Mendeley Desktop© (version 1.16.1, 2016) reference manager software was used to removeduplicates retrieved from systematic review searches as this has recently been recommended as the most effective package, based on the percentage of false negatives and false positives retrieved (Kwon, Lemieux, McTavish & Wathen, 2015). References were loaded as a Research Information Systems (RIS) file into Mendeley. The "Check duplicates" option from the tools menu was run to check for close duplicates, generating a total of 323 duplicates, all of which were merged. This left 1544 publications for screening based on their title and abstracts. After this screening 1461 publications were excluded leaving 83 articles for detailed analysis. A total of 35 articles were retrieved and identified for inclusion in the review (figure 5.1).

The methodological quality of each study was assessed using the PEDro scale, which is a valid (de Morton, 2009) and reliable (Maher, Sherrington, Herbert, Moseley & Alkins, 2003) scale for rating the quality of clinical trials. The scale was modified with respect to three criteria. Half a point was awarded for criterion 1 if the general source of participants was made clear, but a list of criteria to determine eligibility to participate in the study was not made explicit. Similarly, for criterion 4 half a point was awarded if the reviewer was not fully satisfied that baseline measures for the most important prognostic indicators were similar between groups. For criterion 7 half a point was awarded if participants appeared to have received treatment or control conditions as allocated, but an explicit statement to this effect or mention of analysis by intention to treat was absent. Table 5.1 shows how points were awarded for each of the 35 studies included in the review. The quality assessment of the studies was undertaken by a single reviewer.

5.4 Results

5.4.1 General study characteristics

An overview of the study characteristics is shown in table 5.2. Twenty-one of the 35 studies included in this review were carried out using inactive or active, healthy participants. Seven studies used overweight or obese men and women (Trilk *et al*., 2010; Boutcher, Park, Dunn & Boutcher, 2013; Boyd *et al*., 2013; Skleryk *et al*., 2013; Whyte, Ferguson, Wilson, Scott & Gill, 2013; Little *et al*., 2014; Martinez *et al*., 2014), and a further three studies used participants at risk of metabolic disease or type 2 diabetes (Freese *et al*., 2014, 2015; Jung *et al*., 2015). The remaining four of the 35 studies included two studies with children or adolescents (de Araujo *et al*., 2012; Buchan *et al*., 2013), and a single study using the elderly (Adamson *et al*., 2014) and chronic obstructive pulmonary disease patients (Coppoolse *et al*., 1999). A total of 583 participants were allocated to HIT, with 54% of these being male (n = 312, female n = 271). Seventy-seven percent of female participants were included in nine of the 35 studies (Richards *et al*., 2010; Trilk *et al*., 2010; Boutcher *et al*., 2013; Freese *et al*., 2014, 2015; Jung *et al*., 2014, 2015; Klonizakis *et al*., 2014; Kilpatrick *et al*., 2015; Shepherd *et al*., 2015), and six studies used female participants only (Trilk *et al*., 2010; Boutcher *et al*., 2013; Freese *et al*., 2014; Harris, Rakowbowchuk & Birch, 2014; Freese *et al*., 2015). The remaining studies included male and female (n = 15) or male only (n = 13) participants. The mean sample size across the 35 studies was 16 ± 10.

Nineteen of the studies used random assignment of participants to independent groups, in which groups receiving the experimental exercise intervention were compared with control groups receiving no treatment (a control study) or an alternative exercise intervention (a positive-control study). Three of these studies applied random assignment following stratification according to $\dot{V}O_{2max}$ (Matsuo *et al.*, 2014), age (Buchan *et al.*, 2014; Matsuo *et al.*, 2014) or stage of menopause (Freese *et al.*, 2015). Seven studies used counterbalanced or crossover repeated measures designs (Freese, Levine, Chapman, Hausman & Cureton, 2011; Whyte *et al.*, 2013; Oliveira *et al.*, 2014; Jung *et al.*, 2014; Little *et al.*, 2014; Martinez *et al.*, 2014; Kilpatrick *et al.*, 2015), and a further nine studies used quasi-experimental designs without randomisation. Three of these used matched sampling based on waist circumference, sex or $\dot{V}O_{2peak}$ (Burgomaster *et al.*, 2008; Boyd *et al.*, 2013; Harris *et al.*, 2014) with the remaining six studies using non-random allocation to groups (Burgomaster *et al.*, 2006, 2007, 2008; Rakowbowchuk *et al.*, 2008; Nybo *et al.*, 2010; Boutcher *et al.*, 2013). Eleven of the studies were conducted at one of two institutions in Canada; six at McMaster University, Ontario, (Burgomaster *et al.*, 2005, 2006, Gibala *et al.*, 2006; Burgomaster *et al.*, 2007, 2008; Rakowbowchuk., 2008); and five at the University of British Columbia (Boyd *et al.*, 2013; Jung *et al.*, 2014; Little *et al.*, 2014; Martinez *et al.*, 2014; Jung *et al.*, 2015).

The studies achieved a mean PEDro score of 6.27 out of 10 (± 1.46). All the studies included a point measure (i.e. size of treatment effects) and a measure of variability, such as standard deviation, standard error or confidence intervals, for the primary outcomes. A between-group statistical comparison involving different exercise interventions, or comparison of treatment with a control condition, was reported for all studies. Two out of the 35 studies used blinding of assessors and concealed allocation (Heydari *et al.*, 2012; Matsuo *et al.*, 2013) and five studies explained *a priori* power analyses used to determine sample size (Trilk *et al.*, 2010; Freese *et al.*, 2011; Heydari *et al.*, 2012; Matsuo *et al.*, 2013; Martinez *et al.*, 2014). Baseline measures for the most important prognostic indicators were similar between groups for most studies. However, in some instances this was not explicit, and half a point was awarded (Rakobowchuk *et al.*, 2008; Nybo *et al.*, 2010; de Araujo *et al.*, 2012). Generally, it was clear that the number of participants initially allocated to groups, and the number from whom key outcome measures were obtained were the same. There was no mention of analysis by intention to treat in any of the studies, although it was clear that all participants received treatment or control conditions as allocated in 12 of the 35 studies. As discussed above, nine of the 35 studies used a quasi-experimental design with the remaining 26 studies all using random allocation to groups, although the precise method of randomisation was not reported in many studies. Finally, the source of participant recruitment was reported in most studies, but the list of criteria used to determine precise eligibility to partake in the studies was less consistent, with just 22 studies reporting this explicitly.

5.4.2 HIT protocols

Total time commitment of each session (and reporting of warm-up and cool down)

The total time commitment of each session is inclusive of a warm-up and cool down. For 16 of the studies the volume of exercise per session (i.e. the number of high-intensity intervals) progressively increased over the intervention period, thus a range of times were reported to reflect the minimum total time commitment at the start of the intervention and the maximum time commitment performed toward the end of the intervention. The mean time commitment was ~20.5 ± 6.4 to ~25.5 ± 7.4 min. However, 16 of the 35 studies did not explicitly detail warm-up and cool down protocols. Therefore, this value is conservative. One study was notably shorter than the others (10 min) inclusive of a warm-up and cool down (Metcalfe *et al*., 2011).

Mode, frequency and duration of interventions

Four studies used walking and running as the exercise modality (Nybo *et al*., 2010; de Araujo *et al*., 2012; Buchan *et al*., 2013; Oliveira *et al*., 2013). High-intensity 'efforts' were interspersed with passive rest (Oliveira *et al*., 2013) or lower intensity exercise, based on parameters identified during a baseline maximal graded exercise test (de Araujo *et al*., 2012). Nybo *et al*. (2010) used a recovery strategy between bouts of high-intensity treadmill running was not specified. In all the other studies (n = 31) cycle ergometers were used throughout the exercise interventions. Alternating intensities were achieved by changes in the rate of pedalling and the braking force applied against the cycle flywheel (i.e. changes in power output). Frequency of exercise interventions was typically two (n = 2) or three (n = 25) sessions per week. Coppoolse *et al*. (1999) used three HIT sessions in addition to two continuous exercise sessions per week, and Matsuo *et al*. (2013) used an exercise frequency of five sessions per week. A further seven studies were based around a single HIT session, so intervention frequency was not applicable (Freese *et al*., 2011; Oliveira *et al*., 2013; Whyte *et al*., 2013; Jung *et al*., 2014; Little *et al*., 2014; Martinez *et al*., 2014; Kilpatrick *et al*., 2015). Excluding the studies that used a single session, the average training duration for the remaining 28 studies was 5.5 ± 3-weeks (mean ± s), with a modal value of 6-weeks and a range of 10-weeks. The longest studies were 12-weeks (Nybo *et al*., 2010; Heydari *et al*., 2012; Boutcher *et al*., 2013).

Intensity (including interval duration)

The mean interval, or high-intensity 'sprint', duration for all 35 studies was 40 ± 27.4. Four studies used notably shorter intervals of 6-s, 8-s, 10-s and 10–20-s (Adamson *et al*., 2014; Heydari *et al*., 2012; Skleryk *et al*., 2013; Metcalfe *et al*., 2011, respectively), and three further studies used much longer durations of 2–3 min (Nybo *et al*., 2010; Oliveira *et al*., 2013; Matsuo *et al*., 2013). Intensities were based on three approaches: 1) application of a braking force relative to body mass applied against a cycle ergometer flywheel, 2) a fixed percentage of a performance parameter identified during maximal baseline testing (i.e. power and velocity), and 3) physiological responses to exercise. As such the varied approaches to assigning exercise intensity will have resulted in differing aerobic and anaerobic contributions to adenosine triphosphate turnover.

The most common method of assigning exercise intensity, for 18 of the 35 studies, was maximal cycling sprints against a predetermined resistance. Nine of these studies used a resistance proportional to 7.5% of body mass, with 4–8 sprints performed for 30-s (Burgomaster *et al*., 2005, 2006; Gibala *et al*., 2006; Burgomaster *et al*., 2007, 2008; Rakobowchuk *et al*., 2008; Richards *et al*., 2010; Freese *et al*., 2011; Harris *et al*., 2014). This protocol is in-line with the Wingate test (Bar-Or, 1987). Rest in-between intervals was typically 3–4 min. More recently, several studies used a derivative of this protocol to determine intensity. Metcalfe *et al*. (2011) used 7.5% of body mass for 1–2 sprints with a duration of 10–20-s with the aim of reducing the effort required to complete HIT. Other studies varied the resistance by using 5% of body weight (Trilk *et al*., 2010; Skleryk *et al*., 2013) and 6.5–9% of fat free mass (Whyte *et al*., 2013; Freese *et al*., 2014; Zelt *et al*., 2014; Eskelinen *et al*., 2015; Freese *et al*., 2015), whereas Adamson *et al*. (2014) used 6–10 × 6-s sprints against 6–7% of body mass. Six studies used a performance parameter to determine exercise intensity. Coppoolse *et al*. (1999), Dunham & Harms (2012), Boyd *et al*. (2013), and Klonizakis *et al*. (2014) used 5–10 × 60-s cycling sprints at 90–100% of peak power. Work-to-rest ratios between 1:1 and 1:3 were used in these studies. Similarly, de Araujo *et al*. (2012) used 3–6 × 60-s treadmill efforts at 100% peak velocity, with a 1:3 work-to-rest ratio. A single study used maximal effort running sprints within a 20-m distance with a 1:1 work-to-rest ratio (Buchan *et al*., 2013). Eleven studies used physiological responses to exercise to determine exercise intensity; including heart rate (n = 7), maximal oxygen uptake (n = 2) and domains of exercise (n = 2). Studies using heart rate typically used 10 × 60-s cycle efforts at ~90% heart rate maximum (HR_{max}) with a 1:1 work-to-rest ratio (Little *et al*., 2014; Jung *et al*., 2015, 2016), although Heydari *et al*. (2012) used

60 × 8-s cycle sprints at 80–90% HR_{max}, and Nybo *et al*. (2010) used 5 × 2 min treadmill efforts at an intensity > 95% HR_{max}. Matsuo *et al*. (2013) and Oliveira *et al*. (2013) used an exercise intensity equivalent to 85–100% of $\dot{V}O_{2max}$, whereas Martinez *et al*. (2014) and Kilpatrick *et al*. (2015) used contemporary descriptions of exercise intensity based on the presence of 'moderate', 'heavy' and 'severe' domains, defined by their relation to anaerobic or ventilatory threshold, critical power and maximal exercise capacity.

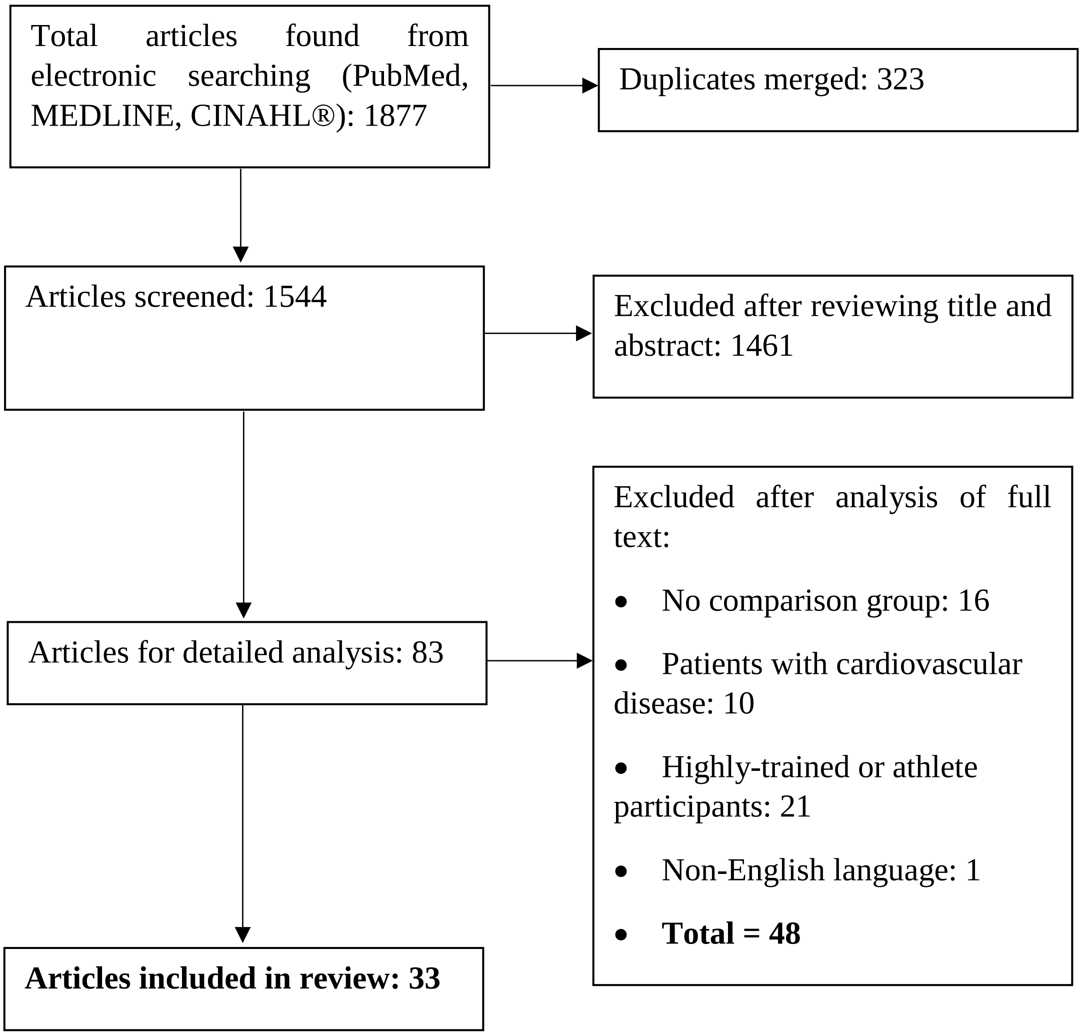

Figure 5.1 Flowchart of the systematic review process.

Table 5.1 Methodology quality of time-efficient HIT studies with a total time commitment per session of ≤ 30 min

	1	2	3	4	5	6	7	8	9	10	Total
Adamson *et al. (2014)*	−	+	−	+	−	−	−	+	+	−	4
Boutcher *et al*. (2013)	±	−	−	+	−	−	−	+	+	−	3.5
Boyd *et al. (2013)*	+	−	−	+	−	+	+	+	+	−	6
Buchan *et al*. (2013)	+	+	−	+	−	+	±	+	+	−	6.5
Burgomaster *et al. (2005)*	±	−	−	+	−	+	±	+	+	−	5
Burgomaster *et al. (2006)*	±	−	−	+	−	+	±	+	+	−	5
Burgomaster *et al. (2007)*	±	−	−	+	−	+	±	+	+	−	5
Burgomaster *et al. (2008)*	+	−	−	+	−	+	±	+	+	−	5.5
Coppoolse *et al. (1999)*	+	+	−	+	−	+	+	+	+	−	7
de Araujo *et al. (2012)*	+	+	−	±	−	+	+	+	+	−	6.5
Dunham & Harms *(2012)*	+	+	−	+	−	+	+	+	+	−	7
Eskelinen *et al*. (2015)	+	+	−	+	−	+	±	+	+	−	6.5
Freese *et al*. (2011)	+	+	−	+	−	+	±	+	+	+	7.5
Freese *et al*. (2014)	+	+	−	+	−	+	+	+	+	−	7

Freese *et al*. (2015)	+	+	−	+	−	+	±	+	+	+	7.5
Gibala *et al. (2006)*	±	+	−	+	−	+	+	+	+	−	6.5
Harris *et al*. (2014)	+	−	−	+	−	+	±	+	+	−	5.5
Heydari *et al. (2012)*	+	+	+	+	+	+	+	+	+	+	10
Jung *et al*. (2014)	+	+	−	+	−	+	−	+	+	−	6
Jung *et al*. (2015)	+	+	−	+	−	−	+	+	+	−	6
Kilpatrick *et al*. (2015)	+	+	−	+	−	+	−	+	+	+	7
Klonizakis *et al*. (2014)	+	+	−	+	−	+	+	+	+	−	7
Little *et al*. (2014)	−	+	−	+	−	+	+	+	+	−	6
Martinez *et al*. (2014)	+	+	−	+	−	+	−	+	+	+	7
Matsuo *et al. (2013)*	+	+	+	+	+	+	+	+	+	+	10
Metcalfe *et al. (2011)*	+	+	−	+	−	+	±	+	+	−	6.5
Nybo *et al. (2010)*	±	−	−	±	−	−	−	+	+	−	3
Oliveira *et al*. (2013)	+	+	−	+	−	+	−	+	+	+	7
Rakobowchuk *et al. (2008)*	+	−	−	±	−	+	±	+	+	−	5

Richards *et al. (2010)*	+	+	−	+	−	+	−	+	+	−	6
Skleryk *et al*. (2013)	±	+	−	+	−	+	+	+	+	+	7.5
Shepherd *et al*. (2015)	+	+	−	+	−	+	+	+	+	−	7
Trilk *et al. (2010)*	±	+	−	+	−	−	−	+	+	+	5.5
Whyte *et al*. (2013)	+	+	−	+	−	+	+	+	+	−	7
Zelt *et al*. (2014)	±	+	−	+	−	+	±	+	+	−	6

\+ Represents criteria achieved and one point is given.

− Represents criteria not achieved and no point given.

± Represents criteria partially achieved and half a point given.

Modified PEDro criteria:

1. Eligibility criteria specified (*criteria partially achieved when source of participants was included but an explicit list of criteria was not*).
2. Participants were randomly allocated to groups.
3. Allocation was concealed.
4. The groups were similar at baseline regarding the most important prognostic indicators (*criteria partially achieved if this was not clear*).
5. There was blinding of all assessors who measured the primary outcomes.
6. Measures of at least one key outcome were obtained from more than 70% of the participants initially allocated to groups.
7. All participants for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least one key outcome were analysed by 'intention to treat' (*criteria partially achieved if an explicit statement that all participants received treatment or control conditions as allocated was not reported*).
8. The results of between-group statistical comparisons are reported for the primary outcome.
9. The study provides the point measures and measures of variability for at least one key outcome.
10. Sample size calculations were explained.

Table 5.2 Overview of studies that have used time-efficient HIT with a total time commitment per session of ≤ 30 min.

Authors	*n* [a]	Population	Age (years) (mean ± *s*)	BMI (kg·m^2) (mean ± *s*)	HIT Protocol	Total time commitment (min) [b]	Intervention duration	Main outcomes
Adamson *et al. (2014)*	6	Elderly	65 ± 4	-	6-10 × 6 s cycle sprints (6-7% BM), 1 min recovery, 2 × per week	~7 – 11	6 weeks	↑ $\dot{V}O_{2max}$ (8%), ↓ blood pressure (9%), improved functional test scores
Boutcher *et al*. (2013)	16	Sedentary, healthy overweight women	23 ± 4.0	27.7 ± 3.2	60 × 8 s cycle sprints (80 – 85% HRpeak [c]), 12 s recovery, 3 × per week	30	12 weeks	↑ $\dot{V}O_{2max}$ (19%), cardiac vagal modulation of heart rate was associated with aerobic training response
Boyd *et al. (2013)*	9	Overweight/ obese men	22.7 ± 3.8	32.3 ± 2.1	8-10 × 60 s cycling sprints (80 rpm at 100% of maximal power [c]), 60 s recovery, 3 × per week	26 – 30	3 weeks	↑ $\dot{V}O_{2max}$ (28%), ↑ COX and PGC-1α, no difference in perceived enjoyment or self-efficacy compared to a lower intensity exercise group
Buchan *et al*. (2013)	42	Adolescents	16.7 ± 0.6	-	4-6 × 30 s running sprints (maximal effort), 20–30 s recovery, 3 × per week	~4 – 6	7 weeks	↑ in vertical jump performance, 10 m sprint, predicted aerobic fitness, ↓ systolic blood pressure (4%), no change in biochemical markers
Burgomaster *et al. (2005)*	8	Healthy	22.1 ± 1	-	4-7 × 30 s cycle sprints (7.5% BW), 4 min recovery, 3 × per week	~18 – 27.5	2 weeks	↑ CS maximal activity (38%), ↑ resting muscle glycogen content (26%), improved exercise test scores
Burgomaster *et al. (2006)*	8	Active, healthy men	21 ± 1	-	4-7 × 30 s cycle sprints (7.5% BW), 4 min recovery, 3 x per week	~18 – 27.5	2 weeks	↑ PDH, ↑ CS maximal activity (11%), ↑ resting muscle glycogen content (50%), ↓ glycogenolysis and lactate production, improved exercise test scores

Burgomaster *et al.* *(2007)*	8	Active, healthy men	22 ± 1	-	4-6 × 30 s cycle sprints (7.5% BW), 4 min recovery, 3 x per week	~18 – 27	6 weeks (followed by 6 weeks detraining)	↑ COX-4 (~35%) and GLUT-4 (~25%) after 1 week and remained higher than baseline after 6 weeks of detraining
Burgomaster *et al.* *(2008)*	10	Healthy	24 ± 1	-	4-6 × 30 s cycle sprints (7.5% BW), 4.5 min recovery, 3 x per week	~20 – 30	6 weeks	↑ protein content of PGC-1α, ↑ markers of carbohydrate and lipid oxidation (similar responses compared to endurance exercise group)
Coppoolse *et al.* *(1999)*	11	COPD patients	63.8 ± 8	25. ± 10	9 × 60 s cycling (90% peak power [c]), 2 min recovery, 3 × per week (+ 2 days of continuous exercise)	30	8 weeks	↑ peak work load (17%), ↓ leg pain at peak power, no changes in VO_2, minute ventilation or CO_2 production
de Araujo *et al.* *(2012)*	15	Obese children	10.7 ± 0.7	30.8 ± 0.7	3-6 × 60 s treadmill efforts (100% peak velocity [c]), 3 min recovery, 2 × per week	~12 – 24	6 weeks	↑ $\dot{V}O_{2peak}$ (14.6%), ↓ insulinaemia (30.5%), ↓ body mass (2.6%), improved exercise test scores
Dunham and Harms *(2012)*	8	Active, healthy	20.2 ± 2.1	24.2 ± 2.2	5 × 60 s cycle bouts (90% of final intensity [c]), 3 min recovery, 3 × per week	23	4 weeks	↑ $\dot{V}O_{2max}$ (~8-10%), ↑ maximum inspiratory pressure (inspiratory muscle strength), improved exercise test scores
Eskelinen *et al*. (2015)	14	Inactive, healthy men	47	25.9	4-6 × 30 s cycle sprints (0.088 kp/kg FFM), 4 min recovery, 3 x per week	~18 – 27	2 weeks	↑ $\dot{V}O_{2peak}$ (6%), ↑ glucose uptake in main working muscles (12%), no difference in FFA uptake, similar to endurance training group
Freese *et al*. (2011)	12	Active, healthy	~21	≤ 30	4 × 30 s cycle sprints (7.5% BW), 4 min recovery	27	Three bouts (two days)	↓ postprandial TG after HIT with energy deficit (21%) and energy balance (10%) compared to control, no difference in responses of insulin, glucose or NEFA
Freese *et al*. (2014)	23	Women at risk of metabolic syndrome	51.7 ± 10.4	31.5 ± 7.1	4-8 × 30 s cycle sprints (9% FFM), 4 min recovery, 3 × per week	23 – 41	6 weeks	Improvements in role-physical (performing daily activities) and vitality (feelings of energy and fatigue)

Freese *et al*. (2015)	22	Women at risk of metabolic syndrome	52 ± 10.6	31.4 ± 7.1	4-8 × 30 s cycle sprints (9% FFM), 4 min recovery, 3 × per week	23 – 41	6 weeks	↓ fasted (12%) and postprandial TG (10%), six weeks of HIT did not magnify the attenuation in postprandial TG
Gibala *et al. (2006)*	8	Active, healthy men	24 ± 1	-	4-6 × 30 s cycle sprints (7.5% BW), 4 min recovery, 3 × per week	~ 18 – 27	2 weeks	↑ maximal activity of COX, improved muscle buffering capacity, ↑ glycogen content, improved exercise test scores (all similar to endurance training exercise group)
Harris *et al*. (2014)	6	Active, healthy females	22 ± 2	23.6 ± 1.8	4 × 30 s cycle sprints (7.5% BW), 4.5 min recovery, 3 x per week	~20	4 weeks	↑ $\dot{V}O_{2max}$ (~15%), ↑ number and mobilisation of circulating angiogenic cells which may enhance vascular repair, work-matched sprint continuous training was just as effective as traditional HIT
Heydari *et al. (2012)*	20	Inactive, healthy men	24.9 ± 4.3	28.4 ± 2.4	60 × 8 s cycle sprints (80 – 90% HR_{max} [c]), 12 s recovery, 3 × per week	30	12 weeks	↑ $\dot{V}O_{2max}$ (~15%), ↓ body mass (1.7%), ↓ in heart rate, ↑ stroke volume, improved forearm vasodilatory capacity, improved arterial stiffness, ↑ baroreceptor sensitivity
Jung *et al*. (2014)	44	Inactive, healthy	-	-	10 × 60 s cycle efforts (~90% HR_{max} [c]), 1 min recovery	~25	Single bout	↑ enjoyment compared to CMI and CVI exercise (> 50% preferred HIT), ↑ pleasure after exercise compared to CVI exercise, but ↓ pleasure compared to CMI at these times, confidence to engage with HIT = CMI, and ↑ than CVI
Jung *et al*. (2015)	15	Inactive with pre-diabetes	51 ± 11	33.1 ± 7.7	10 × 60 s cycle efforts (~90% HR_{peak} [c]), 1 min recovery, 3 × per week	25	4 weeks (unsupervised, at home)	Compared to a moderate-intensity continuous training group: greater adherence to prescribed protocol (89 ± 11% *vs*. 71 ± 31%), more time spent in vigorous physical activity per week measured by accelerometer (24 ± 18 min *vs*. 11 ± 10 min)
Kilpatrick *et al*. (2015)	24	Active, healthy	22 ± 3	24 ± 4	Various – study compared different HIT intervals against continuous exercise	24	Single bouts	Interval protocol produced affective and enjoyment responses similar to moderate continuous exercise and more positive than heavy continuous exercise

Klonizakis *et al*. (2014)	12	Inactive, post-menopausal women	64 ± 7	-	10 × 60 s cycle efforts (100% peak power [c]), 1 min recovery, 3 × per week	26	2 weeks	Improvements in cardiopulmonary function following HIT (trend for decreased blood pressure, significant increase in $\dot{V}O_{2max}$ compared to continuous exercise) but not vascular function (flow mediated dilation)
Little *et al*. (2014)	10	Inactive overweight/ obese	41 ± 11	36 ± 7	10 × 60 s cycle efforts (~ 90% HR_{peak}), 1 min recovery	25	Single bout	Greater and more lasting effects on reducing incremental postprandial glucose compared with continuous moderate intensity exercise
Martinez *et al*. (2014)	20	Inactive overweight/ obese	22 ± 4	29 ± 3	Various – study compared different HIT intervals against continuous exercise	28	Single bouts	Higher pleasure and enjoyment for shorter interval trials
Matsuo *et al. (2013)*	28	Sedentary, healthy men	26.5 ± 6.2	< 25	Various – study included more than one HIT group, 5 × per week	10 – 18	8 weeks	↑ $\dot{V}O_{2max}$ (16.7-22.5%), ↑ left ventricular mass, stroke volume and resting heart rate
Metcalfe *et al. (2011)*	14	Sedentary, healthy men	26 ± 3	-	1-2 × 10-20 s cycle sprints (7.5% BW), ~3.5 min recovery, 3 × per week	10	6 weeks	↑ $\dot{V}O_{2peak}$ (12-15%), ↑ insulin sensitivity (28%)
Nybo *et al. (2010)*	8	Active, healthy men	37 ± 3	-	5 × 120 s treadmill running (> 95% HR_{max}), recovery not specified, 3 × per week	20	12 weeks	↑ $\dot{V}O_{2max}$ (14%), ↑ insulin sensitivity (28%), improved response to OGTT
Oliveira *et al*. (2013)	15	Healthy men	24 ± 4	24.2 ± 2.5	~6-7 × 120 s treadmill efforts (at 100% VO_{2peak} [c]), ~1 min recovery	~19	Single bout	Compared to continuous training HIT resulted in: ↑ felt arousal, ↑ RPE, ↓ pleasure, no difference in enjoyment
Rakobowchuk *et al. (2008)*	10	Inactive, healthy	23.6 ± 3.2	23.6 ± 3	4-6 × 30 s cycle sprints (7.5% BW), 4 min recovery, 3 × per week	~20 - 29	6 weeks	↑ $\dot{V}O_{2peak}$ (~7%), improved popliteal endothelial function and artery distensibility, ↑ anaerobic peak power
Richards *et al. (2010)*	21 19	Sedentary or active, healthy	- -	- -	(Dual study)	18 – 31.5	2 weeks	↑ insulin sensitivity, no change in resting energy expenditure or thermogenic response

					4-7 × 30 s cycle sprints (7.5% BW), 4 min recovery, 3 x per week			
Skleryk *et al*. (2013)	8	Sedentary, obese men	40.2 ± 2.3	32.2 ± 2.1	8-12 × 10 s cycle sprints (5% BW), 80 s recovery, 3 x per week	~18 – 21	2 weeks	No changes in metabolic or skeletal muscle adaptations in the HIT group or the traditional exercise recommendations comparison group
Shepherd *et al*. (2015)	46	Inactive, healthy	42 ± 11	27.7 ± 5	Repeated × 15–60 s sprints (> 90% HR_{max}), 45–120 s recovery, 3 × per week	18 – 25	10 weeks	↑ $\dot{V}O_{2max}$ (9%), improved insulin sensitivity, ↓ abdominal fat mass, improved blood lipids. Also, beneficial effects on health perceptions. Similar benefits compared to moderate-intensity continuous training
Trilk *et al. (2010)*	14	Sedentary overweight/ obese women	30.1 ± 6.8	35.7 ± 6.3	4-7 × 30 s cycle sprints (5% BW), 4 min recovery, 3 x per week	~22 – 31.5	4 weeks	↑ $\dot{V}O_{2max}$ (12%), ↑ stroke volume (11.4%), ↓ resting heart rate (-8.1%)
Whyte *et al*. (2013)	10	Sedentary overweight/ obese men	26.9 ± 6.2	29.9 ± 9.1	4 × 30 s cycle sprints (6.5% FFM), 4.5 min recovery, 3 × per week	24	Single bout	↑ insulin sensitivity (~45%) compared to control (but no difference compared to matched-work extended sprint group), ↑ fat oxidation in the fasted state (63%) 24-h post exercise
Zelt *et al*. (2014)	11 12	Active, healthy men	23 ± 5 22 ± 2	25 ± 3 26 ± 3	(Multiple HIT groups) 4–6 × 30 s *or* 15 s cycle sprints (6.5% FFM), 4.5 min *or* 4.75 min recovery, 3 × per week	~25 – 30	4 weeks	↑ $\dot{V}O_{2peak}$ (4–8%), ↑ lactate threshold (8–16%), critical power (5–7%) and Wingate peak power (6%) (with no significant difference between HIT groups or endurance training comparison group)

Abbreviations: AMPK = 5'-adenosine monophosphate-activated protein kinase; BM = body mass; COPD = chronic obstructive pulmonary disease; CMI = continuous moderate-intensity; CVI = continuous vigorous-intensity; COX = cytochrome c oxidase; CS = citrate synthase; FFA = free fatty acid; FFM = fat free mass; GLUT = glucose transporter; GP = glycogen phosphorylase; HR_{max} = maximum heart rate; MAPK = mitogen-activate protein kinase; NEFA = non-esterified fatty acids; OGTT = oral glucose tolerance test; PDH = pyruvate dehydrogenase; PGC-1α = peroxisome proliferator-activated receptor-γ coactivator-1α; RMR = resting metabolic rate; RPE = rating of perceived exertion; SIRT = sirtuin; TDEE = total daily energy expenditure; TG = triglyceride; $\dot{V}O_{2max}$ = maximal volume of oxygen consumed per minute; $\dot{V}O_{2peak}$ = peak volume of oxygen consumed per minute

[a] Number of participants in HIT group; [b] Values are conservative (several studies do not adequately detail warm-up and cool down procedures); [c] Intensity determined during a baseline maximal graded exercise test

Supervision

One study examined HIT outside of a supervised environment (Jung *et al*., 2015). Participants completed 10 sessions of supervised HIT, and were then asked to carry out the same exercise, three times per week, independently for four weeks. The remaining 32 studies were based on HIT protocols carried out in a controlled environment, and were fully supervised. The presence of a supervisor during exercise is likely to improve the accuracy of the prescribed intervention in terms of intensity and duration of activity. It also allows for closer participant monitoring and facilitation of motivation to complete each trial.

5.4.3 Outcomes

Skeletal muscle remodelling

Five studies demonstrated rapid skeletal muscle remodelling toward a more oxidative phenotype, primarily through influence on PGC-1α and mitochondria biogenesis. Burgomaster *et al*. (2008) reported significant increases in PGC-1α (peroxisome proliferator-activated receptor-γ coactivator) protein content after six weeks of repeated Wingate based HIT. Values were compared to a group who performed continuous endurance exercise and were found to be similar, despite the significantly different total training volumes (~225 *vs*. ~2250 kJ·week^{-1}). Boyd *et al*. (2013) also reported significant increases in PGC-1α whole muscle protein content after training by comparing two HIT protocols with differing intensities in obese men. Skeletal muscle remodelling occurred irrespective of exercise intensity. These studies, and three others (Burgomaster *et al*., 2006; Gibala *et al*., 2006; Burgomaster *et al*., 2007) demonstrate increases in 'upstream signals' that activate PGC-1α and regulate muscle oxidative capacity. Increases in the maximal activity of citrate synthase (~11–38%), and cytochrome *c* oxidase subunit 4 (~35%) were reported in these studies.

Maximal oxygen uptake

Sixteen of the 35 studies reported improvements in maximal oxygen uptake, or cardiorespiratory fitness, measured as $\dot{V}O_{2peak}$ or $\dot{V}O_{2max}$ (Rakobowchuk *et al*., 2008; Nybo *et al*., 2010; Trilk *et al*., 2010; Metcalfe *et al*., 2011; de Araujo *et al*., 2012; Dunham & Harms, 2012; Heydari *et al*., 2012; Boutcher *et al*., 2013; Boyd *et al*., 2013; Matsuo *et al*., 2013; Adamson *et al*., 2014; Harris *et al*., 2014; Klonizakis *et al*., 2014; Zelt *et al*., 2014; Eskelinen *et al*., 2015; Shepherd *et al*., 2015). The average of the baseline values was 34.9 ± 5.5 and increased to 39.5 ± 6.1 ml·kg·min^{-1} after HIT (an increase of 12.6%). In three of these studies the increase in $\dot{V}O_{2max}$ was greater for HIT than for continuous exercise when used as a comparison treatment (Nybo *et al*., 2010; Trilk *et al*., 2010; Boyd *et al*., 2013), and produced similar improvements to continuous exercise in all other studies, despite a reduced volume of exercise. Matsuo *et al*. (2014) high-intensity interval *aerobic* training (18 min duration, exercise volume ~180 kcal) produced greater improvements in $\dot{V}O_{2max}$ than sprint interval training (10 min, ~100 kcal). However, sprint interval training resulted in improvements similar to continuous aerobic training (45 min, ~360 kcal). A single study reported no change in peak oxygen uptake in response to training although the duration of this study was only2-weeks (Skleryk *et al*., 2013). Improved cycling time trial performance (Burgomaster *et al*., 2005, Gibala *et al*., 2006; Burgmaster *et al*., 2006; Dunham & Harms, 2012; de Araujo *et al*., 2012) and functional test scores in elderly participants (get up and go test, sit to stand test, and the 50-m loaded walk test) (Adamson *et al*., 2014) were also reported.

Blood glucose homeostasis

After HIT muscle glycogen content increased by 28–50% in three studies (Burgomaster *et al*., 2005, 2006; Gibala *et al.,* 2006). This is important for optimum substrate utilisation for health and exercise performance. Eskelinen *et al*. (2015) found that after training, insulin stimulated glucose uptake improved only in those muscles that were significantly engaged in the power production during exercise (i.e. quadriceps femoris). Five studies reported increased insulin sensitivity (~28%) following short- and longer-term HIT (Nybo *et al*., 2010; Richards *et al*., 2010; Metcalfe *et al*., 2011; de Araujo *et al*., 2012; Shepherd *et al*., 2015). Insulin sensitivity was determined via response to a 75 g oral glucose tolerance test using the Homeostasis Model Assessment for Insulin Resistance or the Cederholm index; in addition to the hyper-insulinaemic euglycaemic clamp technique, considered to be the gold-standard measurement of insulin sensitivity (Bloomgarden, 2006). Metcalfe *et al*. (2011), insulin sensitivity was determined using the Cederholm index (Ciderolm & Wibell, 1990) which has been shown to correlate well with the insulin clamp method (Piché *et al*., 2007). Improvements in insulin sensitivity appeared to be sex-specific, as mean insulin sensitivity improved in male (n = 7) but not in female participants (n = 8), although Richards *et al*. (2010), using the clamp technique, did not observe any sex differences in improvements (female n = 7). In contrast two studies showed non-significant differences in insulin sensitivity compared to control or traditional exercise recommendations (Whyte *et al*., 2013; Skleryk *et al*., 2013, respectively). A single study measured glucose transporter (GLUT)-4 protein content following HIT and found modest peak increases of ~25% after 6-weeks of training (Burgomaster *et al*., 2007). Compared to baseline, GLUT-4 remained elevated following a further 6-weeks of detraining, but was lower after detraining than at the end of the training period. The findings from Little *et al*. (2014) show a single session of HIT improves post-prandial glucose control in overweight or obese adults for up to 24 h following exercise. The overall effects on glycaemia were superior to continuous moderate-intensity exercise.

Cardiometabolic risk factors

There were improvements in anthropometric characteristics related to cardiometabolic health in five studies, including a significant increase in muscle mass (0.7 kg) and thigh circumference (1.3 cm) (Matsuo *et al*., 2013) and reductions in body mass, body mass index and waist circumference compared to control (de Araujo *et al*., 2012; Heydari *et al*., 2012; Boutcher *et al*., 2013; Shepherd *et al*., 2015). However, 13 of the 35 studies demonstrated no positive improvements in body mass, body mass index or body composition (Burgomaster *et al*., 2007; Nybo *et al*., 2010; Metcalfe *et al*., 2011; Boutcher *et al*., 2013; Boyd *et al*., 2012; Freese *et al*., 2014; Harris *et al*., 2014; Klonizakis *et al*., 2014; Skleryk *et al*., 2014; Zelt *et al*., 2014; Freese *et al*., 2015; Jung *et al*., 2015; Eskelinen *et al*., 2013), whilst the remaining 17 studies did not report changes in anthropometric characteristics. The findings from seven studies (Nybo *et al*., 2010; de Araujo *et al*., 2012; Heydari *et al*., 2012; Buchan *et al*., 2013; Adamson *et al*., 2014; Klonizakis *et al*., 2014; Jung *et al*., 2015) showed reduced systolic blood pressure with an average baseline value of 128.1 ± 14.7 decreasing to 121.3 ± 14.5 mmHg after HIT (a decrease of 5.3%). Reduction was greatest (9%) for hypertensive elderly participants in the Adamson *et al*. (2014) study. Reduction in diastolic blood pressure was reported for one study (Heydari *et al*., 2012), whereas five studies reported no beneficial changes in blood pressure (Rakowbowchuk *et al*., 2008; Matsuo *et al*., 2013; Skleryk *et al*., 2013; Whyte *et al*., 2013; Harris *et al*., 2014).

Resting blood lipids were measured in three studies. Nybo *et al*. (2010), de Araujo *et al*. (2012), and Shepherd *et al*., (2015) found no changes in total cholesterol, low-density lipoprotein cholesterol (LDL-C), triglycerides or high-density lipoprotein cholesterol (HDL-C) for HIT of 6–12-weeks. Postprandial triglyceride was decreased (by 10%) in two studies (Freese *et al*., 2011, 2015) although longer-term HIT did not magnify the attenuation compared to a single exercise session (Freese *et al*., 2015). Furthermore, Whyte *et al*. (2013) reported a 63% increase in fat oxidation in the fasted state on the day following HIT. A single study investigated the effect of cycle ergometer sprints (4 × 30-s) on the thermogenic response to β-adrenergic receptor stimulation, a determinant of energy balance, and found no difference in energy expenditure compared to baseline or sedentary controls (Richards *et al*., 2010).

Myocardium and vasculature

Six studies considered cardiovascular structure and function in *healthy* participants free from chronic cardiovascular lifestyle disease (Rakobowchuk *et al*., 2008; Trilk *et al*., 2011; Heydari *et al*., 2012; Boutcher *et al*., 2013; Harris *et al*., 2014; Matsuo *et al*., 2014). Stroke volume was measured in three of these studies and significantly increased after HIT in all instances. Resting heart rate decreased in three studies, but not in the study by Rakobowchuk *et al*. (2008). These findings suggest improved cardiac function. Furthermore, peripheral artery distensibility and endothelial function are both prognostic indicators of cardiovascular disease, and were significantly improved after six weeks of HIT, comparable to traditional endurance training (Rakobowchuk *et al*., 2008). Improvements in endothelial function and artery distensibility were reported in the popliteal artery (back of the knee), a common site of peripheral vascular disease (Debasso *et al*., 2004), although artery distensibility of the carotid artery was not statistically altered by training in either group. However, arterial stiffness determined by pulse wave velocity between the carotid and femoral arteries was significantly improved after 12-weeks of HIT in the study of Heydari *et al*. (2012). Therefore, it is possible that alterations in central artery distensibility might require a longer training stimulus. Autonomic function (determined via heart rate variability), forearm vasodilatory capacity and baroreceptor sensitivity were also significantly improved. Findings from a single study suggests that HIT could be an effective method to enhance vascular repair as measured by increased mobilisation of haematopoietic angiogenic stem cells that aid vascular repair (Harris *et al*., 2014). One study considered the effects of HIT on left ventricular mass and observed a statistically significant increase (6.5%) after HIT but not aerobic training (Matsuo *et al*., 2014).

Affect (pleasure-displeasure) and enjoyment

Six of the 35 studies included measures related to the tolerability, enjoyment and pleasure associated with performing HIT (Boyd *et al*., 2013; Oliveira *et al*., 2013; Jung *et al*., 2014; Martinez *et al*., 2014; Kilpatrick *et al*., 2015; Shepherd *et al*., 2015). These measures, based on hedonic theory such as dual-mode theory, suggest that affective (pleasure-displeasure) responses during exercise might predict future exercise intentions and exercise adherence. HIT was reported to be more enjoyable than continuous exercise in three studies (Jung *et al*., 2014; Martinez *et al*., 2014; Kilpatrick *et al*., 2015). Furthermore, in the study by Martinez *et al*. (2014) shorter duration HIT (using sprints of 30-s and 60-s) was found to be more enjoyable than longer duration HIT (120-s sprints) and continuous exercise. However, two studies reported no significant difference in perceived enjoyment when comparing HIT with continuous exercise (Boyd *et al*., 2013; Oliveria *et al*, 2013).

Similarly, affective valence (pleasure-displeasure) responses associated with HIT were mixed. Several studies reported higher affective valence responses for HIT compared to 'heavy' continuous exercise, similar to those reported for continuous moderate exercise (Jung *et al*., 2014; Kilpatrick *et al*., 2015). Participants also reported being just as confident to engage in HIT as continuous exercise (Jung *et al*., 2014). When compared to continuous exercise and longer duration HIT, shorter duration HIT was associated with higher affect and post-exercise enjoyment (Martinez *et al*., 2014). In contrast, two studies observed lower affective states for HIT compared to continuous exercise (Boyd *et al*., 2013; Oliveira *et al*., 2013). For example, in the study by Oliveria *et al*. (2013) HIT resulted in decreased affective responses, increased ratings of perceived exertion and increased fatigue after exercise compared to continuous exercise, although enjoyment was not different. The variety of HIT protocols used in these studies, in terms of volume and intensity, probably accounts for much of the variation in measures and is likely to impact significantly on cognitive and behavioural responses to exercise.

Adherence and drop-out

A minimum adherence was not specified as an inclusion criterion in any of the studies. However, three participants were excluded from analysis in one study based on insufficient data and non-compliance with the HIT protocol (Freese *et al*., 2014). Twenty-five of the 35 studies did not mention adherence in the HIT or comparison groups at all. In six of these studies this may have been because of the short or single session nature of the intervention, thus adherence perhaps was not applicable (Freese *et al*., 2011; Oliveira *et al*., 2013; Whyte *et al*., 2013; Jung *et al*., 2014; Martinez *et al*., 2014; Kilpatrick *et al*., 2015). Adherence was reported in nine studies (Metcalfe *et al*., 2011; de Araujo *et al*., 2012; Dunham & Harms, 2012; Buchan *et al*., 2013; Klonizakis *et al*., 2014; Little *et al*., 2014; Matsuo *et al*., 2014; Jung *et al*., 2015; Shepherd *et al*., 2015) with an average rate of adherence of 92 ± 5.6% in the HIT groups.

Adherence to HIT was no different to continuous training in two studies (de Araujo *et al*., 2012; Matsuo *et al*., 2014), and was reported as 98% for all groups combined in one study (Dunham & Harms, 2012). For the 4-week unsupervised period of Jung *et al.*'s (2015) study, adherence in the HIT group (89%) was significantly higher than for the moderate-intensity continuous training group (71%). In one study adherence was 100% although the duration of this study was very short (Little *et al*., 2014). In the study of Richards *et al*. (2010) > 98% of participants completed all of the high-intensity sprints prescribed, with those that did not reporting feelings of nausea as the reason.

Rate of participant drop out was explicitly reported in ten studies (Coppoolse *et al*., 1999; de Araujo *et al*., 2012; Dunham & Harms, 2012; Heydari *et al*., 2012; Freese *et al*., 2014; Klonizakis *et al*., 2014; Matsuo *et al*., 2014; Freese *et al*., 2015; Jung *et al*., 2015; Shepherd *et al*., 2015). For these studies, a total of 60 (out of 270) participants dropped out after allocation to groups; 28 in the HIT groups compared to 32 for the comparison groups. Drop out was reported for a variety of reasons all unrelated to training. No injuries were reported associated with undertaking HIT. Two participants cited 'time commitment' as a reason for dropping out and one participant was excluded based on non-compliance with the HIT protocol (Freese *et al*., 2014). The remaining 25 studies did not explicitly report participant drop out.

Adverse events

None of the studies described their adverse event monitoring protocol, and no adverse events to HIT were reported. One study reported that eight (out of 15) participants partaking in HIT were unable to complete the exercise session as prescribed due to fatigue (Oliveira *et al*., 2013). Although fatigue is a natural response to the exercise undertaken, and not an adverse event *per se*, it is nevertheless important. This study did however use a particularly intense protocol with a high dependence on anaerobic metabolism. Reporting of adverse events is important to determine the safety of HIT in a range of populations.

5.5 Discussion

The main finding from this systematic review is that time-efficient HIT with ≤ 30 min total time commitment per session, inclusive of a warm-up and cool down, elicits rapid adaptations that are important for health. Changes in skeletal muscle oxidative capacity, aerobic fitness, glucose homeostasis and cardiometabolic disease risk factors were similar to those reported in previous reviews of HIT. Also, a small body of recent evidence suggests that HIT can be enjoyable and pleasurable when compared to continuous exercise, a detail that has not been considered in previous reviews. However, while this review supports the *efficacy* of HIT, what remains less clear is how *effective* it is likely to be in a real-world setting. Although the 35 studies in this review met the operational definition of 'time-efficient' (i.e. a total time commitment ≤ 30 min), most studies were only minimally under the volume of activity recommended in traditional exercise guidelines. Furthermore, most studies have used an intensity that might be intolerable for most people. No severe adverse events were observed, and a high adherence and acceptable drop-out rate were reported, but all the studies except one were fully supervised and it is not clear if these findings could be replicated away from a laboratory setting. Adherence, drop-out and adverse event monitoring procedures were generally poorly reported in the studies in this review.

5.5.1 Efficacy of time-efficient HIT

A consistent finding after 2–12 weeks of time-efficient HIT performed 2–3 times per week, was improved maximal oxygen uptake. This occurred irrespective of whether participants were apparently healthy (Rakowbowchuk *et al*., 2008; Nybo *et al*., 2010; Metcalfe *et al*., 2011; Dunham & Harms, 2012; Heydari *et al*., 2012; Matsuo *et al*., 2013; Harris *et al*., 2014; Zelt *et al*., 2014; Eskelinen *et al*., 2015), overweight or obese (Trilk *et al*., 2010; Boutcher *et al*., 2013; Boyd *et al*., 2013), elderly (Adamson *et al*., 2014) or young (de Araujo *et al*., 2012). HIT increased $\dot{V}O_{2max}$ to the same extent as continuous training, despite a lower volume of work, or to a greater extent in three studies (Nybo *et al*., 2010; Trilk *et al*., 2010; Boyd *et al*., 2013). The range of improvements across the studies are in-line with the findings of others (e.g. Sloth *et al*., 2013). The mean increase of 4.6 ml·kg·min^{-1} (12.6%) is higher than reported in a meta-analysis of HIT in sedentary, active and athletic participants (Weston *et al*., 2014a) but lower than a similar meta-analysis in patients with cardiometabolic disease (Weston *et al*., 2014b). In one study, 2-weeks of HIT did not improve $\dot{V}O_{2max}$ (Skleryk *et al*., 2013) suggesting that a minimal threshold of exercise may be required for short-term adaptations to occur. However, in another 2-week study $\dot{V}O_{2peak}$ significantly increased by 6% (Eskelinen *et al*., 2015). The lack of adaptation in the Skleryk *et al*. (2013) study could be attributed to a small sample size (n = 8), but is likely a result of a less intense HIT protocol (8–12 × 10 s sprints against 5% of body weight *vs*. 4–6 × 30 s sprints against 8% of fat free mass in the Eskelinen *et al*. [2013] study). Therefore, the large range of improvements in $\dot{V}O_{2max}$ are likely a result of heterogeneity in terms of the HIT protocols used, the intervention duration, and baseline

$\dot{V}O_{2max}$. Nevertheless, low aerobic capacity is an independent risk factor for cardiovascular disease and type 2 diabetes (Lee *et al*., 1999; Wei *et al*., 1999; Church *et al*., 2004; Katzmarzyk *et al*., 2005; Lee *et al*., 2005), and cardiorespiratory fitness is more strongly associated with all-cause mortality than overall physical activity levels (Lee *et al*., 2011). As such it is an important prognostic indicator of the potential for HIT to reduce chronic disease.

Underlying these improvements in aerobic fitness is the ability of HIT to induce rapid skeletal muscle remodelling toward a more oxidative phenotype, as reflected by intracellular signalling, and the maximal activity and nuclear protein content of mitochondrial enzymes. Most notably is the effect of HIT on PGC-1α, which is a transcription coactivator that interacts with a broad range of transcription factors involved in many biological responses. These include mitochondria biogenesis, glucose and fatty acid metabolism and fibre type switching in skeletal muscle (Liang & Ward, 2006). Also, evidence suggests PGC-1α is a powerful regulator of energy metabolism under conditions of both health and disease (Finck & Kelly, 2006) and is considered the ‘master regulator’ of mitochondria biogenesis (Wu *et al*., 1999). Several mechanistic studies have demonstrated increases in PGC-1α using both Wingate-based HIT (Gibala *et al*., 2009; Little *et al*., 2011a) and reduced-exertion protocols (Little *et al*., 2010; Hood *et al*., 2011) but these studies were not included in this systematic review due to absence of a control or comparison group. However, two studies included in this review also demonstrate significant increases in PGC-1α protein content after time-efficient HIT. Burgomaster *et al*. (2008) observed changes comparable to continuous endurance exercise, whereas Boyd *et al*. (2013) found that adaptations in oxidative capacity were not mitigated when both intensity and volume of HIT were reduced. Furthermore, these studies, and three others (Burgomaster *et al*., 2006; Gibala *et al*., 2006; Burgomaster *et al*., 2007) also show increases in ‘upstream signals’ that activate PGC-1α and regulate muscle oxidative capacity, such as citrate synthase and cytochrome *c* oxidase subunit 4. These rate-limiting enzymes are involved in the citric acid cycle and respiratory electron transport chain, respectively, typically associated with aerobic metabolism. Thus, it is a seemingly paradoxical phenomenon that HIT, which places significant emphasis on anaerobic metabolism, can induce many of the same aerobic and metabolic adaptations as traditional endurance exercise. Taken together this evidence suggests that time-efficient HIT is an efficacious strategy for improving oxidative metabolism and might highlight potential widespread health benefits.

A previous systematic review (Kessler *et al*., 2012) found that HIT did not result in improvements in lipoprotein or lipid profiles. In the current review, two studies (Nybo *et al*., 2010; de Araujo *et al*., 2012) support this finding, with no observed improvements in total cholesterol, LDL-C, HDL-C or triglycerides. Therefore, it seems HIT is less efficacious than traditional exercise guidelines for improving lipoprotein-lipid profiles and that, in contrast to fitness, it is the volume of activity rather than intensity that is associated with these improvements (Durstine, Grandjean, Cox & Thompson, 2002). Also, previous studies have observed positive correlations between changes in adipose tissue and lipoprotein-lipid profiles (Katzmarzyk *et al*., 2001). In this regard, the greater potential for higher-volume exercise to elicit improvements in the lipoprotein-lipid profile might come about via increased potential for reduction of adiposity, mediated via greater exercise-induced increases in caloric expenditure. It might seem unlikely that the small volume of activity associated with HIT would result in sufficient calorific expenditure to create the negative energy balance required for significant weight loss; however, a non-systematic review by Boutcher (2011) produced preliminary evidence to suggest HIT can result in modest reductions in intra-abdominal and subcutaneous adipose tissue. In this review three studies reported significant reductions in body mass, body mass index or waist circumference following 6-12 weeks of time-efficient HIT, whereas 12 studies reported no change. Regardless, HIT interventions should not be judged solely by their effects on body weight since other cardiometabolic risk factors have consistently been shown to improve following HIT.

Skeletal muscle is the largest tissue mass of the body and a major site for glucose disposal. Given that high-intensity exercise places greater reliance on anaerobic metabolism and intramuscular glycogen as fuel (McCartney *et al*., 1986), it is not surprising that HIT has been associated with improving insulin resistance and impaired blood glucose control. Insulin sensitivity improved by ~28% in four studies (Nybo *et al*., 2010; Richards *et al*., 2010; Metcalfe *et al*., 2011; de Araujo *et al*., 2012) and was apparent after just 2-weeks of HIT (Richards *et al*., 2010). Metcalfe *et al*. (2011) insulin sensitivity improved despite a reduced intensity and very low volume protocol with a total duration of just 10 minutes, inclusive of warm-up and cool down. This demonstrates that a very brief and feasible exercise intervention is associated with clinically significant metabolic health outcomes. Insulin stimulated glucose uptake was also shown to improve following HIT (Eskelinen *et al*., 2015) and muscle glycogen content increased by 28–50% (Burgomaster *et al*., 2005, 2006; Gibala *et al*., 2006). Modest peak increases of ~25% for GLUT-4 proteins were found after 6-weeks of Wingate-based HIT and remained elevated following a further 6-weeks of detraining (Burgomaster *et al*., 2007). This response is necessary to replace depleted stored glycogen post-exercise and is caused by up-regulation of glycogen synthase, and via translocation of GLUT-4 to the muscle sarcolemma followed by an increase in the intrinsic activity of the transporters (Furtad, Poon & Klip, 2003; Wojtaszewski *et al*., 2003). However, this increase is significantly lower than values reported in other non-controlled trials with healthy adults (~119–260%, Little *et al*., 2010; Hood *et al*., 2011) and patients with type 2 diabetes (~369%, Little *et al*., 2011b). These studies used longer-duration high-intensity sprints (60 s) with greater emphasis on aerobic metabolism, compared to the 'all-out' or supramaximal (> 100% $\dot{V}O_{2max}$) nature of the sprints used by Burgomaster *et al*. (2007). Therefore, the volume-intensity relationship of HIT could be an important determinant of adaptations to GLUT-4, but has not been explicitly explored. In this review, HIT was also shown to improve post-prandial glucose and lipid oxidation in participants who were healthy, overweight and at risk of metabolic disease (Freese *et al*., 2011; Whyte *et al*., 2013; Freese *et al*., 2015). Collectively, these results suggest time-efficient HIT is a potent means of improving substrate utilisation for health, particularly via improved facilitated diffusion of glucose into the muscle cells where it can be polymerised and stored as glycogen. This might be particularly important since hyperglycaemic blood glucose excursions in non-diabetic states might contribute to the development of macro- and micro-vascular disease risk (Baron, 2001; Ceriello, 2005).

In this review, studies of time-efficient HIT in patients with chronic disease were limited. Jung *et al*. (2015) observed that HIT was tolerable in 15 participants with non-diabetic hyperglycaemia (commonly referred to as pre-diabetes) between the ages of 30- and 60-years. In this study, compared to moderate-intensity continuous exercise, adherence to HIT was greater during 4-weeks of unsupervised training (71 *vs*. 89%, respectively). A single study compared HIT with continuous training in patients with chronic obstructive pulmonary disease (COPD) and reported increased peak work load (17%) and decreased leg pain at peak power after HIT (Coppoolse *et al*., 1999). Impaired exercise tolerance and dyspnoea are prominent complaints in these patients, therefore HIT might be appropriate to address some of the functional impairments in COPD patients. Adamson *et al*. (2014) elderly participants (mean age 65 ± 4 years) were hypertensive at baseline (155 ± 16 mmHg), and following 6-weeks of reduced-exertion HIT (6–10 × 6 s sprints against 6–7% of body mass) reduced systolic blood pressure by 7 mmHg (9%). This decrease in blood pressure is greater than reported for non-hypertensive participants in this review (5.3%, six studies), which suggests a greater response in hypertensive states. However, other studies (Kessler *et al*., 2012) have found no change in blood pressure in patients taking anti-hypertensive medication. It was not possible to determine if the participants in the Adamson *et al*. (2014) study were using anti-hypertensive medication, or whether improvements persisted beyond the transient post-exercise period. Nine studies considered HIT in participants who were overweight and obese (Trilk *et al*., 2010; Boutcher *et al*., 2013; Boyd *et al*., 2013; Skleryk *et al*., 2013; Whyte *et al*., 2013; Little *et al*., 2014; Martinez *et al*., 2014) or at risk of metabolic syndrome, defined as abdominal obesity and one other risk factor (Freese *et al*., 2014, 2015), and found changes in aerobic fitness, muscle oxidative capacity and exercise tolerability to be broadly similar to those of apparently healthy participants. More research is needed to explore the safety and efficacy of HIT before widespread adoption in patients with chronic diseases because the link between time-efficient HIT and the prevention of metabolic and cardiovascular disease could be important.

5.5.2 Effectiveness of time-efficient HIT

Time-efficiency claim

It is recommended in this review that to uphold the time-efficiency claim, the *total time commitment of each session* be the criterion for demarcating if HIT is to be considered time-efficient or not. As a minimum, this duration, inclusive of a warm-up and cool down, should be less than traditional exercise guidelines – which is 30 minutes per session. This seems appropriate because when 'lack of time' is cited as a barrier to exercise, it is probably the perceived day-to-day time commitment that is in mind. Reduced time commitment might improve compliance, and adhering to an exercise programme enhances its effectiveness, so is clearly an important pre-requisite for the success of any intervention. From the 35 studies included in the current review, the mean total time commitment per session, inclusive of a warm-up, recovery in-between high-intensity bouts and a cool down, was ~20.5 to 25.5 min. Three studies had a total time commitment ≤ 10 min; five studies > 15 min; with the remaining 25 studies having a time commitment between 20–30 min. Therefore, even though 35 HIT studies were identified in this review as 'time-efficient', it is clear they do not require appreciably less time to complete than traditional exercise in most cases.

Metcalfe *et al*. (2011) used all-out cycling sprints (2 × 10–20 s bursts) with a total session duration of just 10 min, inclusive of a warm-up and cool down. This was performed three times per week for a total weekly commitment of 30 minutes. Despite the low volume of exercise performed, aerobic capacity ($\dot{V}O_{2peak}$) improved by 12–15% and insulin sensitivity increased by 28% after six-weeks. Participants in this study were sedentary but healthy and HIT was not compared to another exercise intervention, so the results only show that low-volume HIT is better than no intervention at all. Two further studies used a very short total session duration. The study by Adamson *et al*. (2014) used 6–10 × 6 s sprints with a minimum of 1-minute recovery between sprints, whereas Buchan *et al*. (2013) used 30 s of maximal sprinting within a 20-m distance with a further 30 s of recovery between sprints. The total time commitment of these sessions was reported as ~7–11 min and ~4–6 min, respectively. However, in both studies the authors failed to report whether a warm-up and cool down were undertaken. Nevertheless, these studies provide preliminary evidence to suggest low-volume HIT could offer a genuinely time-efficient alternative to conventional exercise training for improving risk factors of cardio-metabolic disease. Two further recent studies (Whyte *et al*., 2013; Harris *et al*., 2014) have used an alternative interpretation of high-intensity training by comparing traditional HIT with sprint continuous training (SCT), which involves one sustained maximal effort sprint without rest periods. In these studies, SCT was work-matched (kJ) for exercise volume and was reported to be more time-efficient than traditional HIT. The average total time commitment was ~3.5 min for these studies, excluding warm-up and cool down. These protocols add to our choices for time-efficient exercise, although it remains unknown if they will be perceived as too intensive, with less favourable affective valence (pleasure) responses. This seems likely because the metabolic cost of the continuous sprint is high, and without recovery periods, could lead to the dramatic decline in pleasure experienced when individuals exercise above and beyond ventilatory threshold, as proposed in Ekkekakis' dual-mode theory (Ekkekakis, 2003). Nevertheless, SCT was well tolerated by the participants in these two studies. The growing trend in HIT research to explore the minimal amount of exercise that is required to improve health should be embraced.

Intensity and affective responses

Dose-response and the intensity-affect relationship are important considerations for the effectiveness of time-efficient HIT. Most studies in this review (n = 16) used a HIT protocol based on the Wingate test (i.e. 30 s maximal cycling against a braking force equal to 7.5% body mass) with the number of sprints performed typically in the region of 4–6. This is a very intense protocol resulting in considerable fatigue and frequent feelings of nausea. Consequently, these protocols are likely intolerable for the general population and would suffer poor adherence since the intensity would present a significant barrier for most people. In addressing concerns related to tolerability of such protocols some studies (n = 13 in this review) have adopted more practical approaches to HIT, but even these are near-maximal with a 1:1 work-to-rest ratio a common feature. Martinez *et al*. (2014) directly compared affective and enjoyment responses to differing training protocols. Inactive overweight or obese adults completed four counterbalanced trials with intensity based around the difference between anaerobic threshold and maximal capacity. A 20-min bout of heavy continuous exercise (10% of the difference), or 24-min of interval exercise for 30-s, 60-s or 120-s (60% of the difference) with a work-to-rest ratio of 1:1 were used. Affect and enjoyment were more positive during and after exercise for the shorter interval trials. The findings from the 30-s and 60-s trials suggest interval exercise well above ventilatory threshold can be pleasurable, which is important in the development of approaches to exercise that maximize physiological benefit without compromising the perceptual response.

A tendency of recent research has been to address psychological constructs related to the tolerability and adherence of HIT in participants at risk of chronic disease. Boyd *et al*. (2013) reported similar levels of enjoyment regardless of exercise intensity in obese men, in addition to high confidence to successfully complete HIT and schedule sessions into their everyday lives. This occurred despite high-intensity exercise being perceived to be less pleasurable and suggests that participants perceived HIT to be manageable. Improved feelings of 'energy' and 'fatigue' in women at risk of metabolic disease, and perceived ability to perform daily activities have also been reported (Freese *et al*., 2014). Kilpatrick *et al*. (2015) found that HIT (10 × 60-s at or 20% above the ventilatory threshold with a 1:1 work-to-rest ratio) produced affective and enjoyment responses equal to moderate continuous exercise, providing further preliminary evidence that HIT may be a viable alternative to continuous exercise in the promotion of health and fitness. Notwithstanding, we do not know if these perceptions can translate into acceptable long-term adherence to HIT. Future research should continue to explore genuinely time-efficient and tolerable approaches to HIT; how intensity influences cognitive and affective responses such as pleasure or displeasure will be important as this might predict adherence.

Adherence and safety

Reporting of adherence was poor, with only seven of the 35 studies stating this clearly. In the studies that did report on this (Metcalfe *et al*., 2011; de Araujo *et al*., 2012; Dunham & Harms, 2012; Buchan *et al*., 2013; Little *et al*., 2014; Matsuo *et al*., 2014; Jung *et al*., 2015), adherence was good, although all but one study was fully supervised. This preliminary evidence suggests time-efficient HIT could encourage the intended effect under ideal circumstances, but it remains equivocal whether it could be similarly beneficial in an unsupervised, real-world setting or even a clinical setting. Jung *et al*. (2015) compared HIT to moderate-intensity continuous training in patients with non-diabetic hyperglycaemia. Patients were asked to maintain unsupervised exercise at home for a period of four-weeks. Exercise adherence was monitored via accelerometery and activity logs, and was greater in the HIT group (89%) compared to the moderate-intensity continuous group (71%). Similarly, participant drop-out was recorded inconsistently across the studies, but no injuries were reported associated with undertaking HIT. No adverse events to HIT were reported in any of the studies, although adverse event monitoring protocols were not described. Tentatively, time-efficient HIT appears to be safe but future studies should explicitly stipulate the reporting of adverse events as this will allow the safety of interventions to be inferred to the populations under investigation, particularly in higher risk patients. Currently, there is insufficient evidence to suggest that HIT be can be adopted by everyone, and the approach could be hazardous for high-risk individuals. Therefore, to ensure an optimal benefit-to risk ratio, appropriate risk stratification and screening measures should be used to classify individuals as low, moderate or high-risk (e.g. ACSM, 2009).

5.5.3 Limitations

Several limitations should be considered when interpreting the findings of this review. Weston *et al*. (2014b), highlights that despite the recent emphasis on time-efficient approaches to HIT (especially in chronic disease) HIT training guidelines have not been developed. Consequently, current approaches to HIT differ in terms of modality; interval duration, frequency and intensity; and the total time commitment of each session. Although this review provides a basis for demarcating approaches to HIT that are genuinely time-efficient from those that do not differ greatly from traditional exercise guidelines, it is difficult to make comparisons when the volume and intensity of protocols are equated and monitored in different ways. Furthermore, determining time-efficiency claims is problematic when exercise procedures including warm-up and cool down, are not reported explicitly in the methods sections of studies. This was an issue for half of the studies included in this review, and as a result estimates of total time commitment will include some error. Future studies should be clear on both the time spent completing high-intensity exercise *and* the total time commitment to complete a single session of HIT, since this is likely to have implications for the effectiveness of the exercise. A further limitation relates to the specialized equipment currently used to carry out HIT, with most studies in this review using a cycle ergometer that allows for a very rapid transition from unloaded pedalling to a high mechanical or electromagnetic braking force. As highlighted by Whyte *et al*. (2013) it is this characteristic that permits generation of high peak power within the first few seconds of high-intensity intervals, and this may be required to elicit the metabolic benefits associated with HIT. It is not clear if general leisure facility bikes could perform this as effectively.

Discrepancies in the terminology used to describe approaches to HIT varies, and has been considered previously (Sloth *et al*., 2013; Weston *et al*., 2014b), with a recommendation that the term 'high-intensity interval training' be used for protocols that adopt an intensity between 80–100% peak heart rate; and 'sprint interval training' be used when intensity ≥ 100% $\dot{V}O_{2max}$. Again, the terms 'low-volume' (Little *et al*., 2011; Hood *et al*., 2012), 'short duration' (Babraj *et al*., 2009), 'reduced-exertion' (Metcalfe *et al*., 2011) and 'reduced-volume' (Skleryk *et al*., 2013) have also been added to the HIT lexicon. None of these terms guarantee HIT will be particularly time-efficient when compared to traditional physical activity guidelines. This review supports the view that we need to establish a commonly accepted definition of HIT (Biddle & Batterham, 2015), but that we also need to clearly distinguish between approaches which are genuinely time-efficient and those that are simply an alternative to traditional exercise guidelines. Methodological limitations relate to small sample sizes in many of the studies in this review. Inadequate concealment of allocation and blinding of assessors were also a weakness, in all but two studies. Finally, a potential source of bias is that 11 of the studies were conducted at two institutions and that overlapping research groups account for a significant proportion of the studies included in this review.

5.6 Conclusions

Time-efficient HIT with ≤ 30 min total time commitment per session elicits rapid biochemical, cellular and physiological adaptations that are beneficial for health. While the efficacy of such exercise is indisputable, what remains less clear is whether this approach to exercise is likely to be effective in real-world situations, and we should be cautious in extrapolating current evidence from a controlled laboratory setting to the public, since limited research currently exists in populations with chronic disease. Although proponents of HIT are not proposing Wingate-based approaches as a strategy to improve public health, at present most research has focussed on protocols that are exclusively or in combination too intense and not appreciably more time-efficient compared to traditional exercise guidelines. However, there is a recent trend to determine the minimal amount of exercise required to produce beneficial changes in a tolerable and genuinely time-efficient manner. A small number of studies have used protocols that are considerably less time intensive than traditional exercise, and others have assessed psychological constructs related to the enjoyment, pleasure and perceived exertion of HIT compared to continuous exercise, with promising preliminary results. These are important considerations because the acceptability and accessibility of the activity to those for whom the intervention is intended is likely to influence adherence.

To further research on HIT, a key challenge is to translate current evidence to a more practical approach that is both tolerable and time-efficient. It is not clear if such approaches could confer all the health benefits of traditional HIT or higher-volume approaches to exercise. However, pragmatically the choice might not be the optimal exercise prescription, but one we might deem to be ‘good enough’. Honesty and clear communication regarding the potential benefit of HIT and the associated time commitment is important because the nurturance of trust in the relationship between the healthcare or fitness professional and patient can in-turn improve adherence to interventions and patients’ health outcomes (Martin *et al*., 2005). If we wish to laud HIT as time-efficient and promote it as an exercise option to promote public health, we need to refine protocols to ensure they can offer this, and we need to provide evidence for their efficacy *and* effectiveness. Studies are required to investigate various approaches to HIT, including genuinely time-efficient and tolerable approaches that do not overly compromise physiological and psychological response to the activity. Therefore, using a series of research studies, Part Three of this thesis will investigate a novel approach to HIT using shorter sprints to make exercise genuinely time-efficient yet tolerable in terms of exercise intensity.

PART THREE: RESEARCH STUDIES

Chapter 6 Overview, Pilot Work, and General Methods

Elements of this chapter were presented at the BASES Annual Conference 2015, and have been published: Haines, M. (2015) Assessing the feasibility of a reduced-exertion, low-volume, high-intensity interval training (HIT) protocol: A pilot study. *Journal of Sports Sciences*, 33, s25 – s31.

6.1 Overview

Following the findings of the systematic review of literature (Chapter 5), data collection for this research project consisted four phases bound by the theme of reduced-exertion high-intensity interval training (REHIT), but which were distinct in focus and application. Figure 6.1 illustrates the four phases of data collection within the thesis, and a brief overview of each phase is provided below. Ethical approval for phases 1 to 3 was obtained from the University of Huddersfield, School of Human and Health Sciences, School Research Ethics Panel (SREP), and was conducted in accordance with the guidelines proposed in the Declaration of Helsinki. Ethical approval for phase 4 was provided by the National Research Ethics Service Committee Yorkshire & The Humber (REC reference 15/YH/0226; IRAS project ID 167716), in addition to NHS Research Management approval from the relevant NHS Trust Research Committee (R&D ID 15/997).

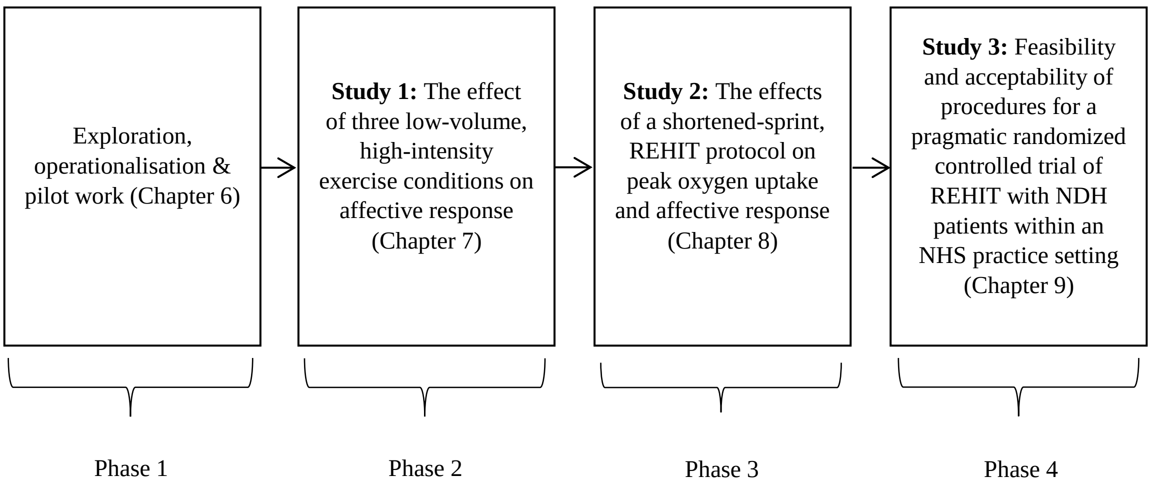

Figure 6.1 Schematic overview of the four phases of data collection within the thesis. Abbreviations: NDH = non-diabetic hyperglycaemia; NHS = National Health Service, REHIT = reduced exertion high-intensity interval training.

Phase 1

The aim of this phase was to explore various HIT protocols and potential outcome variables for use in the later phases of the thesis. Reliability and validity of various measures were considered, with participants from the University of Huddersfield's student and staff body used to trial HIT protocols. This phase culminated in pilot work which aimed to replicate the findings of Metcalfe *et al*. (2011) who reported improvements in $\dot{V}O_{2max}$ and insulin sensitivity following REHIT despite relatively low ratings of perceived exertion, in healthy young participants. The purpose of the pilot work was to assess the prospective feasibility, tolerability, and acceptability of the REHIT protocol for a larger study using NDH patients.

Phase 2

Pilot work in phase 1 revealed that REHIT was perceived to be more strenuous than anticipated, in contrast with the findings of Metcalfe *et al*. (2011). Perceived effort was related to the duration of the sprints (i.e. up to 20 s). Therefore, it was deemed necessary to design a novel approach to REHIT using shortened sprints, to reduce the likelihood of negative affective response associated with completing the activity, with the aim of optimising exercise adherence. Retrospectively, this decision was in-line with current recommendations that research into the health benefits of HIT should focus on protocols with shortened sprints (Vollard & Metclafe, 2017). Thus, study 1 used a randomised, crossover (counterbalanced) design to investigate differences between affective responses to a single bout of three low-volume, high-intensity exercise protocols, including shortened-sprint REHIT.

Phase 3

Study 1 (phase 2) suggested that shortened-sprint REHIT results in more favourable affective responses (i.e. less displeasure, less perceived effort, and more enjoyment). However, it was not known if this approach to REHIT could induce similar improvements in health outcomes. Therefore, study 2 used a randomised, positive-controlled approach to determine if shortened-sprint REHIT would attenuate improvements in $\dot{V}O_{2peak}$, and to measure affective responses during a longitudinal (5–7-week) intervention. Shortened-sprint REHIT was compared against traditional REHIT which was the minimum amount of exercise that had so far been shown to improve $\dot{V}O_{2max}$.

Phase 4

Taken together, the results of study 1 (phase 1) and study 2 (phase 2) suggested that shortened-sprint REHIT could be a genuinely time-efficient and efficacious approach to exercise, yet tolerable and enjoyable. However, the protocol had only been implemented in healthy, young and moderately fit individuals, thus it was not known if the protocol would be similarly acceptable to patients with long-term conditions. Furthermore, it was not clear if such a protocol could be realistically applied in a real-world environment. Accordingly, the aim of study 3 was to describe and report data relevant to the feasibility and acceptability of a shortened-sprint REHIT intervention in NDH patients, with the intention of improving $\dot{V}O_{2peak}$ and blood glucose control as primary outcomes. Moreover, the purpose was to assess whether it would be appropriate to progress to a larger-scale pragmatic trial, and to optimise the design and conduct of any such trial.

6.2 Pilot work

6.2.1 Abstract

Divergence between the evolutionary design of our genome and lifestyle triggers cardiometabolic disease, including diabetes mellitus. Various iterations of low-volume, high-intensity interval training (HIT) can improve risk factors in a manner considered more time-efficient than traditional exercise guidelines. However, the intensity of HIT may present another barrier to participation. Reduced-exertion HIT has shown beneficial effects with relatively low ratings of perceived exertion (RPE) in healthy young participants (Metcalfe *et al*., 2011). The aim of this study was to replicate this finding to assess feasibility for a larger trial using diabetic patients. With institutional ethics approval, 11 recreationally active participants (3 females, 8 males; age, 22.3 ± 7.3 years; stature, 1.73 ± 0.1 m; mass, 71.9 ± 13.6 kg, BMI, 23.8 ± 2.2 kg·m^2) (mean ± SD) took part in a HIT intervention consisting 10 minutes of cycling at 60 W interspersed with 2 × 10–20 s cycling sprints against a braking force equal to 7.5% of body mass. The number of sprints increased over the course of the intervention (2 × 10 s in week 1; 2 × 15 s in weeks 2–3; and 2 × 20 s in week 4). A warm-up (3 min at 30–60 W) and cool down (3 min at 30 W) were also included. Participants performed this activity 2–3 times per week resulting in a total duration of exercise per week of 20–30 minutes. RPE was reported immediately after completion of each HIT session. Whole blood fasting glucose, peak oxygen uptake and body composition were also measured before and after the 4-week intervention. HIT resulted in higher average RPE values (17 ± 1) than those reported by

Metcalfe *et al*. (~13 ± 1). VO_{2peak} was increased post-intervention (49.27 ± 9.17 ml·kg·min^{-1} [95% CI 43.11–55.43]) compared to baseline (48.27 ± 9.23 ml·kg·min^{-1} [95% CI 42.07–54.47]) (p = 0.02). However, fasting glucose and body composition were not different. The results suggest that short duration (4 weeks) reduced-exertion HIT can improve aerobic capacity. However, the intensity of the protocol might be intolerable for most people, presenting a significant barrier to exercise for less fit patients with conditions such as diabetes. The volume-intensity relationship of HIT could be considered *ad infinitum*; however, the acceptability of the activity to those for whom the intervention is intended needs consideration.

6.2.2 Introduction

Divergence between the evolutionary design of our genome and lifestyle triggers cardio-metabolic disease, including diabetes mellitus. Various iterations of low-volume, high-intensity interval training (HIT) can improve risk factors in a manner considered more time-efficient than traditional exercise guidelines. However, the intensity of HIT may present another barrier to participation. Reduced-exertion HIT (REHIT) has shown beneficial effects with relatively low ratings of perceived exertion (RPE) in healthy young participants (Metcalfe, Babraj, Fawkner & Vollard, 2011). The aim of this study was to replicate this finding to assess feasibility for a larger study using non-diabetic hyperglycaemia patients.

6.2.3 Methods

Participants and experimental approach

Eleven participants (3 females; 8 males) volunteered to participate in the study (age, 22.3 ± 7.3 years; stature, 1.73 ± 0.1 m; mass, 71.9 ± 13.6 kg, BMI, 23.8 ± 2.2 kg·m^2; $\dot{V}O_{2peak,}$ 48.3 ± 9.2 ml·kg·min^{-1}). They were included on the basis that they were between 18 and 65 years-old, apparently healthy and low risk according to health screening and risk stratification procedures as per the ACSM’s Guidelines for Exercise Testing and Prescription (ACSM, 2009). Fasting whole blood glucose concentrations also had to be normal. Diagnostically this was defined as a blood glucose concentration < 6.1 mmol·L^{-1}. Since there are insufficient data to accurately define normal glucose levels the term ‘normal’ was used for glucose levels associated with low risk of developing diabetes or cardiovascular disease (World Health Organisation, 2006). This differs from the American Diabetes Association (2013) recommendation that fasting plasma glucose values ≥ 5.6 mmol·L^{-1} and up to 6.9 mmol·L^{-1} be considered as impaired fasting glucose. Exclusion criteria included: diagnosis of type 1 or type 2 diabetes; administration of insulin; a history of end-stage liver or kidney disease, neuropathy or retinopathy; hypertension; cardiovascular disease, or other contraindications to exercise. Participants were also excluded if considered high risk for exercise using standard risk stratification, and if they did not adequately understand verbal explanations or written information given in English. Level of activity and participation in structured exercise varied across the sample and was not proscribed during the study. Participants were recruited from the student population at the University of Huddersfield using convenience sampling. After written and verbal information was provided relating to the study, participants provided written informed consent to take part. The study was approved by the School of Human and Health Sciences, School Research Ethics Panel (SREP).

The first visit to the laboratory involved baseline testing for outcome measures. Fasting whole blood glucose concentration was measured in the morning (following an eight-hour fast) with peak oxygen uptake ($\dot{V}O_{2peak}$) and body composition assessed in the afternoon. Within one week of baseline testing, participants commenced a four-week REHIT intervention. Baseline measures were repeated post-intervention within one week of completing the intervention. Participants were encouraged to continue consuming their normal diet and to maintain normal activity levels throughout the study period. However, a diet and activity log was not kept.

REHIT procedures

The exercise intervention consisted 10 min of cycling at 60 W interspersed with 2 × 10–20 s cycling sprints against a braking force equal to 7.5% of body weight. The number of sprints gradually increased over the course of the exercise intervention (2 × 10 s in week 1; 2 × 15 s in weeks 2–3; and 2 × 20 s in week 4). A warm-up (3 min at approx. 30–60 W) and cool down (3 min at 30 W) were also included. The total duration of each session was 10 min. Participants performed this activity 2–3 times per week resulting in a total duration of exercise per week of 20–30 min. The exercise intervention was adapted from a protocol that has been used in recent research (i.e. Metcalfe *et al*., 2011). All sessions were supervised in a laboratory environment.

Rating of Perceived Exertion

Intensity of exercise was measured via rating of perceived exertion (RPE) using the 15-point Borg scale (Borg, 1970). The scale ranges from 6 “no exertion” to 20 “maximal exertion” with anchors designated for all the odd integers in-between. RPE was recorded immediately upon cessation of each exercise session, with participants asked to retrospectively consider effort for the whole training session, not just the high-intensity bouts.

Peak oxygen uptake ($\dot{V}O_{2peak}$)

An incremental cycling test was used to determine peak volume of oxygen consumed expressed in relative terms per minute; also known as $\dot{V}O_{2peak}$. Participants cycled on an ergometer (Monark 894E) at 50 W for 3 min; thereafter required power to continue cycling was increased by 25 W every 1 min until volitional fatigue or until a pedal revolution of 50–60 rpm could not be maintained (Reaburn, Dascombe, Reed, Jones & Weyers, 2011). $\dot{V}O_{2peak}$ was recorded based on the highest value averaged over 30 s using an online gas analysis system (Cortex Metamax 3B). Several additional criteria were considered to establish if $\dot{V}O_{2max}$ had been reached: a final heart rate within 10 beats·min^{-1} of the age-related maximum, an observed plateau in the oxygen uptake curve, a respiratory exchange ratio of 1.15 or higher and a Rating of Perceived of Exertion (RPE) of 19-20 on the Borg scale (Borg, 1982).

Fasting whole blood glucose

Whole blood glucose concentration was determined from a fingertip capillary blood sample. A warm fingertip was cleaned with a sterile alcohol swab and allowed to dry. Blood samples were collected (approx. 15–50 μl) on Accutrend® glucose test reagent strips (Roche Diagnostics, Lewes, UK) and were immediately assessed based on the reflectance photometry method using an Accutrend® Plus System meter (via the glucoseoxidase/mediator reaction). Capillary puncture was made with Accu-Chek Safe-T-Pro Plus disposable lancets (Roche Diagnostics). Samples were collected in a temperature controlled laboratory at 21°C.

Body composition assessment

Fat mass and fat-free mass were predicted using air displacement plethysmography technology using a Bod Pod® (Cosmed, Leatherhead, UK) which uses the principles of whole body densitometry to estimate the amount of fat and lean tissue. Participants sat inside the Bod Pod® which is a dual chambered, fibreglass plethysmograph, wearing minimal clothing (for accuracy). Other than the requirement to wear minimal clothing the technique is non-invasive.

Statistical analyses

A paired (dependent) samples t-test was used to compare differences between means at baseline and post-intervention, using IBM SPSS Statistics for Windows version 22 (IBM, Armonk, USA). Data were explored for normality by checking histograms and z-scores for skewness and kurtosis. Calculated z-scores for skewness (skewness ÷ standard error skewness) and kurtosis (√kurtosis ÷ standard error kurtosis) were considered normal if they were within ± 1.96 (Field, 2013). Normality was confirmed using Kolmogorov-Smirnov and Shapiro-Wilk tests. All results are reported as the mean ± one standard deviation and 95% confidence intervals. Significance level was set at $p < 0.05$ for all tests.

6.2.4 Results

Rating of Perceived Exertion

REHIT resulted in higher aggregate mean RPE values (17 ± 1, "very hard") than those reported by Metcalfe *et al*. (~13 ± 1, "somewhat hard").

Fasting whole blood glucose

Table 6.1 compares outcome variables at baseline and post-intervention. Fasting whole blood glucose concentration at baseline was 4.0 ± 0.39 mmol·L^{-1} (95% CI 3.73–4.27) and 4.02 ± 0.29 mmol·L^{-1} (95% CI 3.82–4.21) post-intervention but was not statistically significant ($p = 0.76$).

Table 6.1 Summary of statistics comparing measures at baseline and post-intervention.

	Baseline	Post-intervention
Fasting whole blood glucose (mmol·L^{-1})	4.0 ± 0.39 (3.73–4.27)	4.02 ± 0.29 (3.82–4.21)
$\dot{V}O_{2peak}$ (ml·kg·min^{-1})	48.27 ± 9.23 (42.07–54.47)	49.27 ± 9.17 (43.11–55.43) *
Fat mass (kg)	15.47 ± 14.89 (5.46–25.48)	15.31 ± 14.88 (5.31–25.3)
Fat free mass (kg)	56.38 ± 22.36 (41.36–71.41)	56.55 ± 22.47 (41.46–71.65)

Note: Data are presented as mean ± standard deviations (95% confidence intervals).
* Statistically significant in comparison to baseline ($p < 0.05$)
Abbreviations: RPE = rating of perceived exertion, $\dot{V}O_{2peak}$ = peak oxygen uptake.

Peak oxygen uptake ($\dot{V}O_{2peak}$)

$\dot{V}O_{2peak}$ was significantly higher post-intervention (49.27 ± 9.17 ml·kg·min^{-1} [95% CI 43.11–55.43]) compared to baseline (48.27 ± 9.23 ml·kg·min^{-1} [95% CI 42.07–54.47]) ($p = 0.02$, $d = -0.10$).

Body composition assessment

Fat mass and fat-free mass were not significantly different post-intervention compared to baseline (both $p > 0.05$).

6.2.3 Discussion

The main finding of this pilot study was that REHIT resulted in higher mean RPE values (17 ± 1) than those reported by Metcalfe *et al*. (2011) who reported relatively low ratings of perceived exertion using a very similar protocol (~13 ± 1). This was unexpected considering that the participants used in the present study recorded higher baseline fitness values. A plausible explanation is that they could achieve higher levels of anaerobic substrate phosphorylation resulting in greater fatigue and thus higher perceived effort. Accordingly, it seems unlikely that this protocol would be well tolerated by sedentary, obese or diabetic patients. High perception of effort appeared to relate primarily to the duration of the sprints (i.e. some lasted 20 s). Therefore, one of the aims of phase 2 of the research project will be to use a modified REHIT protocol with shortened sprints, with the intention of being less strenuous and more tolerable for less fit or sedentary populations (see Chapter 7). It is not clear if shorter duration sprints will attenuate the health benefits associated with traditional REHIT or higher-volume HIT. However, maximal cycle sprints of a similar duration have been shown to increase the activation of glycogen phosphorylase (Parolin *et al*., 1999). This may act as an important signalling mechanism and could therefore provide sufficient stimulus to increase mitochondrial density, with increased flux through the glycolytic pathway mediating enhanced insulin-stimulated glucose transport. As such, although speculative, protocols using shorter sprints could stimulate glycogenolysis in a manner that could be beneficial in the treatment of hyperglycaemic states.

A secondary finding was that $\dot{V}O_{2peak}$ increased after just four weeks of high-intensity training compared to baseline ($p = 0.02$). This finding is in-line with other research, although the magnitude of increase (~2%) was less than previously reported and the effect size was trivial ($d = -0.10$). Metcalfe *et al*. (2011) used the same protocol and reported improvements in $\dot{V}O_{2peak}$ of 12–15%. The shorter duration of the intervention (4 weeks *vs*. 6 weeks) in the current study, and the heterogeneity in baseline fitness of participants between the two studies, could account for some of this difference. Similar studies of even shorter duration (2 weeks) have also reported increases in aerobic fitness (e.g. Whyte, Gill & Cathcart, 2010; Boyd, Simpson, Jung & Gurd, 2013) although these studies have used more intense protocols, that are likely to be too intense for use in general and clinical populations. Improvements in aerobic fitness following low-volume HIT are likely a result of increased skeletal muscle mitochondrial adaptations (Little, Safdar, Wilkin, Tarnopolsky & Gibala, 2010; Hood, Little, Tarnopolsky, Myslik & Gibala, 2011).

There were no differences between baseline and post-intervention values for fat mass, fat free mass, or fasting whole blood glucose concentrations. However, considering the small sample size and heterogeneity in participant characteristics (e.g. large range of values for fat mass and fat free mass) the study was not adequately powered to test inferences about the intervention. As such, it is difficult to draw confident conclusions from the data. Nevertheless, the main aim of the pilot work was to test whether components of the main study work together, rather than to power the study for inferential statistical testing. In conclusion, the results suggest that short duration (4 weeks) REHIT may increase aerobic capacity, although the effect size was very small. Notwithstanding, the intensity of the protocol might be intolerable for most people, presenting a significant barrier to exercise for habitually sedentary individuals with conditions such as diabetes. The results of this study should be viewed with caution alongside the limitations inherent with such small-scale pilot work. Yet, the perceived intensity associated with the protocol used in this study provides a rationale for exploring similar protocols using shorter sprint durations. The dose-response relationship of HIT could be considered *ad infinitum*; nevertheless, the acceptability of the activity to those for whom the intervention is intended needs further consideration.

6.2.5 Ethical issues raised from pilot work

Table 6.2 summarises ethical issues encountered during operationalisation of procedures throughout Phase 1 of this project. Possible solutions to counter these issues for Phase 4 of the project are also offered, where the aim will be to use REHIT with non-diabetic hyperglycaemia patients in an NHS practice setting (Chapter 9).

Table 6.2 Summary of ethical issues encountered.

Ethical issue	Solution
Participant burden (travel and time)	Requirements for taking part in research, and non-financial compensation, to be clearly described and discussed prior to commencing study. The nature of the exercise intervention is to trial a low-volume approach, so this will minimise time burden.

Adverse outcomes during or after exercise	Strict application of exclusion criteria will minimise risk, and be used alongside appropriate risk stratification prior to commencing exercise. Intensity of exercise will be monitored during supervised sessions, and the intensity of exercise will be tailored relative to individual body mass. Sessions will be carried out in a hospital environment with first aid available.
Discomfort/pain associated with stress of exercise testing and exercise intervention	Requirements for taking part in the research will be clearly described and discussed prior to commencing the study. The nature of the exercise intervention is to trial a low-volume and less strenuous approach to exercise, so this will minimise physical discomfort. Patients can stop exercise at any time, without prejudice or coercion from the researcher, and this will not affect the care they receive.
Withholding standard care	During the study patients will be asked to maintain their normal physical activity and dietary habits. They will be asked to refrain from engaging in new structured exercise programmes during the study period. However, it is envisaged that the extra support offered by taking part in the study is more likely to result in positive behaviour change (adherence to exercise), so any negative effects are minimised.
Blood sampling	Phase 4 requires venous blood sampling to determine HbA_{1c}. Standard procedures for risk management will be adhered to.
Distress at discussing results	It is unlikely that results gathered will cause distress to participants. If the participants do feel some distress at having low fitness (for example), information and advice will be offered by the Chief Investigator (BASES Certified Exercise Practitioner) to offer support. If appropriate, it will be possible to refer the participant back to the healthcare team at the hospital.
Access to personal patient data	First contact will be made by the healthcare (recruitment) team. As such, permission to contact patients will be sought before the Chief Investigator contacts patients. Confidentiality will be upheld for all data.

6.3 General methods

Several procedures and measures are common to the methods of the studies included in this thesis, and are detailed here to aid clarity.

6.3.1 Health screening and exercise familiarisation

For studies 1 and 2, participants were recreationally active and apparently healthy, determined via negative responses to the American Heart Association/American College of Sports Medicine (ACSM) Health and Fitness Facility Pre-Participation Screening Questionnaire. To be included participants also had to be aged between 18- and 65-years, and able to adequately understand verbal instructions and written information given in English. Specific exclusion criteria included diagnosis of diabetes, a history of liver or kidney disease, hypertension that could not be controlled by standard medication, and cardiovascular disease. Individuals considered to be medium or high risk as per the ACSM logic model for cardiovascular disease risk (i.e. ≥ 2 risk factors; ACSM, 2014) were also excluded. The experimental procedures and associated risks were explained to all participants before their participation as part of a familiarisation session. Participants were permitted to observe and trial the exercise conditions. All participants commenced with the first exercise training session within one week of the familiarisation session.

6.3.2 General exercise procedures

For studies 1 and 2, all exercise sessions were performed on a Wattbike cycle ergometer (Wattbike Pro, Nottingham, UK). Saddle height was adjusted for each participant to ensure close to full knee-joint extension (~170°) when the pedal was at the bottom of the cycle. For all exercise conditions, pedal resistance for the bouts of high-intensity cycling was set using the air and magnetic settings to create a flywheel braking force appropriate for peak power generation, as recommended by Wattbike (Wattbike, 2016). This is comparable to typical HIT protocols that have used Monark cycle ergometers which rely on loading weights relative to body mass to create flywheel resistance. However, the Wattbike calculates power output by measuring real time chain tension over a load cell (sampled at 100 Hz) based on known crank length, the average force per crank revolution, and the time taken to complete a crank revolution. Cycle sprints on the Wattbike have been shown to be highly reproducible for absolute and relative peak power (Driller, Argus & Shing, 2013).

Instructions on how to carry out each exercise condition were communicated before and during each session, with standardised verbal encouragement and feedback used throughout the high-intensity periods of exercise to ensure maximal effort. Due to the exercise conditions using different protocols, it was not possible to work match across the conditions. Heart rate was not monitored because the purpose of HIT is to be time-efficient and convenient, so it was deemed that attaching heart rate monitors would negatively impact this feature. However, participants remained in the laboratory for 10 min post-exercise for monitoring of adverse events.

6.3.3 Measurement of perceptual response to exercise

Affect (pleasure-displeasure)

Affective valence (i.e. pleasure-displeasure) was assessed using the single-item, 11-point Feeling Scale (FS) (Hardy & Rejeski, 1989). The FS uses a bipolar scale and ranges from – 5 'very bad' to + 5 'very good', with anchors designated for 0 (neutral) and all odd integers in-between. The stem "How do you currently feel?" was used to measure pleasure throughout exercise at 25%, 50%, 75% and 100% of bout completion for all conditions. These times were selected to capture responses during the warm-up, recovery after a high-intensity bout, and immediately on cessation of exercise. Prior to completing each condition, the FS was explained with the instructions: "During exercise, it is common to experience changes in mood. Some people find exercise pleasurable, whereas others find it to be unpleasant. Also, these feelings may change throughout exercise. When asked, please tell me how you feel at that moment in time using the following scale". The FS was presented to participants using a visual cue card at each time point to ensure accurate reference to the scale. The FS is a measure of core affect and as such is not the same as perceived exertion. These constructs have been shown to be moderately inversely correlated (r = -0.33 to -0.55) demonstrating a degree of discriminant validity (Hardy & Rejeski (1989).

Rating of perceived exertion

Perceived intensity of each condition was monitored using a rating of perceived exertion (RPE) using the 15-point Borg scale (Borg, 1970). The scale ranges from 6 'no exertion' to 20 'maximal exertion' with anchors designated for all the odd integers in-between. As for recording of affect, RPE was measured using a visual cue card throughout exercise at 25%, 50%, 75% and 100% of bout completion, using the stem "How hard are you working at this moment in time?" Strong correlations (r = 0.80 to 0.90) between RPE and exercise intensity have been reported in a meta-analysis (Chen, Fan & Moe, 2010), although these studies are not specific to intermittent exercise which is characteristic of HIT. More moderate correlations have been reported for RPE and heart rate during high-intensity interval cycling (r = 0.63, Green *et al*., 2005).

Enjoyment

Enjoyment was assessed for each condition using the single-item, 7-point Exercise Enjoyment Scale (EES) (Stanley & Cumming, 2009). Anchors are given at every integer, ranging from 1 ‘not at all’ to 7 ‘extremely’. The EES was used following the stem, “Use the following scale to indicate how much you enjoyed this exercise session,” and was recorded 5 min post-exercise. the EES has been provisionally shown to be a valid single-item measure of feeling and felt arousal (Stanley, William & Cumming, 2009) and has been used in other HIT research (e.g. Kilpatrick *et al*., 2015; Smith-Ryan, 2017).

Chapter 7 Study 1: Low-volume exercise and affective response

The content of this chapter has been submitted for publication in the *Journal of Sport and Exercise Psychology*.

The effect of three low-volume, high-intensity exercise conditions on affective response

7.1 Abstract

Despite evidence for the efficacy of regular exercise in treating, delaying or preventing a range of diseases, physical inactivity remains an endemic health problem. Frequently, "lack of time" is cited as the reason for this. Accordingly, recent interest in low-volume, high-intensity exercise has grown exponentially, because this activity is considered more time-efficient, thereby circumventing this barrier. However, the high-intensity nature of this exercise may be another barrier for many people. Hedonistic theories of motivation such as the dual-mode theory, emphasise the importance of avoiding large negative peaks in affective (pleasure-displeasure) response during exercise, since this may result in an avoidance response and poor future exercise adherence. Using a randomised crossover trial, the aim of this research was to consider differences between affective responses to three different low-volume, high-intensity exercise protocols. With institutional ethics approval, 36 participants (29 males, 7 females; age 22.3 ± 4.7 years; mass, 73.2 ± 12.3 kg; BMI, 24.2 ± 2.6 kg·m^2) undertook a single bout of: 1) reduced-exertion high-intensity interval training (REHIT), 2) a novel, shortened-sprint REHIT protocol, and 3) sprint continuous training (SCT). Affect and perceived exertion were recorded throughout exercise at 25%, 50%, 75% and 100% of bout completion, using the Feeling Scale (FS) and the 15-point Borg rating of perceived exertion (RPE) scale, respectively. Enjoyment was recorded 5 min post-exercise using the Exercise Enjoyment Scale (EES). Whole blood lactate concentration was also recorded immediately upon cessation of exercise. A factorial, 3 (Conditions) by 4 (Time) repeated-measures ANOVA revealed significant main effects of Condition and Time for FS and RPE ($p = 0.01_{GG}$). Peak affective valence, was more positive for shortened-sprint REHIT (1.4 ± 1.7 FS units, "fairly good") compared to traditional REHIT (-0.1 ± 1.9, "near neutral") and SCT (-0.8 ± 1.6, "fairly bad"), (both p = 0.001). Traditional REHIT was also associated with greater pleasure than SCT (p = 0.005). Lower RPE was reported after shortened-sprint REHIT (13.9 ± 1.5 units, 'somewhat hard'), compared to traditional REHIT (15.5 ± 1.7, 'hard') and SCT (16.4 ± 1.6, nearly 'very hard'). Again, higher

enjoyment was also associated with shortened-sprint REHIT (all $p < 0.01$). There was no difference in blood lactate concentrations between conditions ($p = 0.59$). The results provide preliminary evidence to suggest that both iterations of REHIT avoid large negative peaks in affective response and may therefore be genuinely time-efficient, yet tolerable approaches to exercise. Shorter sprints may be additionally beneficial in circumventing negative affective responses. These principles may have direct implications for how exercise sessions are structured, but the challenge of translating this evidence to real-world environments remains.

7.2 Introduction

Approaches to high-intensity exercise have evolved since Tabata *et al*. (1996) demonstrated that six-weeks of intermittent exhaustive exercise improved cardiovascular fitness more than moderate-intensity aerobic training. Furtherance of research on high-intensity training has resulted in the emergence of several approaches to low-volume exercise and claims that such protocols could have a fundamental role in health promotion (e.g. Rehn, Winett, Wisløff & Rognmo, 2013; Francois & Little, 2015; Jung *et al*., 2015). High-intensity interval training (HIT) is characterised by brief periods of repeated all-out exercise interspersed with longer periods of recovery. Proponents speculate that this type of exercise could benefit a wide range of people emphasising relative time-efficiency as an important practical benefit to increase exercise adherence in those who otherwise would not engage with more time-consuming approaches. Certainly, the *efficacy* of HIT as a potent means of inducing beneficial biochemical, cellular, and physiological adaptations seems clear. Experimental mechanistic investigations (Gibla *et al*., 2006; Burgomaster *et al*., 2008), randomised controlled trials (Heydari *et al*., 2012; Matsuo *et al*., 2013), and meta-analyses (Weston, Taylor, Batterham & Hopkins, 2014a; Weston, Wilsøff & Coombes, 2014b) attest this point. This type of ativity improves cardiovascular fitness (measured as $\dot{V}O_{2max}$) which is important because low fitness is an independent risk factor for heart disease and type 2 diabetes (Lee *et al*., 2005; Ross *et al*., 2016), and is more closely linked with all-cause mortality than overall volume of exercise (Lee *et al*., 2011). However, what is less clear is how *effective* HIT is likely to be in real-world settings. Concerns have been raised about the likelihood of HIT evoking a high degree of negative affect, or displeasure, which may in-turn lead to an avoidant response with the prospect of future exercise sessions (Hardcastle, Ray, Beale & Hagger, 2014).

Hedonistic theories of motivation, such as dual-mode theory, propose that exercise above a certain intensity threshold relies heavily on anaerobic substrate phosphorylation which results in a cascade of physiological responses that greatly challenge homeostasis (Ekkekakis *et al*., 2008). These perturbations may be closely linked to affect (Cabanac, 2006), and such feelings of displeasure could in-turn predict future engagement in that activity and long-term exercise adherence (Williams *et al*., 2008; Williams *et al*., 2012). A central tenet within this framework for some time, has been that people typically choose not to engage in activities that they find aversive (Pollock, 1978). Thus, one of the primary reasons for the advocacy of HIT – that it might appeal to individuals who otherwise would not engage with more time-consuming exercise – is juxtaposed with speculation that the intensity is likely to pose a significant barrier for many. If one barrier (time) is replaced with another (intensity), HIT is unlikely to result in improved adherence compared to traditional exercise guidelines. However, critiques based on hedonicity have mostly relied on *continuous* exercise above the ventilatory threshold, which may be wholly inappropriate for understanding intensity-affect-adherence relationships associated with HIT, since the intermittent nature of the activity fundamentally alters the exercise experience.

There is a dearth of research addressing the perceptual response to HIT. Oliveira *et al*. (2013) reported lower affective valence (greater displeasure) during HIT compared to continuous training, measured using the Feeling Scale (FS) (Hardy & Rejeski, 1989). However, enjoyment measured 10-min post-exercise was not significantly different. More recently, Decker & Ekkekakis (2017) observed lower pleasure and enjoyment for HIT compared to moderate-intensity continuous exercise. Notwithstanding, the protocols in these two studies used very high intensities. Participants were required to undertake six or seven 2-min treadmill sprints at an intensity equivalent to $\dot{V}O_{2peak}$, or 4 × 3 min intervals at 115% of power achieved at ventilatory threshold, respectively. Such protocols rely heavily on sustained anaerobic metabolism, whereas more moderate approaches to HIT with differing interval and recovery periods might yield different results. Contrasting research has shown HIT can produce affective and enjoyment responses that are more positive than for heavy continuous exercise, like those of moderate continuous exercise (Kilpatrick, Greely & Collins, 2015). Also, Jung *et al*. (2014) assessed a lower-volume approach to HIT, using a 1:1 work-to-rest ratio eliciting a heart rate of ~90% maximum, and compared this to both moderate- and vigorous-intensity continuous exercise. HIT resulted in more pleasant affective responses than vigorous continuous exercise, but was less pleasant that moderate exercise. Furthermore, in comparison to moderate continuous exercise, greater enjoyment and improved confidence to engage with HIT have been reported, despite more negative affective states (Bartlett *et al*., 2011; Kilpatrick, Greely & Collins, 2015).

What is clear is that affective responses to HIT have thus far been inconsistent, most likely due to the differing protocols that have been used in terms of intensity, frequency, duration, and recovery associated with the high-intensity bouts of exercise. The acceptability and tolerability of these protocols to those for whom the intervention is intended should be a foremost consideration, and several attempts have been made to consider the minimal amount of exercise that could confer health benefits. Metcalfe and colleagues (2011; 2016a) used a reduced-exertion HIT (REHIT) protocol with a total duration of 10 min, inclusive of a warm-up and cool down. Participants completed 2 × 10–20-s cycle sprints against a braking force equivalent to 5–7.5% of body mass, performed three times per week over a 6-week period. $\dot{V}O_{2peak}$ improved by 10–15%, although large interindividual variability was observed. The acceptability of such a minimalist approach to HIT could be important for sedentary individuals and those with chronic disease. For example, skeletal muscle insulin sensitivity is an important biomarker in the development of type 2 diabetes and metabolic syndrome (Petersen *et al*., 2007; Defronzo & Tripathy, 2009), and is a principal target for preventative strategies such as exercise. So far, the effects of REHIT on insulin sensitivity in healthy participants have been conflicting (Metcalfe *et al*., 2011; 2016a). Other, studies using participants with type 2 diabetes have shown that insulin sensitivity or glycaemic control are not improved after REHIT, yet increases in $\dot{V}O_{2max}$ remain (Revdal, Hollekim-Strand & Ingul, 2016; Ruffino *et al*., 2016). Metcalfe *et al*. (2015) demonstrated that improvements in $\dot{V}O_{2max}$ are associated with activation of molecular signalling pathways that lead to increased gene expression of peroxisome proliferator-activated receptor-γ coactivator (PGC)-1α, which is considered important for mitochondria biogenesis and energy metabolism under conditions of both health and disease (Wu *et al*., 1999; Finck & Kelly, 2006). In this regard, REHIT seems to be comparable to more traditional higher-volume HIT in terms of adaptations to $\dot{V}O_{2max}$, but not insulin sensitivity (e.g. Burgomaster *et al*., 2008; Boyd *et al*., 2013).

Two further studies have used an alternative form of high-intensity exercise known as sprint continuous training (SCT), which involves one sustained maximal effort sprint without rest periods (Whyte *et al*., 2013; Harris *et al*., 2014). In these studies, SCT was compared to traditional HIT and work-matched (kJ) for exercise volume. The average total time commitment was ~3.5 min for these studies, excluding warm-up and cool down. These protocols add to our choices for time-efficient exercise, although it remains unknown if they will be perceived as too intensive, with less favourable pleasure responses. This seems likely because the metabolic cost of the continuous sprint is high and, without recovery periods, could lead to the dramatic decline in pleasure experienced when individuals exercise above and beyond ventilatory threshold, as proposed in Ekkekakis' dual-mode theory (Ekkekakis, 2003).

An additional psychological theory known as the *peak-end rule* proposes that memory associated with the pleasure or displeasure of exercise is influenced, in part, by the moment a 'peak' affective response is experienced (Redelmeirer & Kahneman, 1996; Kahneman, 1999; Fredrickson, 2000). In relation to HIT and REHIT, the peak moment of displeasure is likely to occur during the high-intensity bout of exercise and could influence retrospective evaluations of the activity, impacting motivational factors related to future adherence. During HIT, at the start of a high-intensity bout sensation is related to muscle resistance to external force, but becomes a function of duration when work is extended over time (Cafarelli *et al*., 1977). As such, the duration of the high-intensity bout is important. Traditional REHIT uses a 20-s maximal-effort cycling sprint against a load equivalent to 7.5% of body mass which is likely to result in considerable fatigue, and even feelings of nausea, particularly in previously non-active individuals. Given that shorter intervals are associated with more favourable affect and enjoyment compared to longer intervals (Freese *et al*., 2014), the perceived effort and affective response to intermittent exercise seems to relate primarily to the duration of sprints. Therefore, it is plausible that adapting REHIT using shorter duration maximal efforts would result in a more favourable perceptual response.

The perceptual response to low-volume HIT, such as REHIT and SCT, is an important consideration in relation to exercise adherence and is currently underexplored. Furthermore, hedonistic theories of motivation have only been considered for higher-volume HIT. The challenge remains to explore approaches to low-volume exercise that provide meaningful benefits to health without overly compromising perceptual response. Therefore, because affective responses to the various iterations of low-volume, high-intensity exercise might predict future engagement in that activity, there is a need to identify practical approaches that are tolerable and genuinely time-efficient. The aim of the present randomised crossover study was to consider differences between perceptual responses to three different low-volume, high-intensity exercise protocols: traditional REHIT, shortened-sprint REHIT, and SCT. The experimental hypothesis was that shortened-sprint REHIT would result in more favourable affective responses (less displeasure) compared to traditional REHIT and SCT.

7.3 Methods

7.3.1 Participants and experimental approach

An *a priori* power analysis was performed using G*Power© software (version 3.1.9.2, 2017) for comparison between three dependent means for the primary outcome, that is ratings of affective valence (pleasure-displeasure) during high-intensity exercise. This was based on an anticipated medium-to-large effect size (ES) (i.e. ES = 0.5–0.8; Cohen, 1988), an alpha criterion of 0.05, and power of 0.8 (1 – beta). This is proportionate with effect size assumptions made in similar studies (e.g. Martinez *et al*., 2014; Kilpatrick *et al*., 2015; Decker & Ekkekakis, 2017). These estimations also assumed that the sphericity assumption associated with repeated measures would be met. Sample size calculations require assumptions that cannot be tested until the data has been collected, and are thus inherently hypothetical. Analysis indicated that a total of 19–45 participants were required to reach 0.8 statistical power, dependent on effect size (i.e. 0.5–0.8). Using emails and word of mouth, a convenience sample of 36 participants (29 males, 7 females; age 22.3 ± 4.7 years; stature, 1.7 ± 0.1 m; mass, 73.2 ± 12.3 kg; BMI, 24.2 ± 2.6 kg·m^2) was recruited, consisting students (78% of the sample) or those who worked in full-time or part-time occupations. Health screening and familiarisation were conducted as per the General Methods (section 6.3.1, pp. 118).

Participants were informed of the benefits and risks of the research prior to signing an informed consent form, before undertaking a single bout of three separate high-intensity exercise conditions: 1) traditional REHIT, 2) shortened-sprint REHIT, and 3) SCT. A randomised, counterbalanced crossover design was used to reduce the chances of the order of exercise sessions, or other factors, adversely influencing results. The three exercise conditions were grouped into six possible orders with participants randomly assigned to these using a random number generator. Participants visited the laboratory separated by a minimum of 48 h in-between sessions. Participants were asked to refrain from intense physical activity the day before each session and to delay participation if fatigue or musculoskeletal injury was present from previous sessions, or other activities. Again, participants were instructed to refrain from engaging in any recovery modalities following exercise and to avoid alcohol; they were also instructed to follow their normal diet. However, diet and physical activity were not monitored in this study. Allocation concealment and blinding of assessors who measured outcome measures were not possible. Ethical approval to carry out the study was obtained by the

University of Huddersfield, School of Human and Health Sciences, School Research Ethics Panel.

7.3.2 HIT conditions

General exercise procedures were applied as per the General Methods (section 6.3.2, pp. 118). Participants remained in the laboratory for 10 min post-exercise for monitoring of adverse events. During this time, whole blood samples were analysed for lactate concentration to consider acid-base balance as an indicator of the extent of anaerobic substrate phosphorylation in response to exercise. The total volume of work (kJ) completed was also calculated upon completion of each exercise condition.

Traditional REHIT

REHIT was performed as per the research of Metcalfe *et al*. (2011) and consisted a total of 10 min cycling, inclusive of 2 × 20 s maximal effort 'sprints' against a braking force appropriate for peak power generation. Exercise intensity in-between sprints was low (~60 W). The 10 minutes of cycling was also inclusive of a warm-up (3 min at ~30–60 W) and cool down (3 min at ~30 W). The total duration of high-intensity exercise (40 s) is equivalent to what was used in the latter half of the six-week study of Metcalfe *et al*. (*ibid*.). A schematic overview of the REHIT condition can be seen in Figure 7.1 a.

Shortened-sprint REHIT

Shortened-sprint REHIT was designed to match the traditional REHIT in terms of the total time spent doing high-intensity exercise (i.e. 40 s). However, with the aim of reducing the perceptual response associated with prolonged maximal efforts, this time was broken up into smaller periods. Therefore, participants performed a total of 10 min cycling, inclusive of 8 × 5 s maximal effort 'sprints' against a braking force appropriate for peak power generation. Similarly, exercise intensities in-between sprints were low (~60 W), and a warm-up (3 min at ~30–60 W) and cool down (2 min at ~30 W) were included within the 10-minute session (Figure 7.1 b).

Sprint continuous training (SCT)

In existing SCT studies, high-intensity exercise has been work-matched (kJ) to sprint interval training (Whyte *et al*., 2013; Harris *et al*., 2014). That is, participants performed the same volume of work as that completed during 20 min of HIT, but in a single bout. The total duration of high-intensity effort in these studies was 3.3–3.5 min. In the current study, it was not possible to work match SCT to the other conditions, because REHIT and shortened-sprint REHIT used different protocols. Instead a decision was made to mimic the total duration of high-intensity exercise as per the previous SCT studies, whilst ensuring the protocol was time-efficient and in-line with the REHIT protocols. Therefore, in this study SCT consisted a total of 8 minutes cycling, inclusive of a warm-up (3 min at ~30–60 W), a 3-min extended sprint, and a cool down (2 min at ~30 W) (see Figure 7.1 c). During the extended sprint, participants were encouraged to pedal with maximal effort whilst considering the duration of the bout. Thus, an element of ‘pacing’ was inherent to this. Whereas the braking force in the studies of Whyte *et al*. (2013) and Harris *et al*. (2014) were reduced (5%–6.5% of body mass, respectively) to ensure maintenance of an appropriate cadence (> 50 rpm), this was not required in the current study. The Wattbike measures force applied through the cranks onto the chain and is independent of cadence, with power uninfluenced by resistance from the magnetic or airbrake systems. Therefore, participants could pedal against a braking force appropriate for peak power generation as per the other conditions, whilst maintaining a pedal cadence appropriate for maximal effort over an extended time.

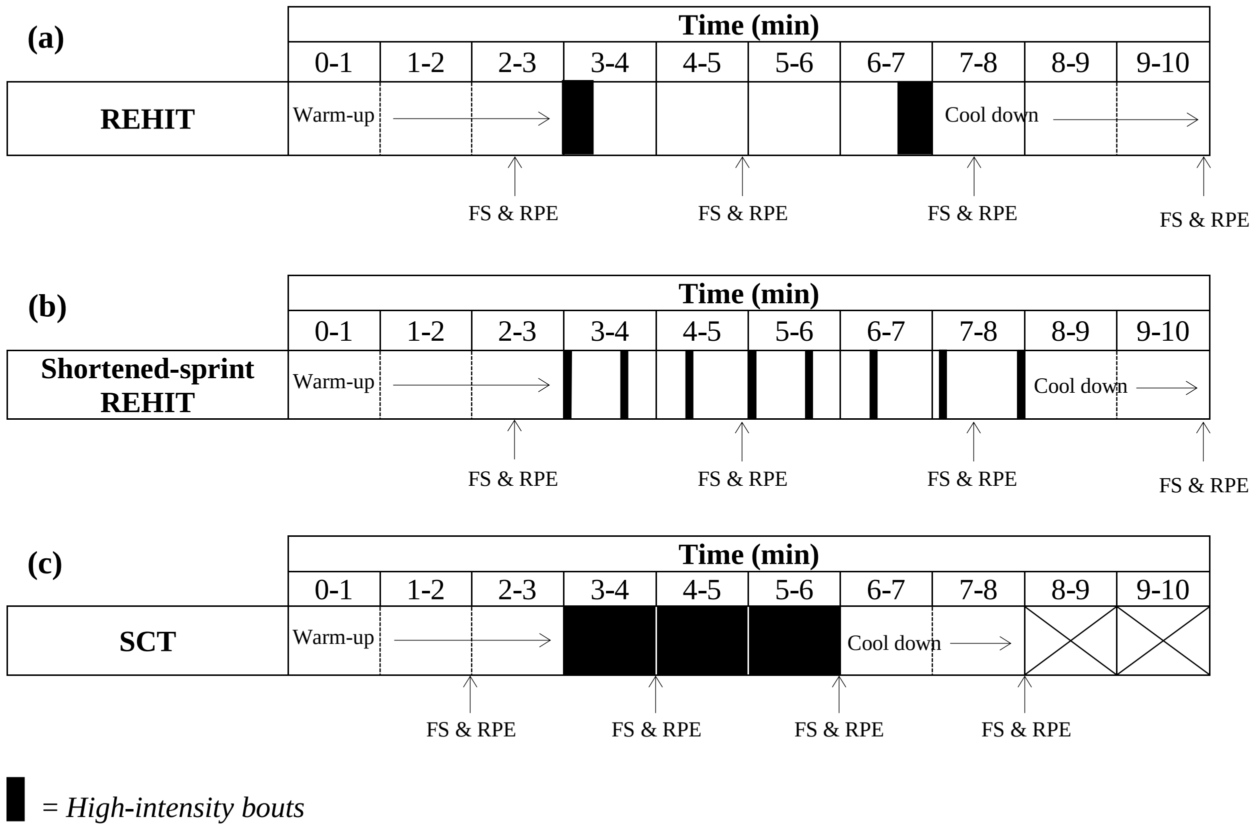

Figure 7.1 Schematic overview of the three exercise conditions. Abbreviations: REHIT = reduced exertion high-intensity interval training, SCT = sprint continuous training, FS = feeling scale; RPE = rating of perceived exertion.

7.3.3 Measures

Affect (pleasure-displeasure)

Affective valence (i.e. pleasure-displeasure) was designated the primary outcome variable and was assessed using the Feeling Scale (FS) (Hardy & Rejeski, 1989) as detailed in the General Methods (section 6.3.3, pp. 119). The stem "How do you currently feel?" was used to measure pleasure throughout exercise at 25%, 50%, 75% and 100% of bout completion for all conditions (Figure 7.1 a-c). For traditional REHIT and shortened-sprint REHIT this equated to 2:30 min, 5 min, 7:30 min, and 10 min. For SCT the equivalent times were 2 min, 4 min, 6 min, and 8 min owing to the reduced total duration of this protocol. These times were selected to capture responses during the warm-up, recovery after a high-intensity bout, and immediately on cessation of exercise.

Rating of perceived exertion

Perceived intensity of each condition was monitored using a rating of perceived exertion (RPE) using the 15-point Borg scale (Borg, 1970) as per the General Methods (section 6.3.3, pp. 119).

Enjoyment

Enjoyment was assessed for each condition using the Exercise Enjoyment Scale (EES) (Stanley & Cumming, 2009) as per the General Methods (section 6.3.3, pp. 120).

Blood lactate

Whole blood lactate concentration was determined from a fingertip capillary blood sample. Participant's fingertips were cleaned with a sterile alcohol swab and allowed to dry. Blood samples were immediately collected (~5 μl) on Lactate Pro Test Strips™ (HaB International Ltd, UK) and assessed based on the amperometric titration method using a Lactate Pro™ analyser (via the potassium ferricyanide/lactate oxidase reaction). Capillary puncture was made with Accu-Chek Safe-T-Pro Plus disposable lancets (Roche Diagnostics, Lewes, UK). Samples were collected in a temperature controlled laboratory at 21°C immediately after completion of exercise, after recording of FS and RPE. Coefficient of variation values between 2.8% and

5.0% have been reported for the Lactate Pro™, which is an acceptable level of reproducibility (Baldari *et al*., 2009).

7.3.4 Statistical analyses

Statistical analyses were carried out using IBM SPSS Statistics version 22 (IBM, Armonk, USA) with the criterion for statistical significance set at $p < 0.05$. Before analyses, data were explored to check assumptions of statistical tests. Normality of data and identification of potential outliers were assessed via visual inspection using histograms and box plots, in addition to a Shapiro-Wilk normality test which is considered the preferable method for a sample size < 50 (Ghasemi & Zahediasl, 2012). Data were then analysed in two phases. The first phase included descriptive analysis of the sample and a factorial (two-way, condition [3]-by-time [4]) repeated measures analysis of variance (RMANOVA) for FS and RPE. The sphericity assumption was checked using Mauchly's test, with Greenhouse-Geisser (denoted $_{GG)}$ correction applied to the degrees of freedom when this was violated. Significant main effects were considered using *post-hoc* Bonferroni-corrected pairwise comparisons. In addition, a series of one-way RMANOVA's were conducted to examine differences in enjoyment, blood lactate, and total work performed. Effect sizes were quantified using the partial eta squared (η^2) statistic to examine the magnitude of differences between the three exercise conditions, with values of 0.1, 0.3, and > 0.5 considered to be a small, medium, and large effect, respectively. Furthermore, prior to carrying out the RMANOVA, possible covariates (age and mass) and factors (gender) – that were not part of the main experimental manipulation but could influence the dependent variable – were included in a preliminary ANOVA analysis to check for independence of the predictor variable, and were found to be non-significant. The second phase used separate one-way RMANOVA to assess differences in FS and RPE for the three exercise conditions for each time point (i.e. 25%, 50%, 75%, and 100% of bout completion). For *post-hoc* analyses, familywise error rate was controlled using Bonferroni corrections by adjusting the level of significance for each test such that the overall type 1 error rate (alpha) across all comparisons remained at 0.05. Mean differences and pooled standard deviation were used to calculate Cohen's *d* to indicate the magnitude of differences between two specific conditions (Cohen, 1992), interpreted using a modified scale proposed to better define the thresholds for moderate and large effects: 0.0–0.19 'trivial', 0.2–0.59 'small', 0.6–1.19 'moderate', 1.2–1.99 'large' and > 2.0 'very large' (Hopkins, 2016).

7.4 Results

7.4.1 Descriptive data

All participants completed all three conditions (no dropouts) and undertook each one as allocated. Outcome measures were obtained from all participants for FS, RPE, EES, and total work. For blood lactate, it was not possible to record a value, due to equipment or measurement error, in four instances (11% of participants). Several adverse events, defined as any untoward occurrence that happened during the conduct of the study, were reported. Seven incidences of mild to moderate nausea or light headedness were reported for REHIT, five for shortened-sprint REHIT, and three for SCT. Additionally, two participants vomited following REHIT and one participant vomited after shortened-sprint REHIT. There were no instances of syncope or musculoskeletal injuries in response to any of the conditions. All adverse events were classified as not serious.

7.4.2 Affect (pleasure-displeasure)

Mauchly's test indicated that the assumption of sphericity was violated for the main effect of Time, $\chi^2(5) = 35.51$, $p = 0.01$, and for the interaction effect, $\chi^2(20) = 40.28$, $p = 0.01$. Therefore, degrees of freedom were corrected using Greenhouse-Geisser estimates of sphericity ($\varepsilon = 0.73$ for the main effect of Time and 0.76 for the interaction effect). A factorial, 3 (Conditions) by 4 (Time: 25%, 50%, 75%, 100% of bout duration) repeated-measures ANOVA on FS showed a significant main effect of Condition, $F(2, 70) = 54.66$, $p = 0.01$, $\eta^2 = 0.61$. *Post-hoc* tests revealed FS to be significantly lower (greater displeasure) during traditional REHIT and SCT compared to shortened-sprint REHIT (both $p = 0.001$), in addition to FS being lower for SCT compared to traditional REHIT ($p = 0.005$) (Figure 7.2). There was also a main effect of Time, $F(2.2, 77.08) = 197.29$, $p = 0.01_{GG}$, $\eta^2 = 0.85$. *Post-hoc* tests showed that FS was significantly lower at all time points compared to the first time-point (25% of bout duration, taken towards the end of the warm-up) (all $p = 0.001$). A quadratic trend was apparent, whereby FS decreased at 50% and 75% of bout duration compared to the previous time points (both $p = 0.001$), but then did not change at 100% of bout duration (after completion of the cool down) ($p = 0.541$). FS ratings declined during the bouts in all three conditions, but the decrease was larger in the traditional REHIT and SCT conditions compared to shortened-sprint REHIT (at 50%, 75%, and 100% of bout duration, all $p = 0.001$). Peak FS occurred at 75% of bout duration for all three conditions with values of 1.4 ± 1.7 ('fairly good'), -0.2 ± 1.9 (near 'neutral') and -0.9 ±

1.5 (‘fairly bad’) reported for shortened-sprint REHIT, traditional REHIT and SCT, respectively. Additionally, SCT was less pleasurable compared to traditional REHIT at 75% (p = 0.03) and 100% (p = 0.02), but not at 50% (p = 0.51) of bout completion. There was also a significant Condition × Time interaction effect, $F(4.57, 159.91) = 12.55$, $p = 0.01_{GG}$, $\eta^2 = 0.26$. This indicates that the condition had different effects on FS depending on the time point (% bout completion). Looking at Figure 7.2, steeper slopes of change were evident for REHIT and SCT compared to shortened-sprint REHIT. These data are summarised in table 7.1.

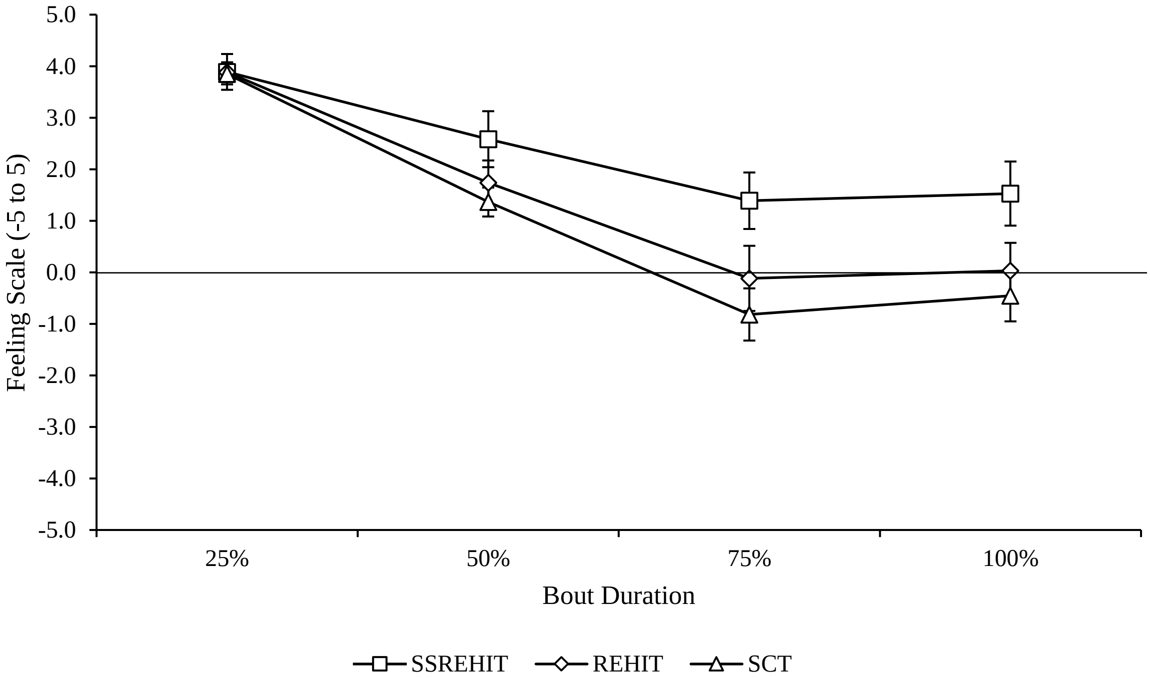

Figure 7.2 Feeling Scale (FS) responses during the three low-volume, high-intensity training conditions. Abbreviations: REHIT = reduced-exertion, high-intensity interval training, SCT = sprint continuous training, SSREHIT = shortened-sprint, reduced-exertion, high-intensity interval training. Note: Data are presented as mean ± 95% confidence intervals.

7.4.3 Rating of perceived exertion

Mauchly’s test indicated that the assumption of sphericity was violated for the main effect of Time, $\chi^2(5) = 25.92$, $p = 0.01$, and for the interaction effect, $\chi^2(20) = 52.96$, $p = 0.01$. Therefore, degrees of freedom were corrected using Greenhouse-Geisser estimates of sphericity ($\varepsilon = 0.76$ for the main effect of Time and 0.68 for the interaction effect). A factorial, 3 (Conditions) by 4 (Time: 25%, 50%, 75%, 100% of bout duration) repeated-measures ANOVA on RPE showed a significant main effect of Condition, $F(2, 70) = 33.02$, $p = 0.01$, $\eta^2 = 0.46$. *Post-hoc* tests revealed RPE to be significantly higher during traditional REHIT and SCT compared to shortened-sprint REHIT (both $p = 0.001$), in addition to RPE being higher for SCT compared to traditional REHIT (p = 0.40). There was also a main effect of Time, $F(2.27, 79.44) = 307.89$, $p = 0.01_{GG}$, $\eta^2 = 0.90$. *Post-hoc* tests showed a quadratic trend whereby RPE increased at 50% and 75% of bout duration compared to the previous time points, and then decreased at 100% of bout duration (all p = 0.001). Peak RPE occurred at 75% of bout duration for all three conditions with values of 13.9 ± 1.5 ('somewhat hard'), 15.5 ± 1.7 ('hard') and 16.4 ± 1.6 (nearly 'very hard') reported for shortened-sprint REHIT, traditional REHIT and SCT, respectively. Shortened-sprint REHIT was perceived to be less strenuous than traditional REHIT and SCT at 50%, 75%, and 100% of bout duration (all $p < 0.05$). Additionally, traditional REHIT was less strenuous compared to SCT at 75% of bout completion (p = 0.01), but not at other time points. There was also a significant Condition × Time interaction effect, $F(4.01, 143.09) = 10.31$, $p = 0.01_{GG}$, $\eta^2 = 0.23$. This indicates that the condition had different effects on RPE depending on the time point (% bout completion). Looking at the Figure 7.3, the increase in RPE was steeper for traditional REHIT and SCT than for shortened-sprint REHIT. These data are summarised in table 7.1.

Table 7.1 Comparison of outcome measures for the three low-volume, high-intensity training conditions.

	SSREHIT	REHIT	SCT	SSREHIT vs REHIT		SSREHIT vs SCT		REHIT vs SCT	
				P =	*d =*	*P =*	*d =*	*P =*	*d =*
FS									
25%	3.9 ± 1.1	3.9 ± 0.6	3.8 ± 0.6	NS	0	NS	0.11	NS	0.17
50%	2.6 ± 1.7*^	1.7 ± 1.3ᶲ	1.4 ± 0.9ᶲ	0.01	0.59	0.01	0.88	0.51	0.27
75%	1.4 ± 1.7*^	-0.1 ± 1.9^ᶲ	-0.8 ± 1.6*ᶲ	0.01	0.83	0.01	1.15	0.03	-0.55
100%	1.5 ± 1.9*^	0 ± 1.7^ᶲ	-0.5 ± 1.5*ᶲ	0.01_{GG}	0.83	0.01_{GG}	1.17	0.02_{GG}	0.31
Average	2.3 ± 1.2	1.4 ± 1.9	1 ± 2.1	-	-	-	-	-	-
RPE									
25%	7.9 ± 1.1	8.3 ± 1.7	7.9 ± 1	NS	-0.28	NS	0	NS	0.29
50%	12 ± 1.7*^	12.6 ± 1.8ᶲ	13.5 ± 1.5*ᶲ	0.04	-0.34	0.01	-0.94	0.4	-0.54
75%	13.9 ± 1.5*^	15.5 ± 1.7^ᶲ	16.4 ± 1.6*ᶲ	0.01	-1	0.01	-1.61	0.01	-0.55
100%	12.1 ± 2*^	13.2 ± 2.1ᶲ	13.5 ± 2.3*ᶲ	0.01	-0.11	0.01	-0.23	0.49	-0.12
Average	11.5 ± 2.5	12.4 ± 3	12.8 ± 3.6	-	-	-	-	-	-
EES	5.2 ± 1.1*^	4.2 ± 1.4^ᶲ	3.4 ± 1.3*ᶲ	0.01	0.79	0.01	1.49	0.01	0.59
Blood Lactate (mmol/L^{-1})	13.1 ± 3.5	13.5 ± 3.5	13 ± 3.2	NS	-0.11	NS	0.03	NS	0.15
Total Work (kJ)	507.2 ± 66.6*^	470.4 ± 71.2^ᶲ	438.5 ± 64.9*ᶲ	0.01	0.53	0.01	1.04	0.01	0.47

Note: Data are presented as mean ± standard deviations.
* Statistically significant in comparison to REHIT ($p < 0.05$)
^ Statistically significant in comparison to SCT ($p < 0.05$)
ᶲ Statistically significant in comparison to SSREHIT ($p < 0.05$)
Abbreviations: EES = exercise enjoyment scale, FS = Feeling Scale, GG = Greenhouse-Geisser, NS = not statistically significant, REHIT = reduced-exertion, high-intensity interval training, RPE = rating of perceived exertion, SCT = sprint continuous training, SSREHIT = shortened-sprint, reduced-exertion, high-intensity interval training

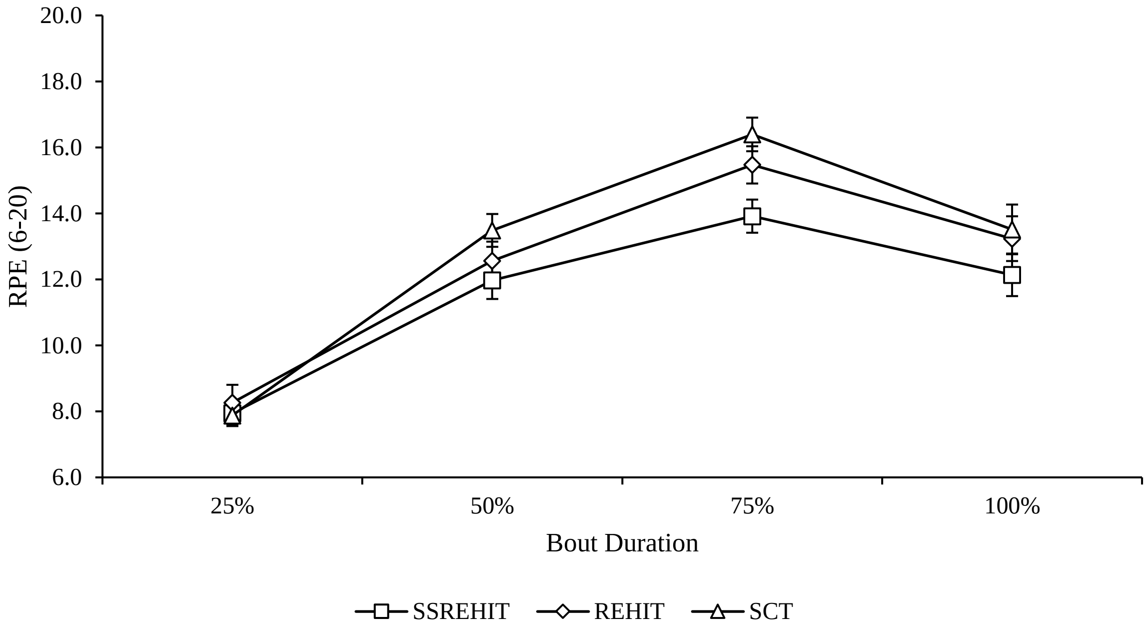

Figure 7.3 Rating of Perceived Exertion (RPE) responses during the three low-volume, high-intensity training conditions. Abbreviations: REHIT = reduced-exertion, high-intensity interval training, RPE = Rating of Perceived Exertion, SCT = sprint continuous training, SSREHIT = shortened-sprint, reduced-exertion, high-intensity interval training. Note: Data are presented as mean ± 95% confidence intervals.

7.4.4 Enjoyment

A one-way, RMANOVA revealed a statistically significant main effect between the conditions for enjoyment, $F(2, 70) = 73.12$, $p = 0.01$, $\eta^2 = 0.68$. *Post-hoc* tests showed EES ratings were significantly higher for shortened-sprint REHIT (5.2 ± 1.1, 'quite a bit') compared to traditional REHIT (4.2 ± 1.4, 'moderately', $p = 0.001$, $d = 0.79$) and SCT (3.4 ± 1.3, 'slightly', $p = 0.001$, $d = 1.49$), and that ratings were also significantly higher for traditional REHIT compared to SCT ($p = 0.001$, $d = 0.59$) (Figure 7.4).

7.4.5 Blood lactate

A one-way, RMANOVA revealed no statistically significant main effect between the conditions for post-exercise blood lactate, $F(1.64, 57.22) = 0.46$, $p = 0.595$, $\eta^2 = 0.01$. Blood lactate values were 13.1 ± 3.5, 13.5 ± 3.5, and 13 ± 3.2 $mmol \cdot L^{-1}$ for shortened-sprint REHIT, traditional REHIT and SCT, respectively.

7.4.6 Total work

A one-way, RMANOVA revealed a statistically significant main effect between the conditions for total work performed, $F(2, 68) = 43.16$, $p = 0.01$, $\eta^2 = 0.73$. *Post-hoc* tests showed total work completed was significantly higher for shortened-sprint REHIT (511.4 ± 62.5 kJ) compared to traditional REHIT (473.8 ± 72.9 kJ, $p = 0.001$, $d = 0.53$) and SCT (448.4 ± 64.3, $p = 0.001$, $d = 1.04$), and that total work was also significantly higher for traditional REHIT compared to SCT ($p = 0.002$, $d = 0.47$) (Figure 7.5).

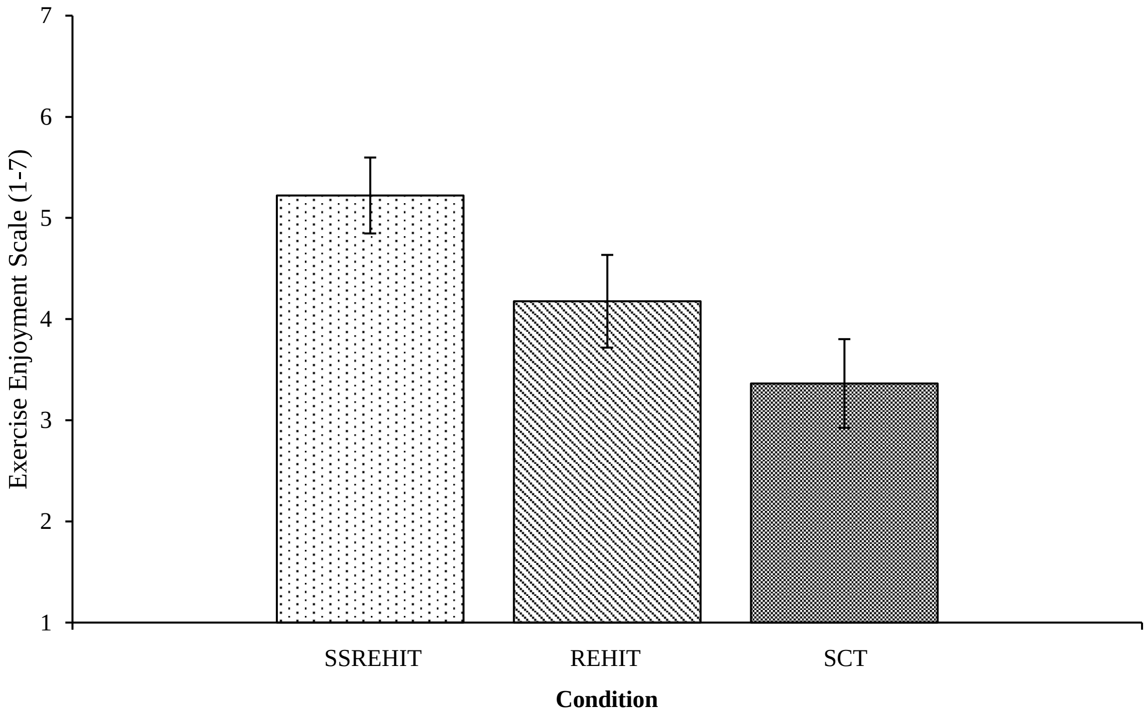

Figure 7.4 Enjoyment responses after the three low-volume, high-intensity training conditions. Abbreviations: REHIT = reduced-exertion, high-intensity interval training, SCT = sprint continuous training, SSREHIT = shortened-sprint, reduced-exertion, high-intensity interval training. Note: Data are presented as mean ± 95% confidence intervals.

7.5 Discussion

The premise for advocating HIT as a means of achieving a more active lifestyle is predicated on the assumption that avoiding the most commonly cited barrier to exercise – lack of time – will lead to greater exercise adherence. However, the intensity of this type of exercise could similarly discourage participation if it is deemed overly strenuous. The aim of the current research was to investigate perceptual responses to low-volume, high-intensity exercise including REHIT, which is focussed on the minimal amount of exercise that can convey health benefits. Fundamentally, whether this exercise can be shown to be efficacious and safe, yet at the same time appealing, tolerable, and sustainable will be decisive in terms of its effectiveness in real-world settings and as a public health strategy (Decker & Ekkekakis, 2017). Although some research has considered perceptual responses to traditional higher-volume HIT, there is limited data on affective response to low-volume HIT or REHIT. As such, this is the first study to empirically compare affective responses during three different low-volume, high-intensity exercise conditions.

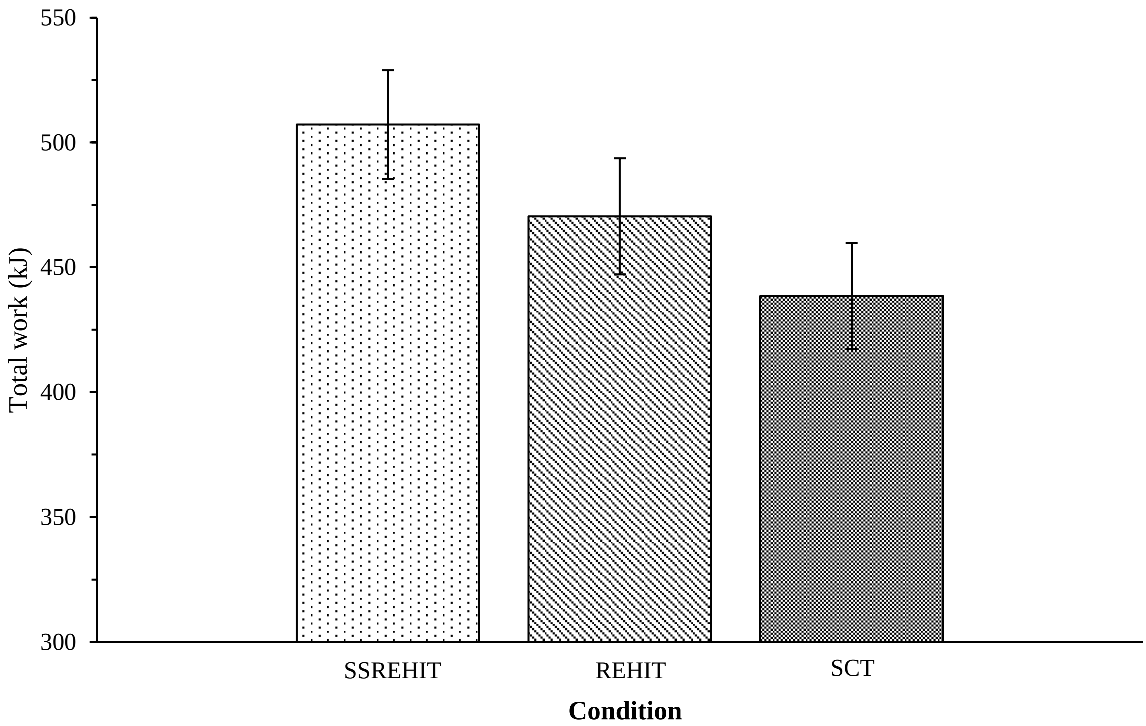

Figure 7.5 Total work performed for the three low-volume, high-intensity training conditions. Abbreviations: REHIT = reduced-exertion, high-intensity interval training, SCT = sprint continuous training, SSREHIT = shortened-sprint, reduced-exertion, high-intensity interval training. Note: Data are presented as mean ± 95% confidence intervals.

The main finding of this study was that shortened-sprint REHIT was more enjoyable, with lower perceived exertion, and more favourable affective responses compared to traditional REHIT and SCT. Although affective responses decreased throughout all conditions (i.e. diminishing pleasure over time), the slopes of change were steeper during traditional REHIT and SCT, illustrated by significant and meaningful Condition × Time interactions for FS (p = 0.01_{GG}, $\eta^2 = 0.26$, Figure 7.2). Similarly, the increase in RPE was sharper during REHIT and SCT than for shortened-sprint REHIT ($p = 0.01_{GG}$, $\eta^2 = 0.23$), particularly between 25%, 50% and 75% of bout completion for SCT, and between 50% and 75% of bout completion for REHIT (Figure 7.3). These data provide preliminary evidence to suggest that shorter intervals do not compromise perceptual response to the same degree as longer intervals, and therefore could reduce the likelihood of REHIT evoking a high degree of negative affect, which could in-turn improve exercise adherence. Shortened-sprint REHIT and traditional REHIT conditions were matched in terms of the total time spent completing high-intensity exercise (i.e. 40 s; 8 × 5 s vs 2 × 20 s, respectively), yet despite the reduced recovery time between bouts, both FS and RPE were more favourable at 50%, 75%, and 100% of bout completion for shortened-sprint REHIT. This suggests perception is related to the duration of muscle action to external force during high-intensity sprints, rather than the number of high-intensity sprints per se.

Affective valence is an important part of the exercise experience as pleasure-displeasure responses may predict future engagement with that exercise. The dual-mode theory has been used to describe the affective response to *continuous* exercise, where intensities above the ventilatory threshold are accompanied by a cascade of biochemical, neuroendocrine, autonomic, cardiovascular, and respiratory changes that dramatically challenge maintenance of homeostasis (Ekkekakis *et al*., 2008). Recent research has started to consider responses to intermittent exercise including HIT (Jung *et al*., 2014; Kilpatrick *et al*., 2015, Martinez *et al*., 2015; Decker & Ekkekakis, 2017). However, the present study is the first-time affective responses have been considered for low-volume, HIT. The mean FS response for shortened-sprint REHIT was 2.3 ± 1.2 units, which was higher than for traditional REHIT (1.4 ± 1.9) and SCT (1 ± 2.1). This value is also higher than those reported for higher-volume HIT in the studies of Kilpatrick *et al*. (2015) and Decker & Ekkekakis (2017). Indeed, the FS responses recorded for shortened-sprint REHIT in the present study were more like the responses for moderate-intensity continuous exercise in these two studies. However, average responses for affect may be misleading as the periods of low-intensity recovery may disguise in-task peaks associated with the high-intensity bouts of exercise. Peak FS values for higher-volume HIT have been reported as slightly below zero, where 0 is ‘neutral’ and -1 is ‘fairly bad’ (i.e. Jung *et al*., 2014; Decker & Ekkekakis, 2017). Others have reported peak FS values in the region of 2 to 3, where 3 is ‘good’ and 5 is ‘very good’ (i.e. Kilpatrick *et al*., 2015; Martinez *et al*., 2015). These differences are likely to be consequential, and caused by the differing protocols that have been used in terms of intensity, frequency, and duration of bouts; in addition to the time at which affective responses were recorded.

In the current study, peak FS responses occurred at 75% of bout duration in all three conditions. However, pleasure remained significantly and meaningfully higher for shortened-sprint REHIT with a rating of 1.4 ± 1.7 FS units, compared to -0.1 ± 1.9 for traditional REHIT (p = 0.01, d =

0.83) and -0.8 ± 1.6 for SCT, respectively (p = 0.01, d = 1.15). Pleasure was also significantly and meaningfully higher for traditional REHIT compared to SCT (p = 0.03, d = -0.55). Referring to the verbal labels associated with these numerical ratings, affective response during shortened-sprint REHIT was 'fairly good', 'neutral' during traditional REHIT, and 'fairly bad' during SCT. It has been suggested that hedonicity (i.e. pleasure-displeasure) is an important signal for behaviour choices, and that minimising bi-dimensional displeasure is key to achieving optimal behaviour (Cabanac, 2006). Therefore, given that people typically choose not to engage in behaviours they find aversive, it seems likely that the specific SCT protocol used in this study would not be adhered to in the long-term by most people. However, the responses relating to perception of displeasure were minimised during shortened-sprint REHIT, so this may be a genuinely time-efficient and tolerable approach to exercise and a viable alternative to current exercise guidelines. Despite the difference in affective response, there was no difference in mean blood lactate concentrations across the three conditions.

Several studies have recorded RPE following REHIT. In their original study, Metcalfe and colleagues (2011) reported improvements in $\dot{V}O_{2max}$ in healthy but sedentary participants despite modest required effort, with RPE values of 13 ± 1 ('somewhat hard'). Using the same protocol, Haines (2015) observed higher mean RPE ratings (17 ± 1, 'very hard') in recreationally active participants. It is not clear why more active participants should perceive REHIT to be harder, although a plausible explanation is that they could achieve higher levels of anaerobic substrate phosphorylation resulting in greater fatigue and thus higher perceived effort. More recently, other studies have reported REHIT sessions to be well tolerated with RPE values of 14 ± 2 in sedentary men and women (Metcalfe *et al*., 2016b), and 13.6 ± 1.1 in men with type 2 diabetes (Ruffino *et al*., 2016). However, in all these studies RPE was collected at the end of training sessions with participants asked to retrospectively consider effort for the whole training session, not just the high-intensity bouts. It is reasonable to expect perceptual response *during* REHIT to be very different, because there is a general shift in affective valence toward pleasure, regardless of intensity, after the cessation of exercise. Also, dose-response effects may occur during exercise and then dissipate before post-exercise measurements of affect are recorded (Ekkekakis, 2008). Furthermore, as highlighted by Decker & Ekkekakis (2017), the peak-end rule contests that memory associated with pleasure-displeasure responses are influenced by specific episodes: the moment a distinct 'peak' is experienced, and the 'end' of the activity – with the duration having little effect. As such, even if most of the time during REHIT is spent at a low-intensity, the high-intensity bouts could produce a negative affective peak of which the magnitude could impact motivational factors related to future adherence. Therefore, to capture a more complete depiction of responses, measurements were taken during exercise in the current study. As for FS, peak RPE occurred at 75% of bout completion in all conditions. RPE was significantly and meaningfully lower for shortened-sprint REHIT compared to traditional REHIT (and SCT.An assumption of dual-mode theory is that there exists a distinction between core affect, such as hedonistic pleasure or pain, and more distinct emotional experiences such as enjoyment that require cognitive appraisal and appreciation of the totality of the experience (Wankel, 1993; Russell & Barrett, 1999). Although affective valence and enjoyment overlap, they are not identical constructs. Nonetheless, they are both important perceptions in understanding the exercise experience (Martinez *et al*., 2015). Research has shown that enjoyment responses to HIT are similar or higher than those for moderate-intensity continuous exercise (Kilpatrick *et al*., 2015; Jung *et al*., 2015; Thum, Parsons, Whittle & Astorino, 2017). In contrast, the specific HIT protocols used by Oliveira *et al*. (2013) and Decker & Ekkekakis (2017) were deemed to be less enjoyable than moderate-intensity continuous exercise. In the current study, post-exercise enjoyment was statistically and meaningfully higher for shortened-sprint REHIT (5.2 ± 1.1 EES units, 'quite a bit') compared to traditional REHIT (4.2 ± 1.4, 'moderately', p = 0.01, d = 0.79), and SCT (3.4 ± 1.3, 'slightly', p = 0.01, d = 1.49). This is in-line with the findings of Martinez *et al*. (2015) who reported greater enjoyment for shorter intervals over longer ones. It remains speculative why high-intensity intermittent exercise can result in more favourable affective and enjoyment responses compared to continuous exercise. The nature of the activity may provide a succession of positive accomplishments as high-intensity bouts are completed; and breaking the activity into smaller bursts could make the activity appear more manageable or prevent monotony. Similarly, in the current study it is a plausible explanation that exposure to 5 s sprints during shortened-sprint REHIT was of insufficient duration to induce the physiological responses that are associated with more negative affective and enjoyment responses.

Although shortened-sprint REHIT elicits minimal displeasure, suggesting this protocol is tolerable, it remains to be seen if it can produce beneficial adaptations for health such as increased cardiovascular fitness. The least volume of exercise which has so far been shown to improve $\dot{V}O_{2max}$, is 40 s of high-intensity cycling per session (Metcalfe *et al*., 2011, 2016b) – as used in the REHIT condition in this study. The shortened-sprint REHIT protocol also used 40 s of high-intensity cycling, but divided into 5 s bursts. Some evidence and mechanistic reasoning suggest this shortened-sprint protocol could also improve fitness. To meet the extreme demands of maximal activity during HIT, energy is derived from phosphocreatine and the rapid onset of glycogenolysis (Margaria, Edwards & Dill, 1933; Jones *et al*., 1985). Glycogen is the primary substrate and is catalysed by the rate-limiting enzyme glycogen phosphorylase. Parolin *et al*. (1999) demonstrated that glycogen phosphorylase is rapidly activated within the first 6 s of maximal-intensity cycling, probably due to calcium ion release from the sarcoplasmic reticulum. Furthermore, Gibala (2017) has speculated that during HIT, it is the dramatic *rate* at which myocellular fuel stores are changing, not the total amount of fuel depletion that is the signal for a cascade of events which promote skeletal muscle remodelling. One of the signalling molecules involved in this process, 5'-adenosine monophosphate protein kinase (AMPK), is regulated by glycogen availability (McBride, Ghilagaber, Nikolaev & Hardie, 2009). Therefore, it is plausible that the first few seconds of the high-intensity bouts are particularly important, and by reducing the total duration of each one it may be possible to reduce accumulated fatigue which could avoid a reduction in the effectiveness of later bouts. The idea that the intensity, rather than the total volume, of high-intensity exercise is significant has received some empirical support. A meta-analysis of 34 studies concluded that improvement in $\dot{V}O_{2max}$ is not attenuated with fewer bouts of high-intensity exercise, and may possibly even be enhanced (Vollard, Metcalfe & Williams, 2017). Moreover, AMPK activation has been observed in response to a single 30 s cycle sprint (Guerra *et al*., 2010; Fuentes *et al*., 2012), and there is a dramatic decline in glycogenolytic rate after the first high-intensity sprint (Jones *et al*., 1985; Parolin *et al*. 1999) – both of which reinforce the idea that the quality of short sprints could be a key determinant of the training stimulus.

Several limitations should be considered alongside the findings of this study. The three exercise conditions were not work matched and this creates a confound that limits comparison between protocols. There was a significant difference between the total work completed for each condition and although this improves ecological validity, because participants had more flexibility and autonomy as they would in a real-world setting, it is possible that the magnitude of physiological adaptations in longer-term studies would be affected by total work performed. The lower total work for the SCT condition was expected given that the protocol was 2 min shorter than for the other conditions. Nevertheless, difference in total work is not likely to be the most salient consideration because a core principle of dual-mode theory is that intensity, not duration or work completed, drives the affective response (Kilpatrick, Kraemer, Bartholomew, Acevedo & Jarreau, 2007; Kilpatrick *et al*., 2015).

A further limitation relates to use of a Wattbike for the protocols in this study. Most HIT studies have used cycle ergometers that allow for a very rapid transition from unloaded pedalling to a high mechanical or electromagnetic braking force. Whyte *et al*. (2013) highlights it is this characteristic that permits generation of high peak power within the first few seconds of high-intensity intervals, and this may be required to elicit the metabolic benefits associated with HIT. Although the Wattbike upholds this feature and allows for pedalling against a braking force appropriate for peak power generation, the force is not specifically 7.5% of body mass as used in most HIT studies. This makes comparisons between studies more difficult, in an area of research where differences in study findings may already be obscured by methodological differences. Furthermore, it is not clear if general leisure facility bikes could be used to perform HIT as effectively.

Another limitation relates to the sample which was taken primarily from a convenient undergraduate student population. Although baseline fitness was not assessed, nor was a detailed evaluation of exercise history, the participants were both relatively young and more active than the general population. Indeed, they derived from a pool of interested sport and exercise science students, who may have knowledge of the hypotheses of the study which could have influenced their perceptual response to the exercise conditions. As such the findings from this study cannot be generalised to the wider population, particularly those who are sedentary or who have chronic disease. Future research should address perceptual response to shortened-sprint REHIT in these populations.

Finally, the REHIT protocols in this study were based on the protocols used by Metcalfe *et al*. (2011), but used high-intensity bout duration representative of what was used in the latter stages of this study. It is likely that perceptual response would be different if the total volume of high-intensity exercise was progressively built-up over several weeks. Again, further studies should address perceptual response to REHIT using longitudinal studies.

In summary, this study provides preliminary evidence to suggest that perceptual response to shortened-sprint REHIT, in terms of pleasure-displeasure, perceived effort, and enjoyment; was more favourable compared to traditional REHIT and SCT. Affective valence remained positive throughout exercise. By reducing the duration of the high-intensity sprints, it is possible that shortened-sprint REHIT could be a genuinely time-efficient, appealing, and tolerable form of exercise to combat the burden of physical inactivity. Moving forward, physiological adaptations to shortened-sprint REHIT should be addressed through longitudinal research to see if such approaches could confer the same health benefits of higher-volume HIT. A key challenge remains to translate current evidence to practical approaches that are both tolerable and time-efficient in real-world settings.

Chapter 8 Study 2: Shortened-sprint REHIT, $\dot{V}O_{2max}$ and affect

Elements of this chapter will be presented at the BASES Annual Conference 2017, and the content has been submitted for publication in the *Journal of Science and Medicine in Sport*.

The effects of a shortened-sprint, reduced-exertion, high-intensity interval training (REHIT) protocol on peak oxygen uptake and peak affective response

8.1 Abstract

The minimum amount of exercise that has been shown to improve peak oxygen uptake ($\dot{V}O_{2peak}$) is REHIT incorporating two 20 s maximal exertion cycle sprints within a 10-min exercise session (Metcalfe *et al*., 2011). However, hedonistic theories of motivation propose that exercise above a certain intensity threshold results in physiological responses that negatively influence affective valence (i.e. increasing sensations of displeasure). This could lead to avoidance of the activity and poor exercise adherence. Given that sensation of exertion is a function of intensity and duration, it is plausible that reducing the time spent 'sprinting' may attenuate any negative affect associated with periods of high-intensity exercise. Accordingly, the aims of this study were to investigate affective response to a novel, shortened sprint REHIT protocol; and to test the effect of this protocol on $\dot{V}O_{2peak}$. With institutional ethics approval, 24 men (age 21.2 ± 1.9 years; mass, 80.2 ± 6.8 kg; BMI, 25.5 ± 1.8 kg·m^2) were randomly assigned to one of two conditions: 1) shortened-sprint REHIT (8 × 5 s sprints), or 2) traditional REHIT (2 × 20 s sprints). Participants completed 15 exercise sessions over a 5–7-week period, with $\dot{V}O_{2peak}$ determined using a ramp cycling test pre- and post-intervention. Affect and rating of perceived exertion (RPE) were measured during exercise using the Feeling Scale (FS) and the 15-point Borg scale, respectively. Enjoyment was recorded 5-min after cessation of activity using the Exercise Enjoyment Scale. Factorial (condition × time) mixed ANOVA's were used to compare differences between groups. Affective valence was more favourable for shortened sprint REHIT compared to traditional REHIT (1.6 ± 0.6 vs 0.2 ± 1 FS units, respectively; where 1 is 'fairly good' and 0 is 'neutral'; p = 0.001, d = 1.62). Similarly, peak RPE values were lower for shortened-sprint REHIT (14.4 ± 0.9 vs 16.2 ± 1.1, p = 0.001, d = -1.71). However, there was no difference in enjoyment. Compared to baseline, $\dot{V}O_{2peak}$ increased in both groups (6% for shortened sprint REHIT [d = -0.36] and 9% for traditional REHIT [d = -0.53], both p = 0.01), although there was considerable heterogeneity in training response within each group. The results suggest both conditions improve fitness without overly

compromising cognitive and affective response, and as such may be genuinely time-efficient yet tolerable approaches to exercise. The challenge of translating this research into real-world practice remains.

8.2 Introduction

The idea that our biology works best at relatively high levels of physical activity is not new (Mayer, Purnima, & Mitra, 1956). Indeed, regular skeletal muscle action might be an integral requirement for normal genotypic expression and good health (Booth *et al*., 2002a), hence regular physical activity and structured exercise are established preventative and therapeutic adjuncts in the management of several chronic diseases. However, a significant challenge to prescribing exercise relates to poor adherence which is typically reported at between 40% and 50%, or lower in patients with chronic disease (Hallal *et al*., 2012; Qiu, Sun, Cai, Liu & Yang, 2012). Perceived lack of time is the most commonly cited internal barrier to exercise (Reichart, Barros, Dominigues & Hallal, 2007; Korkiakangas, Alahuhta & Laitinen, 2009) and conflicts with current guidelines for health which promote relatively high volumes of continuous moderate-to-vigorous intensity exercise (e.g. Haskell *et al*., 2007; O'Donovan *et al*., 2010). Therefore, the challenge of encouraging individuals and populations to engage in more physical activity remains.

Recent research on the benefits and efficacy of low-volume, high-intensity interval training (HIT) may help to overcome this barrier. HIT is characterised by brief periods of repeated high-intensity, or 'all-out', intervals of exercise interspersed with longer periods of recovery, and is considered more time-efficient than traditional exercise strategies. However, claims relating to time-efficiency are disputed because some iterations of HIT do not require appreciably less time to complete than conventional physical activity programmes (e.g. Whyte *et al*., 2013) – imposed by the inclusion of a warm-up, periods of rest in-between high-intensity intervals, and a cool down. Further concerns have been raised about the likelihood of high-intensity exercise evoking a high degree of negative affect, or displeasure, which may in-turn lead to an avoidant response and poor exercise adherence (Hardcastle, Ray, Beale & Hagger, 2014). Thus, a growing trend in HIT research is to explore the minimal amount of exercise that is required to improve health in a genuinely time-efficient and tolerable manner (Gaesser & Angadi, 2011; Freese *et al*., 2014; Kilpatrick *et al*., 2015; Vollard & Metcalfe, 2017).

Metcalfe and colleagues developed a reduced-exertion HIT (REHIT) protocol with the aims of being more time-efficient, less strenuous, and more applicable to an inactivepopulation

(Metcalfe *et al*., 2011; Metcalfe *et al*., 2016b). This protocol requires a total of 10 min cycling, inclusive of a warm-up and cool down, and comprises 2 × 10–20-s cycle sprints against a braking force equivalent to 5%–7.5% of body mass, performed three times per week over a 6-week period. In these studies, although changes in insulin sensitivity were equivocal, cardiovascular fitness (measured as $\dot{V}O_{2peak}$) improved by 10–15%, which is consistent with more conventional HIT (e.g. Rakobowchuk *et al*., 2008; Heydari *et al*., 2012; Matsuo *et al*., 2013). Increased mitochondria biogenesis and markers of oxidative capacity such as citrate synthase, via activation of adaptive cellular signalling pathways and increases in peroxisome proliferator-activated receptor-γ coactivator (PGC)-1α gene expression, may explain this adaptation – once considered exclusive to aerobic exercise (Gillen *et al*. 2014; Metcalfe *et al*., 2015). This is clinically important since cardiovascular fitness, or $\dot{V}O_{2max}$, is a powerful predictor of morbidity and mortality. A series of large scale observational studies demonstrate a protective effect of fitness on cardiovascular disease and all-cause mortality, even when other predictors of mortality such as dyslipidaemia are present (Blair *et al*., 1995; Blair *et al*. 1996; Sui, Laditka, Hardin & Blair, 2007a). Similar studies have demonstrated a protective effect of fitness in populations with diabetes, obesity, and hypertension (Church, LaMonte, Barlow & Blair, 2005; Sui, LaMonte & Blair, 2007b, Sui *et al*., 2007c). Attributable fractions – which depend on the strength of association between an exposure and an outcome, and on the prevalence of that risk factor in the population – estimate that low cardiorespiratory fitness accounts for substantially more deaths than obesity, diabetes, and dyslipidaemia (Blair, 2009). Fitness is more closely linked with all-cause mortality than the overall volume of exercise (Lee *et al*., 2005; Lee *et al*., 2011; Ross *et al*., 2016). Thus, the potential for REHIT to induce rapid improvements in $\dot{V}O_{2max}$ in a genuinely time-efficient manner is valuable if protocols can be adopted by the general population.

Whether REHIT is acceptable, accessible, and tolerable for those for whom it is intended is an utmost consideration. Currently, there is a dearth of research on the perceptual response to REHIT, so it is not known if such protocols are appropriate for sedentary or clinical populations. Ratings of perceived exertion (RPE) have been collected in response to REHIT in a small number of studies and have generally been rated between 'somewhat hard' and 'hard' (i.e. ~14 on the 15-point Borg scale) using sedentary but healthy men and women (Metcalfe *et al*., 2011; 2016b), and men with type 2 diabetes (Ruffino *et al*., 2016). However, using the same protocol, Haines (2015) observed higher mean RPE ratings (17 ± 1, 'very hard') in recreationally active participants. It is not clear why more active participants should perceive

REHIT to be harder, although it is possible that they could achieve higher levels of anaerobic substrate phosphorylation resulting in greater fatigue and hence higher perceived effort. It is important to note that RPE was measured after completion of REHIT in these studies, and that perceptual response *during* the exercise bout could be very different. The peak-end rule contests that memory associated with affective valence (pleasure or displeasure) of exercise is influenced by two specific episodes: the moment a distinct 'peak' affective response is experienced, and the 'end' of activity (Redelmeirer & Kahneman, 1996; Kahneman, 1999; Fredrickson, 2000; Ekkekakis, 2008). During REHIT the peak moment could relate to displeasure associated with the time, albeit minimal, spent completing high-intensity exercise and could influence retrospective evaluations of that activity. To capture a more complete depiction of affective responses, measurements should be taken throughout exercise. Other hedonic theories of motivation – such as dual-mode theory (Ekkekakis, Hall & Petruzzello, 2005) – have been applied to more strenuous HIT (e.g. Freese *et al*., 2014; Jung *et al*., 2014, Kilpatrick, Greely & Collins, 2015; Decker & Ekkekakis, 2017), and have been used to question the likely adoption of this type of exercise in public health settings (Hardcastle, Ray, Beale & Hagger, 2014). Accordingly, there is a need to consider these assumptions with REHIT.

The sensations of exertion and affect in response to exercise depend on the type of work performed by skeletal muscle and resistance to external force (Cafarelli, 1982; Cabanac, 2006). When the work is extended over time however, the sensation of the exertion becomes a function of duration (Cafarelli, Cain & Stevens, 1977). If hedonicity is an important signal for behaviour optimisation, these considerations highlight the importance of dose-response for approaches to REHIT that aim to maximise physiological benefit without overly compromising perceptual response. Attempts to minimise any negative affect associated with periods of high-intensity exercise will be important, and one practicable method of achieving this is to lower the duration of the high-intensity sprints. Therefore, in the present study a shortened-sprint REHIT protocol was used with the sprints reduced to 5 seconds, compared to 20 seconds for traditional REHIT. However, the overall time spent completing high-intensity work was matched to that of Metcalfe and colleagues (i.e. 40 s; Metcalfe *et al*., 2011, 2016b). In theory, such an approach could be beneficial as the adaptations associated with HIT may be explained, in part, by rapid glycogen depletion which is limited to ~15 s of the initial sprints (Parolin *et al*., 1999), meaning that protocols with shorter sprints could be just as effective (Metcalfe *et al*., 2015). Preliminary data suggests that a single bout of this shortened-sprint REHIT protocol is associated with a more favourable perceptual response, that is less displeasure, compared to traditional REHIT (Chapter 7). However, it is not known if shortened-sprint REHIT attenuates improvements in $\dot{V}O_{2peak}$, or how perceptual responses change over time. Therefore, the aims of the current study were twofold: 1) to test the effects of shortened-sprint REHIT on $\dot{V}O_{2peak}$, and 2) to measure perceptual response to REHIT across a 5–7-week intervention.

8.3 Methods

8.3.1 Participants and experimental approach

Participants were recruited through emails and word of mouth at the University of Huddersfield. All participants were students, recreationally active, and apparently healthy determined as per the General Methods outlined in section 6.3.1 (pp. 118).

A convenience sample of 24 men (age 21.2 ± 1.9 years; stature, 1.8 ± 0.1 m; mass, 80.2 ± 6.8 kg; BMI, 25.5 ± 1.8 kg·m^2) agreed to take part in the research. Participants were informed of the benefits and risks of the research prior to signing an informed consent form, before random assignment (via a random number generator) to one of two exercise intervention groups: 1) traditional REHIT (n = 12), or 2) shortened-sprint REHIT (n =12). The first visit to the laboratory involved study familiarisation and baseline measurement of peak oxygen uptake ($\dot{V}O_{2peak}$) and fat mass. Within one week of the baseline testing session participants commenced the intervention. Baseline measures were repeated post-intervention within one week of completing the intervention. Participants were encouraged to continue consuming their normal diet and to maintain normal physical activity levels throughout the study period. However, diet and physical activity were not monitored. Allocation concealment and blinding of assessors who measured outcome measures were not possible. This study was conducted in accordance with the guidelines proposed in the Declaration of Helsinki, with ethical approval to carry out the study obtained by the University of Huddersfield, School of Human and Health Sciences, School Research Ethics Panel.

8.3.2 REHIT procedures

Participants were required to partake in a total of 15 sessions of REHIT or shortened-sprint REHIT. They were permitted to achieve this by completing two or three sessions per week until the target had been accomplished. Thus, the intervention lasted 5–7 weeks dependent on the frequency of sessions per week. This flexibility within the study design was used to aid compliance with the programme, and to more closely mimic how REHIT might be used in a real-life setting. All exercise sessions were performed as per the General Methods (section 6.3.2, pp. 118).

Instructions on how to carry out each REHIT protocol were communicated before and during each session, with standardised verbal encouragement and feedback used throughout the high-intensity periods of exercise to ensure maximal effort. The two conditions in this study were not work matched (kJ), but were matched in terms of duration of warm-up, total duration, and total time spent completing high-intensity exercise (cycle sprints). Heart rate was not monitored because the purpose of REHIT is to be time-efficient and convenient, and it was deemed that attaching heart rate monitors would negatively impact this feature. However, participants remained in the laboratory for at least 5 min post-exercise for monitoring of adverse events.

Traditional REHIT

Traditional REHIT was performed in-line with Metcalfe *et al*. (2011) and consisted a total of 10 minutes cycling, inclusive of one (first session only) or two (all other sessions) maximal effort 'sprints' against a braking force appropriate for peak power generation. The duration of the sprints increased from 10 s for sessions 1 to 3; to 15 s for sessions 4 to 7; and to 20 s for sessions 8 to 15. Exercise intensity in-between sprints was low (~60 W). The 10 minutes of cycling was also inclusive of a warm-up (3 min at ~60 W) and cool down (3 min at ~30-60 W). A schematic overview of the REHIT protocol can be seen in Figure 8.1.

Shortened-sprint REHIT

Shortened-sprint REHIT was designed to match the traditional REHIT protocol in terms of the total time spent doing high-intensity exercise. However, with the aim of reducing the perceptual response associated with prolonged maximal efforts, this time was broken up into shorter periods. Therefore, participants performed a total of 10 minutes cycling, inclusive of 2 (first session only), 4 (sessions 2 and 3), 6 (sessions 4 to 7), or 8 (sessions 8 to 15) × 5 s maximal effort 'sprints' against a braking force appropriate for peak power generation. Again, exercise intensities in-between sprints were low (~60 W), and a warm-up (3 min at ~60 W) and cool down (2 min at ~30-60 W) were included within the 10-minute session (Figure 8.2).

8.3.3 Measures

Peak oxygen uptake ($\dot{V}O_{2peak}$)

$\dot{V}O_{2peak}$ was designated the primary outcome measure and was determined using a ramp cycling test (expressed in relative terms per minute). Participants cycled on a magnetically braked ergometer (Ergomedic 839E Digital, Monark, Vansbro, Sweden) starting at 20 W, with required power to continue cycling increased by 15 W every 1 min thereafter, until volitional exhaustion or until a pedal cadence of 50–60 rpm could not be maintained. The Monark 839E ergometer provides for a constant rate of work independent of pedal cadence, however this lower threshold was set to avoid over-exertion. Participants respired through a face mask connected via a sample line and volume transducer to an online gas analysis system (Metamax 3B, Cortex, Leipzig, Germany). Respiratory volume, expired oxygen and carbon dioxide, and respiratory exchange ratio were measured with $\dot{V}O_{2peak}$ taken as the highest value averaged over 10 s periods. Several additional criteria were considered to establish if $\dot{V}O_{2peak}$ had been reached: an observed plateau in the oxygen uptake curve, a respiratory exchange ratio of 1.15 or higher, and a Rating of Perceived of Exertion (RPE) of 19-20 on the Borg scale (Borg, 1982).

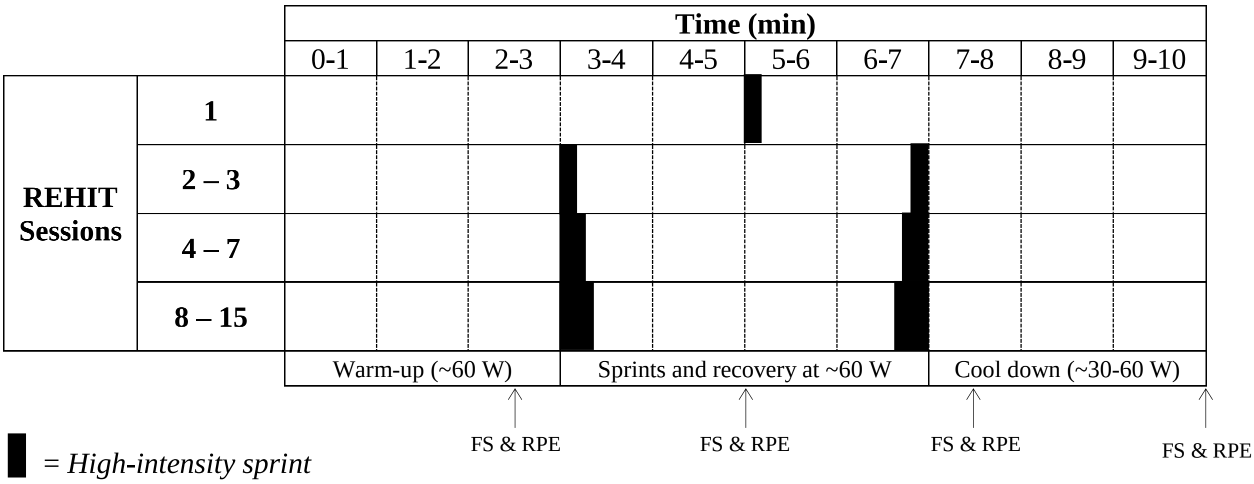

Figure 8.1 Schematic overview of the traditional REHIT training protocol. Abbreviations: REHIT = reduced-exertion, high-intensity interval training, FS = Feeling Scale; RPE = rating of perceived exertion.

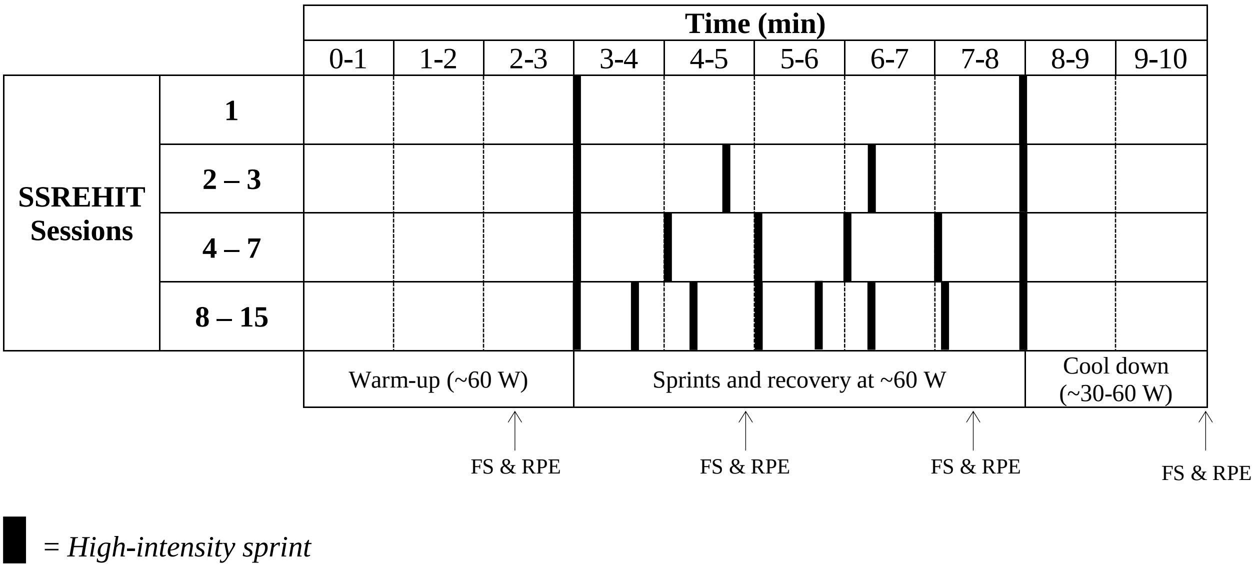

Figure 8.2 Schematic overview of the shortened-sprint REHIT training protocol. Abbreviations: FS = Feeling Scale, REHIT = reduced-exertion, high-intensity interval training; RPE = rating of perceived exertion; SSREHIT = shortened-sprint, reduced-exertion, high-intensity interval training.

Body composition assessment

Fat mass and fat-free mass were predicted using air displacement plethysmography technology using a Bod Pod® Model 2007A (COSMED, Leatherhead, UK), using software version 4.2, which uses the principles of whole body densitometry to estimate the amount of fat and lean tissue. The Bod Pod® is a dual chambered, fibreglass plethysmograph which uses a two-point calibration before each use: baseline calibration with the chamber empty, and calibration using a 50-L calibration cylinder. Following this, participants were instructed to sit motionless inside the Bod Pod®, wearing minimal clothing (for accuracy) while the Bod Pod® software predicted body surface area (based on measured stature and body mass) and body volume as per the equation of Dempster & Aitkens (1995). Body density was then calculated from body volume (body mass ÷ body volume) and applied to the Siri equation (Siri, 1961) to predict body composition. For each test, two measures were completed using predicted thoracic gas volume values provided by the Bod Pod® software. If the two tests differed by more than 150 ml, additional tests were performed until two tests were within 150 ml. Other than the requirement to wear minimal clothing the technique is non-invasive. Both relative and absolute measures of reliability have reported that air displacement plethysmography is a reliable method for predicting body composition in adults (Noreen & Lemon, 2006; Anderson, 2007; Tucker, Lecheminant & Bailey, 2014).

Affect (pleasure-displeasure)

Affective valence (i.e. pleasure-displeasure) was assessed using the Feeling Scale (FS; Hardy & Rejeski, 1989) as detailed in the General Methods (section 6.3.3., pp. 119). The stem "How do you currently feel?" was used to measure pleasure at 25%, 50%, 75%, and 100% of bout completion for both exercise conditions (figures 8.1 & 8.2). Values for 75% of bout completion were then used for further analyses. This time-point captured responses at their peak value, in-line with previous research using these protocols (Chapter 7). FS responses were recorded during sessions 1-3, 4-5, 7-9, and 15; with aggregate mean values for sessions 1-3, 4-7, and 8-15 recorded for analysis. These sessions were chosen to capture responses across the intervention reflecting the gradual progression in the number of high-intensity sprints per session.

Rating of perceived exertion

Intensity during REHIT was monitored using rating of perceived exertion (RPE) using the 15-point Borg scale (Borg, 1970) as per the General Methods (section 6.3.3., pp. 119). As for recording of affect, RPE was measured using a visual cue card during exercise at 25%, 50%, 75%, and 100% of exercise completion using the stem "How hard are you working at this moment in time?" Again, peak values at 75% were used for analyses. RPE was measured during the same sessions as for affect.

Enjoyment

Enjoyment was assessed using Exercise Enjoyment Scale (EES) (Stanley & Cumming, 2009) as detailed in the General Methods (section 6.3.3., pp. 120). Enjoyment was measured for the same sessions as affect and RPE, as outlined above.

8.3.4 Statistical analyses

Statistical analyses were carried out using IBM SPSS Statistics version 22 (IBM, Armonk, USA) with the criterion for statistical significance set at $p < 0.05$. Before analyses, data were explored to check assumptions of statistical tests. Normality of data and identification of potential outliers were assessed via visual inspection using histograms and box plots, in addition to a Shapiro-Wilk normality test. Data were then analysed in two phases. The first phase included descriptive analysis of the sample and a factorial (two-way, condition [2]-by-time [2]) mixed analysis of variance (ANOVA) for $\dot{V}O_{2peak}$ and fat mass. Homogeneity of variance between groups was checked using Levene's test, although mixed ANOVA is generally considered to be robust to violations of this assumption (Field, 2013). Bonferroni correction was used to control for familywise error rate. Effect sizes were calculated using partial eta squared (η^2) to examine the magnitude of differences between the exercise conditions, with values of 0.1, 0.3, and > 0.5 considered to be a small, medium, and large effect, respectively. Paired samples t-tests were used to test for significant differences between values measured pre-intervention and post-intervention within each group, with Cohen's *d* used to indicate the magnitude of differences between conditions (Cohen, 1992). This was calculated using mean differences and pooled standard deviation, and interpreted using a modified scale: 0.0–0.19 'trivial', 0.2–0.59 'small', 0.6–1.19 'moderate', 1.2–1.99 'large' and > 2.0 'very large' (Hopkins, 2016). The second phase used a factorial (two-way, condition [2]-by-time [3]) mixed ANOVA for FS, RPE, and enjoyment; with aggregate mean values for sessions 1–3, 4–7, and 8–15 recorded for analysis. The sphericity assumption was checked using Mauchly's test, with Greenhouse-Geisser correction (denoted $_{GG}$) applied to the degrees of freedom when this was violated. For *post-hoc* analyses, familywise error rate was controlled using Bonferroni corrections by adjusting the level of significance for each test such that the overall type 1 error rate (alpha) across all comparisons remained at 0.05. Again, effect sizes were calculated using partial η^2.

8.4 Results

8.4.1 Descriptive data

The characteristics of the participants for each condition are shown in table 8.1. At baseline, $\dot{V}O_{2peak}$ (46.2 ± 7 vs 44.7 ± 6.8 ml·kg·min^{-1}) and fat mass (16.2 ± 5.8 vs 14.8 ± 5.3 %) between groups were similar. Twenty-one participants completed all 15 exercise sessions within 5–7 weeks. Three participants took 8 weeks to complete all sessions due to missing several sessions. There were no dropouts and each participant undertook each exercise condition as allocated with outcome measures obtained from all participants. Several adverse events, defined as any untoward occurrence that happened during the conduct of the study, were reported. Five incidences of mild to moderate nausea or light headedness were reported (two for shortened-sprint REHIT and three for traditional REHIT), and one participant vomited following traditional REHIT. There were no instances of syncope or musculoskeletal injuries in response to any of the exercise sessions. All adverse events were classified as not serious.

Table 8.1 Participant characteristics and changes in primary outcomes after the shortened-sprint REHIT and traditional REHIT interventions.

	SSREHIT		REHIT		SSREHIT Pre vs post		REHIT Pre vs post	
	Pre	Post	Pre	Post	*P* =	*d* =	*P* =	*d* =
Age (years)	20.9 ± 1.4	-	21.4 ± 2.4	-	-	-	-	-
Mass (kg)	80.7 ± 6.3	80.4 ± 6.4	79.6 ± 7.6	79.6 ± 7.2	0.10	0.05	0.38	0
BMI (kg·m^2)	25.6 ± 2	25.5 ± 2.1	25.4 ± 1.7	25.3 ± 1.7	0.12	0.05	0.41	0.06
$\dot{V}O_{2peak}$ (ml·kg·min^{-1})	46.2 ± 7	48.8 ± 6.6*	44.7 ± 6.8	48.7 ± 7.7*	0.01	-0.36	0.001	-0.53
$\dot{V}O_{2peak}$ (L·min^{-1})	3.7 ± 0.6	3.9 ± 0.6*	3.6 ± 0.6	3.9 ± 0.7*	0.01	-0.32	0.001	-0.44
Fat mass (%)	16.2 ± 5.8	16.2 ± 6.1	14.8 ± 5.3	14.9 ± 5.5	0.97	0	0.44	-0.02

Note: Data are presented as mean ± standard deviations.

* Statistically significant in comparison to pre-value ($p < 0.05$)

Abbreviations: REHIT = reduced-exertion, high-intensity interval training, SSREHIT = shortened-sprint, reduced-exertion, high-intensity interval training, $\dot{V}O_{2peak}$ = peak oxygen uptake per minute.

8.4.2 Peak oxygen uptake

A factorial, 2 (Conditions) by 2 (Time: pre- and post-intervention) mixed ANOVA on $\dot{V}O_{2peak}$ showed a significant main effect of Time, $F(1, 22) = 30.61$, $p = 0.001$, $\eta^2 = 0.58$. Values increased from baseline by 6% for shortened-sprint REHIT (pre: 46.2 ± 7 vs post: 48.8 ± 6.6 ml·kg·min^{-1}, $d = -0.36$) and by 9% for traditional REHIT (pre: 44.7 ± 6.8 vs post: 48.7 ± 7.7 ml·kg·min^{-1}, $d = -0.53$) (Figure 8.3). However, ANOVA revealed the difference between groups was not statistically significant. Also, the interaction effect was not significant. Figure 8.4 shows variability in training responses for which the range was large in both conditions (-2.4% to 22.5% for shortened-sprint REHIT, and -1.7% to 19.5% for traditional REHIT).

8.4.3 Fat mass

There was no statistically significant difference between fat mass at baseline and post-intervention for either condition. Similarly, there was no difference between groups (table 8.1 and Figure 8.4).

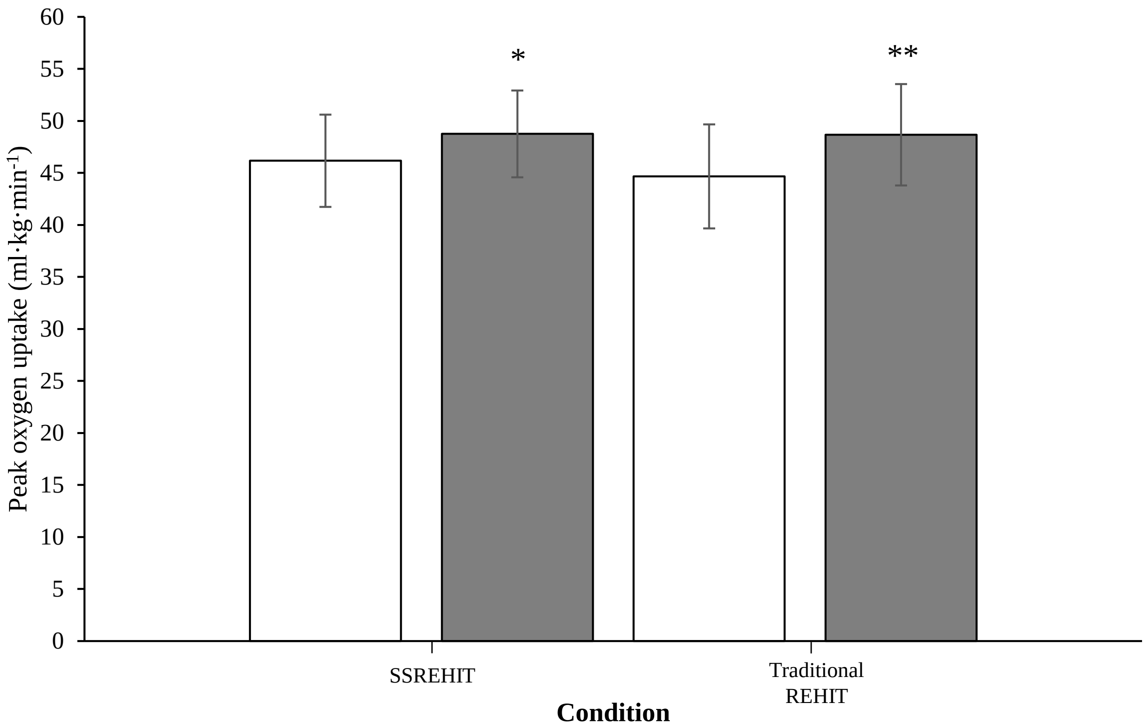

Figure 8.3 Peak oxygen uptake pre- (white bars) and post-intervention (grey bars) for SSREHIT and traditional REHIT. Abbreviations: REHIT = reduced-exertion, high-intensity interval training, SSREHIT = shortened-sprint, reduced-exertion, high-intensity interval training. Note: Data are presented as mean ± 95% confidence intervals. * Statistically significant in comparison to pre-value ($p \leq 0.01$). ** Statistically significant in comparison to pre-value ($p \leq 0.001$).

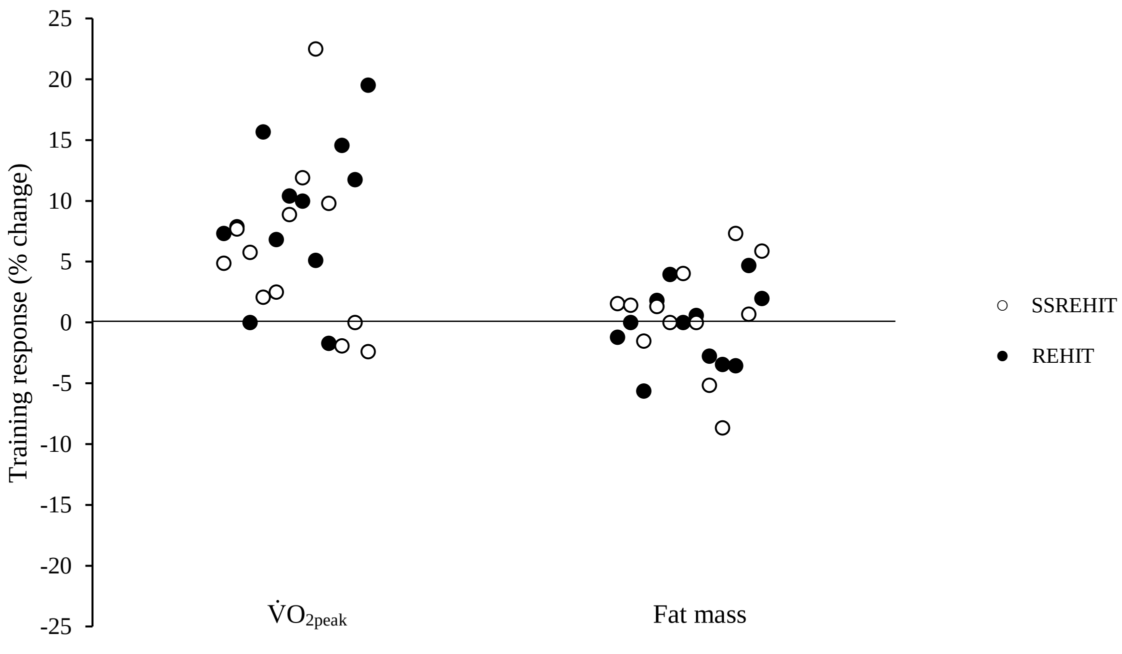

Figure 8.4 Variability in training responses following SSREHIT and traditional REHIT. Dots represent the training adaptation for individual participants in each condition. Abbreviations: REHIT = reduced-exertion, high-intensity interval training, SSREHIT = shortened-sprint, reduced-exertion, high-intensity interval training.

8.4.4 Affect (pleasure-displeasure)

A factorial, 2 (Conditions) by 3 (Time: sessions 1–3, 4–7, 8–15) mixed ANOVA on FS showed a significant main effect of Time, $F(2, 44) = 89.43$, $p = 0.001$, $\eta^2 = 0.80$. *Post-hoc* tests revealed FS to be significantly lower (more displeasure) during sessions 4–7 and 8–15 compared to the preceding time points (both $p = 0.001$, Figure 8.5). There was also a significant difference between groups, $F(1, 22) = 13.36$, $p = 0.001$, $\eta^2 = 0.38$, with mean FS values of 3.1 ± 0.9 (sessions 1–3), 2.2 ± 0.6 (session 4–7), and 1.6 ± 0.6 (session 8–15) for shortened-sprint REHIT; compared to 2.2 ± 0.7, 1.2 ± 1, and 0.2 ± 1 FS units for traditional REHIT at the same time points. FS responses were lowest during sessions 8–15 in both conditions, corresponding to 'fairly good' and 'neutral' for shortened-sprint REHIT and traditional REHIT, respectively. There was also a significant Condition × Time interaction effect, $F(2, 44) = 3.2$, $p = 0.05$, $\eta^2 = 0.13$. This indicates that the condition had a small effect on FS depending on the time point (sessions). Looking at Figure 8.5, steeper slopes of change were evident for traditional REHIT compared to shortened-sprint REHIT between sessions 4–7 and 8–15. These data are summarised in table 8.2.

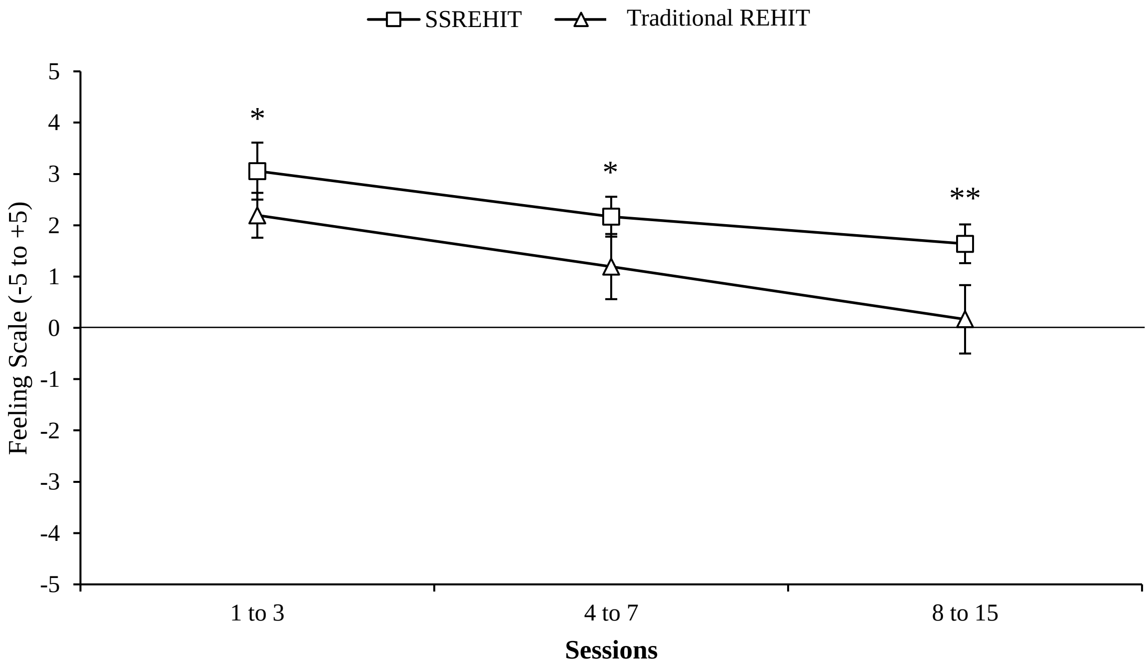

Figure 8.5 Peak Feeling Scale (FS) responses during shortened-sprint REHIT and traditional REHIT across the intervention. Responses were recorded at 75% of bout completion. Abbreviations: REHIT = reduced-exertion, high-intensity interval training, SSREHIT = shortened-sprint, reduced-exertion, high-intensity interval training. Note: Data are presented as aggregate mean ± 95% confidence intervals. * Significant difference between groups ($p \leq 0.01$). ** Significant difference between groups ($p \leq 0.001$).

Table 8.2 Comparison of perceptual response for both exercise conditions.

	SSREHIT	Traditional REHIT	SSREHIT vs Traditional REHIT	
			P =	*d =*
FS				
Sessions 1–3	3.1 ± 0.9*	2.2 ± 0.7	0.01	1.06
Sessions 4–7	2.2 ± 0.6*	1.2 ± 1	0.01	1.16
Sessions 8–15	1.6 ± 0.6*	0.2 ± 1	0.001	1.62
Average	2.3 ± 0.7	1.2 ± 1	-	-
RPE				
Sessions 1–3	10.4 ± 1.3*	13.1 ± 1.6	0.001	-1.77
Sessions 4–7	12.8 ± 1.1*	15.3 ± 1.1	0.001	-2.17
Sessions 8–15	14.4 ± 0.9*	16.2 ± 1.1	0.001	-1.71
Average	12.5 ± 2	14.9 ± 1.6	-	-
EES				
Sessions 1–3	4.8 ± 0.9	4.5 ± 1	0.37	0.30
Sessions 4–7	4.4 ± 0.9	4.1 ± 1	0.41	0.30
Sessions 8–15	4 ± 1	3.7 ± 1.3	0.49	0.25
Average	4.4 ± 0.4	4.1 ± 0.4	-	-

Note: Data are presented as aggregate mean ± standard deviations.
* Statistically significant in comparison to traditional REHIT ($p < 0.05$)
Abbreviations: EES = exercise enjoyment scale, FS = feeling scale, REHIT = reduced exertion high-intensity interval training, RPE = rating of perceived exertion, SSREHIT = shortened-sprint reduced-exertion high-intensity interval training.

8.4.5 Rating of perceived exertion

A factorial, 2 (Conditions) by 3 (Time: sessions 1–3, 4–7, 8–15) mixed ANOVA on RPE showed a significant main effect of Time, $F(2, 44) = 282.48$, $p = 0.001$, $\eta^2 = 0.93$. *Post-hoc* tests revealed RPE to be significantly higher during sessions 4–7 and 8–15 compared to the preceding time points (both $p = 0.001$, Figure 8.6). There was also a significant difference between groups, $F(1, 22) = 25.83$, $p = 0.001$, $\eta^2 = 0.54$, with mean RPE values of 10.4 ± 1.3 (sessions 1–3), 12.8 ± 1.1 (session 4–7), and 14.4 ± 0.9 (session 8–15) for shortened-sprint REHIT; compared to 13.1 ± 1.6, 15.3 ± 1.1, and 16.2 ± 1.1 RPE units for traditional REHIT at the same time points. RPE responses were highest during sessions 8–15 in both conditions, between ‘somewhat hard’ and ‘hard’ for shortened-sprint REHIT, and ‘hard’ and ‘very hard’ for traditional REHIT. There was also a significant Condition × Time interaction effect, $F(2, 44) = 5.5$, $p = 0.007$, $\eta^2 = 0.20$. This indicates that the condition had a small effect on RPE depending on the time point (sessions). Figure 8.6 highlights steeper slopes of change for shortened-sprint REHIT compared to shortened-sprint REHIT between sessions 4–7 and 8–15. These data are summarised in table 8.2.

8.4.6 Enjoyment

Mauchly's test indicated that the assumption of sphericity was violated for the main effect of Time, $\chi^2(2) = 10.82$, $p = 0.004$. Therefore, degrees of freedom were corrected using Greenhouse-Geisser estimates of sphericity ($\varepsilon = 0.71$ for the main effect of Time). A factorial, 2 (Conditions) by 3 (Time: sessions 1–3, 4–7, 8–15) mixed ANOVA on EES showed a significant main effect of Time, $F(1.43, 31.37) = 23.34$, $p = 0.001_{GG}$, $\eta^2 = 0.52$. *Post-hoc* tests revealed enjoyment to be significantly lower during sessions 4–7 and 8–15 compared to the preceding time points ($p = 0.008$ and 0.001, respectively, Figure 8.7). However, there were no differences between groups and no significant interaction effect. These data are summarised in table 8.2.

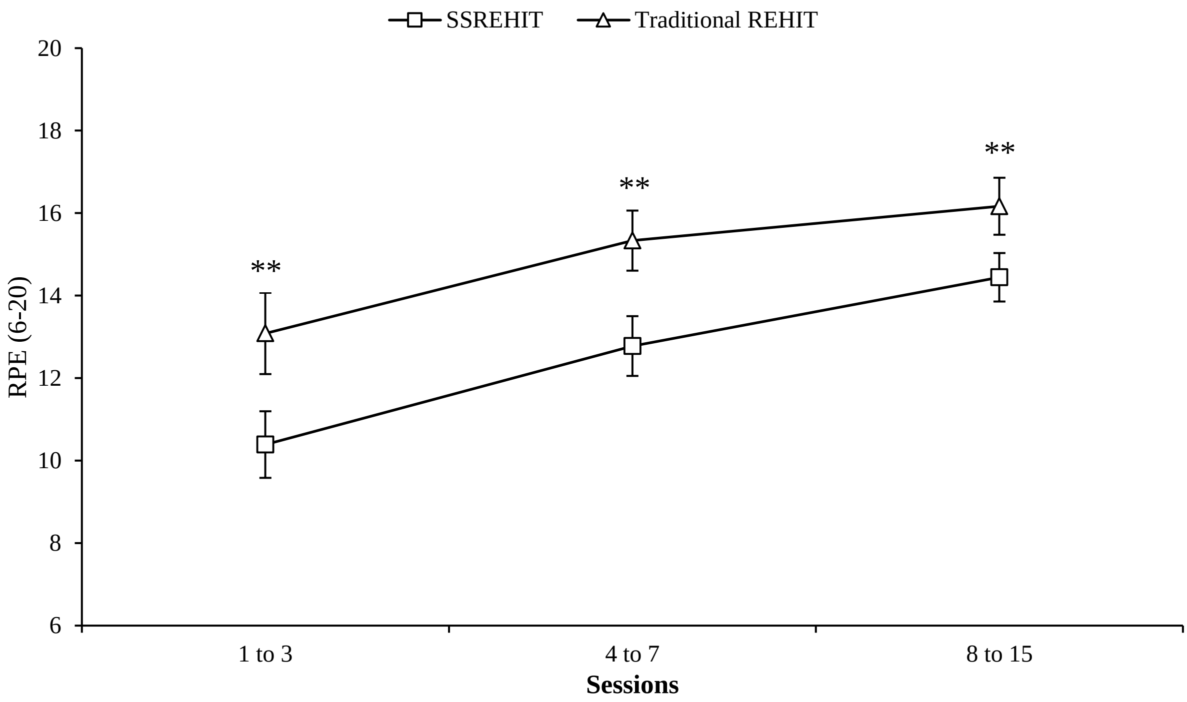

Figure 8.6 Peak RPE responses during SSREHIT and traditional REHIT across the intervention. Responses were recorded at 75% of bout completion. Abbreviations: REHIT = reduced-exertion, high-intensity interval training, RPE = rating of perceived exertion, SSREHIT = shortened-sprint, reduced-exertion, high-intensity interval training. Note: Data are presented as aggregate mean ± 95% confidence intervals. ** Significant difference between groups ($p \leq 0.001$).

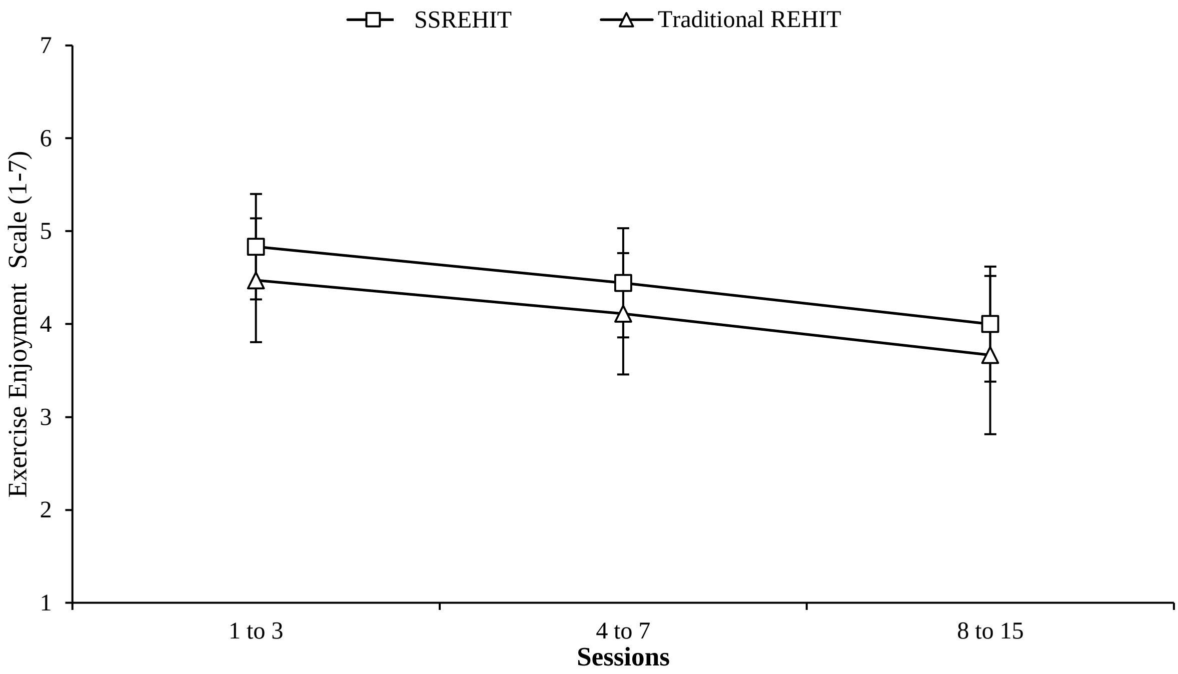

Figure 8.7 Enjoyment responses following shortened-sprint REHIT and traditional REHIT across the intervention. Responses were recorded 5 min after cessation of exercise. Abbreviations: REHIT = reduced-exertion, high-intensity interval training, SSREHIT = shortened-sprint, reduced-exertion, high-intensity interval training. Note: Data are presented as aggregate mean ± 95% confidence intervals.

8.4 Discussion

The minimum amount of exercise that has so far been shown to improve cardiovascular fitness is REHIT incorporating two 20 s maximal exertion cycle sprints within a 10-min low-intensity exercise session (Metcalfe *et al*., 2011; 2016b). Although this approach has been generally well tolerated, based on ratings of perceived exertion taken at the end of exercise, it is possible that peak affective responses (i.e. pleasure-displeasure) could be low *during* the 20-s sprint which might result in future avoidance of the activity. To circumvent overly compromising perceptual response, REHIT can be adapted by reducing the duration of the high intensity sprints, whilst simultaneously increasing the frequency of sprints to maintain the same overall duration of high-intensity activity (e.g. 8 × 5 s sprints). A single bout of exercise using this protocol has been shown to result in more favourable perceptual responses (Chapter 7). However, it is unclear if this shortened-sprint REHIT protocol can elicit the same benefits to health. Using a randomised positive-controlled approach, the present study compared the effects of shortened-sprint REHIT and traditional REHIT on $\dot{V}O_{2peak}$ and adiposity, in addition to perceptual response during exercise throughout a longitudinal intervention. The foundation for the study was that for REHIT to have any impact on public health, it needs to be shown to be both efficacious and safe, yet at the same time appealing, tolerable, and sustainable.

The main finding was that 5–7 weeks of both traditional REHIT and shortened-sprint REHIT results in improved cardiovascular fitness. Compared to baseline, $\dot{V}O_{2peak}$ increased by 9% for traditional REHIT and by 6% for shortened-sprint REHIT (both $p = 0.01$). The differences between groups was not statistically significant ($p = 0.78$). The small sample size may have resulted in insufficient power to detect statistically significant differences, leading to a type II error. A post hoc statistical power calculation for the post-exercise $\dot{V}O_{2peak}$ values revealed a calculated power of 0.06. However, post-hoc power analyses are fundamentally flawed because they are typically only calculated for non-significant results (i.e. $p \geq 0.05$), so associated analyses will produce a low post-hoc power result, which can be misinterpreted as the study having inadequate power (Hoenig & Heisey, 2001; Levine & Ensom,2001). Regardless, the increases reported in the current study are in-line with previous research that has used REHIT with sedentary participants and type 2 diabetes patients (7–10% increase, Metcalfe *et al*., 2016b; Ruffino *et al*., 2016); but lower than other research using healthy, young participants (12–15% increase, Metcalfe *et al*., 2011). Compared to these studies, which used 18 to 24 sessions over a 6–8-week period, the present study used less sessions (15 across a 5–7-week period) demonstrating that REHIT interventions consisting fewer sessions can also bring about training adaptations. Although the improvements in $\dot{V}O_{2peak}$ were not as high as those reported for higher-volume and more strenuous HIT (e.g. Weston *et al*., 2014a; Milanović, Sporiš & Weston, 2015), they are nevertheless likely to be clinically important, because large scale observational research has demonstrated that every 3.5 $mL \cdot kg^{-1} \cdot min^{-1}$ increase in aerobic exercise capacity confers a 12% improvement in survival (Myers *et al*., 2002). Similarly, each 1 $mL \cdot kg^{-1} \cdot min^{-1}$ advantage in $\dot{V}O_{2peak}$ has been shown to provide a 9% improvement in survival in patients with coronary heart disease (Vanhees, Fagard, Thijs, Staessen & Amery, 1994). Considering these findings, the potential for both traditional REHIT and shortened-sprint REHIT to bring about rapid improvements in fitness in a time-efficient manner is notable. In the present study, there was a mean increase of 4 $mL \cdot kg^{-1} \cdot min^{-1}$ and 2.8 $mL \cdot kg^{-1} \cdot min^{-1}$ for the traditional REHIT and shortened-sprint REHIT protocols, respectively.

Considerable heterogeneity in training response was observed for $\dot{V}O_{2peak}$. Figure 8.4 shows that the change ranged from ~ -2% to 20% in both training groups. These findings support similar inter-individual variation reported following both REHIT (Metcalfe *et al*., 2016b) and higher-volume HIT (Bacon, Carter, Ogle & Joyner, 2013; Gurd *et al*., 2016), and emphasise the importance of looking beyond typical responses when interpreting exercise intervention outcomes. For example, in the shortened-sprint REHIT group in the current study, five out of

12 participants had no or little measurable adaptation to $\dot{V}O_{2peak}$ in response to the training programme, despite a favourable group mean adaptation. The notion of 'responders' and 'non-responders' in terms of $\dot{V}O_{2peak}$ was established for continuous aerobic exercise in the seminal, multi-centre, exercise training trial known as the HERITAGE Family Study (Bouchard *et al.*, 1999). It seems that this phenomenon might explain responses to HIT and REHIT too, and such underlying error should be considered when attempting to translate research into real-world practice. Furthermore, the small sample size used in the current and other REHIT studies make the mean results susceptible to the influence of individual variation in response, and this could reduce the reliability of results. Attempts have been made to identify sufficiently discrete genetic biomarkers to predict $\dot{V}O_{2max}$ responses to endurance training (Timmons *et al.*, 2010), and as recommended by Metcalfe *et al.* (2016b), it needs to be established whether this can also be applied to intermittent exercise. Preliminary research shows that individual patterns of response differ between endurance training and HIT, suggesting that non-response to endurance training might not necessarily predict response to HIT (Bonafiglia *et al.*, 2016).

Although REHIT is time-efficient, which may encourage participation for individuals who otherwise would not engage with more time-consuming exercise, it is likely to result in similarly poor adherence if it is perceived to be too strenuous. As such, affective valence is an important part of the exercise experience because pleasure-displeasure responses during activity may predict future engagement with that exercise. This reasoning is based on the dual-mode theory which is predicated on the notion that intensities above the ventilatory threshold are accompanied by a cascade of physiological responses that dramatically challenge maintenance of homeostasis during continuous exercise (Ekkekakis *et al.*, 2008). Research has started to investigate this issue for HIT (e.g. Jung *et al.*, 2014; Kilpatrick *et al.*, 2015, Martinez *et al.*, 2015; Decker & Ekkekakis, 2017); however, only a single study has measured these responses during REHIT. It was found in Chapter 7 that peak FS responses during a single session were significantly and meaningfully higher (more pleasurable) for shortened-sprint REHIT (1.4 ± 1.7 FS units), compared to traditional REHIT (-0.1 ± 1.9) (p = 0.01, d = 0.83), where 1 is 'fairly good', 0 is 'neutral', and -1 is 'fairly bad'. The results of the present study support these findings, with peak FS values significantly higher for shortened-sprint REHIT compared to traditional REHIT at all time points (see table 8.2). To achieve progressive overload of participants, the number of sprints completed in the shortened-sprint REHIT protocol increased as the intervention progressed with 8 × 5 s maximal effort sprints used from session 8 onwards. There was a significant main effect for Time (p = 0.001, η^2 = 0.80) indicating diminishing pleasure as the number of sprints increased over time. However, importantly average FS responses did not enter the negative domain (i.e. < 0) at any point, suggesting the protocol was well tolerated in this regard. Average FS responses remained above 0 for traditional REHIT also, but only just. Aggregate mean peak displeasure was observed during sessions 8–15 for both conditions with values of 1.6 ± 0.6 and 0.2 ± 1 FS units for shortened-sprint REHIT and traditional REHIT, respectively.

RPE scores recorded for traditional REHIT were higher than previously described. Other researchers (e.g. Metcalfe *et al*., 2011; 2016b) have consistently reported values of ~14 RPE units, that is between ‘somewhat hard’ and ‘hard’. In the present study, average RPE during sessions 8–15 was 16.2 ± 1.1, or between ‘hard’ and ‘very hard’. This difference could be explained by individual variation in terms of participant exercise history or baseline fitness, but more likely reflects the differing times at which these values were recorded. Metcalfe and colleagues collected RPE values at the end of training sessions with participants asked to retrospectively consider effort for the whole training session, not just the high-intensity bouts; whereas in the present study values were recorded at their peak *during* exercise (at 75% of bout completion, in-line with the study conducted in Chapter 7). It is important to capture a representative depiction of responses during activity because dose-response effects may occur during exercise but then dissipate before post-exercise measurements are recorded, or they may simply be hidden by the general shift in affect toward pleasure after the cessation of exercise (Ekkekakis, 2008). These exhortations regarding measurement of perceptual response are important because they could be decisive in relation to motivational factors related to future exercise adherence. The peak-end rule suggests that memory associated with perceptual responses are influenced by the moment a distinct ‘peak’ is experienced, as highlighted by Decker & Ekkekakis (2017). In the current study, RPE values recorded for shortened-sprint REHIT were significantly lower than for traditional REHIT (between-groups main effect, p = 0.001, $\eta^2 = 0.54$). Specifically, mean RPE was lower at all time points, with large to very large magnitude based differences recorded (all p = 0.001, see table 8.2 and Figure 8.6). A plausible explanation for the difference in RPE could be that when physical activity is extended over time, the sensation of the exertion becomes a function of duration (Cafarelli, Cain & Stevens, 1977). Alternatively, the successive completion of more regular intervals may repeatedly bolster confidence within a single session, or simply the 5-s sprints may have been of insufficient duration to induce the metabolic, pulmonary, and physiological responses that are associated with more negative perceptual changes.

Despite the differences in RPE and FS between shortened-sprint REHIT and traditional REHIT, there was no difference in enjoyment associated with completion of exercise, recorded 5 min after cessation of activity ($p = 0.387$). There was a trend toward higher EES values for shortened-sprint REHIT, but the magnitude of these differences was small (table 8.2). Given that traditional REHIT was more strenuous, the results support those of Bartlett *et al*. (2010) in that higher-intensity exercise can be perceived to be just as enjoyable as less-intense exercise. It should be noted that although affective valence and enjoyment overlap, they are not identical constructs. An assumption of dual-mode theory is that there exists a distinction between core affect, such as hedonistic pleasure or pain, and more distinct emotional experiences such as enjoyment that require cognitive appraisal and appreciation of the totality of the experience (Wankel, 1993; Russell & Barrett, 1999). Nonetheless, they are both important perceptions in understanding the exercise experience for REHIT (Martinez *et al*., 2015). Taken together, the enjoyment and perceptual responses and the improvements in cardiovascular fitness, suggest both REHIT protocols used in this study are genuinely time-efficient, yet tolerable and sufficiently enjoyable. The challenge remains to translate this evidence into real-world scenarios for patients with long-term conditions, but it seems reasonable to speculate that REHIT could be both efficacious and effective. Research continues to address the minimal amount of exercise that can confer health benefits. Songsorn *et al*. (2016) recently demonstrated that a single 20-s cycle sprint per training session did not provide a sufficient stimulus for improving $\dot{V}O_{2max}$. Nevertheless, several meta-analyses have shown that protocols using lower intensity or shorter sprint durations do not attenuate the improvement in $\dot{V}O_{2max}$, and could even enhance the response by ~1.8 ± 2.7 $mL \cdot kg^{-1} \cdot min^{-1}$ (Milanović, Sporiš & Weston, 2015; Vollard, Metcalfe & Williams, 2017). Although these analyses were for more strenuous HIT, they provide a rationale for future investigations to specifically consider REHIT with a focus on dose-response relationships.

It is not possible from the current study to determine the mechanisms that caused the increase in $\dot{V}O_{2peak}$. However, following a single bout of REHIT average *vastus lateralis* muscle glycogen concentrations have been shown to reduce by ~20% immediately and for 3 hours post-exercise (Metcalfe *et al*., 2015). Skeletal muscle glycogen content is an important acute regulator of metabolism and may also have a role as a signalling molecule for exercise-induced adaptations (Jensen & Richter, 2012). Therefore, such a pronounced disturbance to muscle energy stores could be associated with activation of signalling pathways, including activation of PGC-1α which is considered the 'master regulator' of mitochondria biogenesis and skeletal muscle remodelling towards a more oxidative phenotype (Wu *et al*., 1999), and may explain adaptations in $\dot{V}O_{2peak}$ in the current study. To further the research agenda on REHIT it would be valuable to determine if these changes are induced by protocols that use shortened sprints of < 20 s duration, such as the protocol used in the current study.

The aim of this study was to investigate a novel approach to REHIT using shortened sprints, to determine whether it attenuates adaptations to $\dot{V}O_{2peak}$. Alongside this, it was important that the intensity used during the sprints did not overly compromise cognitive and affective responses. The results suggest that the specific shortened-sprint REHIT protocol used in this study could be used as a convenient and time-efficient exercise option. However, there are several limitations which need to be considered. First, in lowering the duration of the sprints, it was necessary to counter this by increasing the number of sprints per session to match the total duration of high-intensity exercise (i.e. the protocol was adapted so that 2 × 20 s sprints were replaced with 8 × 5 s sprints). This significantly reduces rest between sprints and could adversely influence recovery and perceptual response. Although this was not the case in the present study, other research using higher-volume HIT has reported that increasing the number of sprint repetitions negatively affects perceived exertion and feelings of pleasure (Little *et al*., 2011b; Frazão *et al*., 2016). Furthermore, it is possible that increasing the number of sprints could result in 'pacing' strategies that affect the 'all-out' nature of the sprints which might be necessary for optimal adaptation (Vollard, Metcalfe & Williams, 2017). The current study was carried out in a controlled laboratory environment and participants received verbal encouragement to work maximally during each sprint. Effort may diminish for later sprints in unsupervised real-world settings. Therefore, the need to carefully balance the frequency, duration, and intensity of sprints is a challenging issue.

Second, for optimal benefit in treating physical inactivity related disease, REHIT also needs to improve other biomarkers of health. Presently, the effect of REHIT on insulin sensitivity is unclear (Metcalfe *et al*., 2011; 2016a; Ruffino *et al*., 2016) and it is unlikely that REHIT would result in sufficient calorific expenditure to create the negative energy balance required for significant weight loss. Although some research supports the notion that higher-volume and more strenuous HIT can result in reductions in fat mass (e.g. Whyte *et al*., 2010; Heydari *et al*., 2012), this may be related to reduction in energy intake through suppression of appetite (Boutcher, 2011). Metcalfe *et al*. (2016) reported systemic concentrations of the appetite stimulating hormone acylated ghrelin were reduced by > 50% in the immediate REHIT post-exercise period, which is in-line with research that suggests suppression occurs at higher exercise intensities (Broom, Stensel, Bishop, Burns & Miyashita, 2007; Broom, Batterham, King & Stensel, 2009; Wasse, Sunderland, King, Miyashita & Stensel, 2013). Other studies have shown that more strenuous HIT can transiently suppress appetite, although the associated effects on *ad libitum* food intake are equivocal (Deighton, Barry, Connon & Stensel, 2013; Beaulieu, Olver, Abbott & Lemon, 2015; Holliday & Blennin, 2017). Long-term studies using overweight individuals need to be carried out in real-world environments to determine if REHIT can effectively reduce adiposity. In the current study, exercise did not change fat mass under either condition, but this was not surprising as participants were simply instructed to follow their normal diet, rather than undergoing strict dietary control. Third, adverse events to REHIT (and HIT) must be considered carefully. Although most HIT studies report that exercise is well tolerated, procedures for reporting adverse events are poorly communicated. In the present study, there were several cases of nausea, light-headedness, or vomiting in response to the intensity of exercise; and whilst this only happened in a few instances, it would be likely to negatively impact on future engagement with this type of activity for many people.

Several sample and research design limitations should also be considered alongside the findings of this study. The sample were not representative of inactive, obese, or other populations with chronic disease, and as such responses in these groups could be different. The sample was derived from a convenient pool of interested sport and exercise science students, who may have had knowledge of the hypotheses of the study which could have influenced their perceptual response to the exercise conditions. Differences in expectations can be explicitly or implicitly communicated to individual groups, although discussion of this nature between participants and researcher was consciously restricted. Nevertheless, the nature of studying humans as they interact with their environment is neither stable, free from influences, or confounding variables – and the significance of behavioural factors for the validity of physiological research should be considered (Grossman, 2005). Again, although baseline fitness values were similar between the groups, participant characteristics were not matched. A matched samples design would minimise the influence of differences between individuals biasing results. Using such an approach permits the benefits of a within participant design (i.e. less biological variation), whilst avoiding temporal order effects that can influence results, although it is not clear which variables are most influential in exercise intervention research. It is conceivable that participants with lower baseline fitness might obtain greater increase than more well-trained participants.

A further limitation relates to use of a Wattbike for the protocols in this study. Although the Wattbike allows for a very rapid transition from unloaded pedalling to a high braking force, which is required for generation of high peak power within the first few seconds of the high-intensity sprints, most other studies have used ergometers that allow for specific loads equivalent to 7.5% of body mass. This is unlikely to greatly effect results, but makes comparison between studies more problematic, because the protocols used differ somewhat in terms of how resistance was applied. Similarly, other REHIT studies have used three sessions per week, whereas in the present study participants could choose to complete two or three sessions per week (until the target number of sessions was completed). Whilst this adds an element of ecological validity, it makes direct comparison to other protocols less straightforward. Participants were also advised to maintain their normal physical activity and dietary behaviours throughout the duration of the study. Monitoring of daily activity and diet would have been more robust. Hence, these limitations create confounds that limit the validity of the results. Finally, a measure of exercise intentions to predict future exercise behaviour would have been a valuable additional measure during this study.

In conclusion, both REHIT protocols improved cardiovascular fitness whilst minimising negative affective responses during activity, although there was large heterogeneity in training response. Given that low fitness is an important precursor of mortality, REHIT could be a genuinely time-efficient, yet tolerable and enjoyable alternative or adjunct to usual exercise guidelines, to reduce the burden of physical inactivity. Shortened-sprint REHIT resulted in more favourable perceived exertion and pleasure responses. Despite this, there was no difference in enjoyment between the groups. Future research should systematically investigate optimal dose-response of REHIT and associated physiological adaptations to elucidate the minimal amount of exercise that can improve health. The challenge of translating this research into real-world practice remains.

Chapter 9 Study 3: Feasibility of REHIT for NDH patients

Feasibility and acceptability of procedures for a pragmatic randomized controlled trial of REHIT with non-diabetic hyperglycaemia patients within an NHS practice setting

9.1 Abstract

Formal Medical Research Council (MRC) guidance highlights the requirement for greater attention to be given to the initial development of healthcare interventions. This is particularly relevant to exercise interventions, because often they are shown to treat patients and bring about intended effects under ideal circumstances, but fail to demonstrate effectiveness when translated to demonstrable benefits in real-world contexts. The aim of the current research was to carry out a feasibility study to describe and report data relevant to the acceptability of a reduced-exertion high-intensity interval training (REHIT) intervention in non-diabetic hyperglycaemia (NDH) patients, delivered in an NHS practice setting. The purpose was to assess whether it would be appropriate to progress to a larger-scale pragmatic trial, and to optimise the design and conduct of any such trial. Methodological issues were used to analyse the problems that arose in the feasibility study. The intention was to recruit 40 participants from a single centre, which was considered adequate to meet the objectives of the study. Patients were eligible to take part if they were diagnostically defined as NDH based on a glycated haemoglobin (HbA_{1c}) value of 42–46 mmol·mol. The study revealed several feasibility issues including eligibility, challenges to recruitment, patient consent, and poor clinician engagement. These findings form the basis for important learning in relation to the potential for transfer of a REHIT intervention into real-life scenarios with specific populations, which must be sensitive to features of the local context such as the built environment, socioeconomic status, and the specific needs of individuals with chronic disease. Despite the simplicity and convenience of using HbA_{1c} to screen for diabetes risk, the process of accurately screening and case finding eligible patients was problematic. However, some aspects of the intervention worked well. Adherence to the exercise intervention was very high, with 97% of sessions completed for the participants that finished the study. Given the issues, it is prudent to recommend that the trial is not feasible in its current form. The small sample ($n = 6$) recruited for this trial limits interpretation of data, and it is not possible to estimate variability of intended outcomes to use in a formal sample size calculation for a full-scale trial. However, this

preparatory stage of trial design pre-empted problems with the intervention that could be changed to optimise the design and conduct of a larger-scale pragmatic trial to improve transferability into real-world practice. Solutions to the issues identified in this study revolve around using a dedicated local recruiter with a strong relationship among the healthcare team and patients, using participant incentives to take part, and allowing for a longer recruitment period. It follows that a compromise must be made between scientific robustness and generalisability to routine real-world contexts.

9.2 Introduction

Encouraging individuals and populations to lead healthier lifestyles is inherently challenging because interactions between behavioural, biological, and environmental factors are complex. Therefore, attempts to tackle problems such as physical inactivity and obesity increasingly use complex interventions, conventionally defined as having several interacting components (Craig *et al*., 2008). Such approaches can be practically and methodologically difficult, and physical activity interventions may pose many extra problems identified as common to complex interventions. For example, it can be difficult to standardise the design and delivery of physical activity interventions because it is unethical to proscribe other healthy behaviours external to the intervention (Hawe, Shiell, Riley & Gold, 2004); they are likely to be sensitive to features of the local context (Wolff, 2001; Rychetnik, Frommer, Hae & Schiell, 2002); they can be organisationally and logistically difficult to apply (Petticrew *et al*., 2005); and causal chains linking intervention with outcomes can be complex (Victora, Habicht & Bryce, 2004). Consequently, it is important that sufficient initial development of interventions is undertaken to consider methodological bias and imprecision that could undermine eventual implementation in practice, and to assess whether it is fundamentally appropriate and ethical to proceed with a large-scale trial (Craig *et al*., 2008; Hubbard *et al*., 2016).

Formal MRC guidance highlights the requirement for greater attention to be given to the initial development of healthcare interventions because many interventions fail to demonstrate effectiveness when translated to demonstrable benefits in real-world contexts (Øvretveit, 2004; Collier, 2009). This is relevant for exercise interventions because, although evidence for their efficacy in treating disease is strong, there is a dearth of evidence for their effectiveness in real-world settings (Beedie *et al*., 2015). Many studies intending to examine exercise effectiveness use laboratory-style methods and controls that would be impractical and uneconomical in real-world interventions (Beedie, Mann & Jimenez, 2014). These concerns are potentially decisive because effectiveness is what matters to patients and commissioners (Beedie *et al*., 2015). As outlined by Bugge *et al*. (2003), common recommendations include the need for thorough feasibility work as part of the preparatory stage of trial design to pre-empt problems with the exercise intervention and to ensure transferability into real-world practice. Such feasibility studies are described as research completed before a main study to answer questions relating to whether a study can be done. This differs to a pilot study which is a miniature version of a main study to test whether components of the main study work together (Arain, Campbell, Cooper & Lancaster, 2010). The aims of such developmental work must compromise between scientific robustness (internal validity) and generalisability to routine real-world contexts (external validity) which are typically inversely related (Godwin *et al*., 2003). Explanatory trials focus on establishing efficacy with resultant high internal but low external validity; whereas pragmatic trials focus on effectiveness in real-world contexts with resultant lower internal but higher external validity (Schwartz & Lellouch, 1967; Bugge *et al*., 2013).

Despite the importance of building the foundation for planned intervention studies, several issues relating to feasibility trials exist. Arain *et al*. (2010) highlighted the inappropriate emphasis on null hypothesis significance testing in the reporting of feasibility trials. Such studies are typically insufficiently powered to test the effectiveness hypotheses associated with the planned main large-scale trial. Indeed, small studies with many of the features of a major study, such as randomisation and hypothesis testing, may be labelled a 'pilot' or 'feasibility' trial because they do not have the statistical power to test clinically significant hypotheses. This practice misses the point of a feasibility trial which is to describe issues such as screening, recruitment, adverse events, completion, and adherence. A review of published pilot or feasibility trials revealed that half of the studies did not primarily address methodological issues preparatory to planning a subsequent study (Shanyinde, Pickering & Weatherall, 2011). In these instances, pilot and feasibility designation for a trial, seems to indicate little more than inconclusive results or lack of adequate sample size. Further issues relate to publication bias and peer review norms which may require researchers to perform null hypothesis significance testing, and misguided conclusions that non-significant statistical tests of appropriately small-scale studies are indicative of poor feasibility (Tickle-Degnen, 2013). Such misinterpretations may result from the largely arbitrary criterion of $p < 0.05$ (Cohen, 1994), ignorance relating to statistical power, or a fundamental misunderstanding regarding the purpose of feasibility research, which aims to descriptively assess the intervention plan rather than test the hypotheses of the main trial (Leon, Davis & Kraemer, 2011).

The present feasibility study relates to a complex intervention to carry out a reduced-exertion, high-intensity interval training (REHIT) programme within a specialist diabesity service in an NHS Trust hosptital. The expression ‘diabesity’ is used to describe the co-existence of the obesity and type 2 diabetes epidemics (Haines, Rajeswaran, Ramasamy & Hastings, 2016). The service was initiated in 2007 to address the growing prevalence of people with diabesity in the locality. The aim of the service was to manage the complex healthcare needs of people with diabesity and to simultaneously optimise glycaemic control and weight management (Rajeswaran, Pardeshi, Srinivasan, 2012). There is also an intermediary group of patients whose blood glucose levels are higher than normal but not high enough to be diagnosed as diabetic. This population are referred to as having non-diabetic hyperglycaemia (NDH) or ‘pre-diabetes’, which are umbrella terms to describe intermediate hyperglycaemic states (Yudkin & Montori, 2014). Hyperglycaemic blood glucose excursions in pre-diabetic states contribute to the development of macro- and micro-vascular disease risk (Baron, 2001; Ceriello, 2005), and without intervention it is estimated that up to 70% of patients in this group will eventually develop type 2 diabetes (DeVegt *et al*., 2001; Vendrame & Gottlieb, 2004). Furthermore, more than 50% of those living in England, who are overweight (BMI > 25 $kg{\cdot}m^2$) and ≥ 40-years-old already have NDH (Mainous III *et al*., 2014). Therefore, interventions – such as increased physical activity – for individuals who are diagnostically considered to have NDH are high priority, as they provide a substantial opportunity for preventing future burden of diabetes on patients, the NHS, and the UK economy (Diabetes UK, 2009). Tier 3 weight management services that include physical activity have been shown to be effective in patients with type 2 diabetes (Taylor, 2015). However, delivering interventions in primary care within a busy practice setting requires considerable time and demanding skills that the multidisciplinary team may not have specialist training in. In the current study, the Principal Investigator (a BASES Accredited Sport and Exercise Scientist and Certified Exercise Practitioner) was used to deliver the intervention as part of the existing service.

Evidence supporting the efficacy of exercise and physical activity as preventative or therapeutic treatments for a range of chronic diseases, including obesity and diabetes, is incontrovertible (Jones *et al*., 2011). However, what is less clear is how effective these interventions are in real-world contexts. It is generally thought that half of people who start an exercise programme stop within the first six months (Robinson & Rogers, 1994; Dishman & Buckworth, 1997) – thus poor adherence is considered a significant issue, particularly in those with chronic disease (Qiu *et al*., 2012), because adhering to the programme is clearly a pre-requisite for the success of any intervention. The most commonly cited barrier to undertaking physical activity is perceived 'lack of time' (Reichart *et al*., 2007; Korkiakangas, Alahuhta & Laitinen, 2009). Consequently, there has been a recent interest in high-intensity interval training, or HIT, which is characterised by brief periods of repeated very high-intensity exercise interspersed with longer periods of recovery. HIT is considered more time-efficient than traditional exercise guidelines which promote 150 to 300 min of moderate-intensity physical activity per week (Haskell *et al*., 2007; O'Donovan *et al*., 2010). However, critics of HIT have highlighted that the intensity of this type of activity may present an additional barrier for many, and that HIT is not appreciably more time-efficient compared to traditional exercise guidelines when inclusive of a warm-up, cool down, and recovery in-between high-intensity bouts (Whyte *et al*., 2013; Hardcastle *et al*., 2014). These concerns may be critical because the acceptability and tolerability of exercise interventions to those for whom they are intended is of primary importance (Haines *et al*., 2012). More recently attempts have been made to modify HIT to make it genuinely time-efficient (Metcalfe *et al*., 2011, 2016; Ruffino *et al*., 2016). This approach is known as reduced-exertion HIT (REHIT). The affective response (i.e. pleasure-displeasure) associated with HIT and REHIT is also important, as this may predict future exercise behaviour (Jung *et al*., 2014; Decker & Ekkekakis, 2017; see Chapters 7 & 8).

At the time of developing the proposal for this research, sparse academic literature had considered HIT or REHIT in a real-world context, or in patients with NDH. Two studies used REHIT with laboratory style methods (Metcalfe *et al*., 2011, 2015), and a further two studies had considered higher-volume HIT in patients with type 2 diabetes (Little *et al*., 2011b; Gillen *et al*., 2012). Also, Jung *et al*. (2015) measured adherence to higher-volume HIT over one month following a supervised laboratory intervention in individuals with NDH. Two further studies had used HIT in real-world settings, with group exercise sessions held outdoors in a public park (Lunt *et al*., 2014) or group cycling sessions within a university gym (Shepherd *et al*., 2015). To the authors knowledge, no studies had considered REHIT using NDH patients within an NHS setting. Furthermore, the HIT protocols and clinical endpoints differed across these studies. Two outcomes were of special interest: maximal oxygen uptake (or cardiovascular fitness) and blood glucose control. Although the effect of HIT on fitness was generally consistent, the effect on blood glucose control was less clear. Also, most were small studies making it difficult to draw inferences about the likely success of the planned trial in the specific NHS Trust used in this study. Success of the intervention was likely to be sensitive to features of the local context, such as cultural diversity, the built environment, socioeconomic status, and public transport. Therefore, feasibility work implementing REHIT into usual care was required. The aim of this preliminary study was to describe and report data relevant to the feasibility and acceptability of a REHIT intervention in NDH patients, with the intention of improving cardiovascular fitness and blood glucose control as primary outcomes. Moreover, the purpose was to assess whether it would be appropriate to progress to a larger-scale pragmatic trial, and to optimise the design and conduct of any such trial.

9.3 Methods

9.3.1 Participants

Patients with NDH, diagnostically defined as a glycated haemoglobin (HbA_{1c}) value of 42–46 mmol·mol (or 6.0–6.4%), were recruited from one UK hospital. This criterion aligns with recommendations from the World Health Organisation (John, 2012).

Inclusion

- Accessing the NHS Trust Weight Management Service (Specialist Diabesity Clinic)
- Aged between 18 and 65 years (inclusive)
- Diagnosed as NDH (using standard criteria)
- Male or female
- Any ethnicity
- Not currently partaking in a new structured exercise intervention
- Considered low or medium risk for exercise using standard risk stratification (ACSM logic model for cardiovascular disease risk [ACSM, 2014])

Exclusion

- < 18 years
- ≥ 66 years
- Currently partaking in a new structured exercise intervention
- Euglycaemic
- Diagnosed with type 1 or type 2 diabetes; taking insulin; history of end stage liver or kidney disease, neuropathy or retinopathy; has hypertension that cannot be controlled by standard medication; has cardiovascular disease, or another contraindication to exercise

- Considered high risk for exercise using standard risk stratification (ACSM logic model for cardiovascular disease risk [ACSM, 2014])
- Unable to adequately understand verbal explanations and written information given in English (no funds available in trial for translation services)

9.3.2 Recruitment

The Chief Investigator (BASES Accredited Sport and Exercise Scientist) formed a recruitment team at the hospital consisting several consultants, registrars, and a physiotherapist who all worked within the specialist diabesity service. A clinical trials assistant or clinical nurse specialist was not available to assist with recruitment for the trial. Patient eligibility to partake in the study was initially identified by the consultants via direct contact in clinic, and by registrars accessing patient records and contacting eligible patients by telephone. Eligible patients were then given study information (letter of invitation and patient information sheet, see appendices 10 and 11). If the patient was interested they provided verbal consent for the Chief Investigator to contact them to arrange a mutually convenient time to meet at the clinic (at the hospital) to discuss the study. During this initial appointment eligibility was confirmed, including further risk stratification using the American Heart Association/American College of Sports Medicine (ACSM) Health and Fitness Facility Pre-Participation Screening Questionnaire and the ACSM logic model for cardiovascular disease risk (ACSM, 2014). Patients considered high-risk were excluded from the study. The potential benefits, risks, and burdens associated with taking part in the trial were explained, and participants were given the opportunity to ask questions. Recruitment was free from undue influence from the recruiters, and coercion or other inducements were not used. Funds were not available to reimburse participants for taking part or for travel expenses. Written informed consent was obtained face to face at this initial appointment. Participants who consented had some baseline measures taken immediately by the Chief Investigator (blood pressure and body composition). At this point arrangements were made for the participant to undergo an electrocardiogram (ECG) to screen for ischaemic heart disease, and a blood test to confirm HbA_{1c} prior to starting the trial. Dates were agreed for further baseline testing (a fitness test) and the start of the REHIT intervention, pending satisfactory results from the ECG and blood test. Eligible patients who were contacted and decided not to participate in the trial were asked to give a reason for declining which was recorded, if agreed by the patient. The recruitment period was fixed at ten months (between March and December 2016).

9.3.3 Sample size

As this study was a feasibility trial no formal sample size calculation was undertaken. However, a proposed sample size of 40 (20 per group) was considered adequate to meet the objectives of the study, and was more than the recommendations given by Julious (2005) and van Belle (2002), who suggested 12 patients per arm is appropriate for a pilot study. If recruitment rate permitted, it was decided that the aim would be to increase the sample size (maximum 60) so that it would be consistent with the median sample size found in a review of 79 pilot studies by Billingham, Whitehead & Julious (2013). Sample sizes within this range are recommended for a feasibility trial that aims to estimate variability (via standard deviation) which can then be used in a formal sample size calculation for a full-scale trial (Lancaster, Dodd & Williamson, 2005; Sim & Lewis, 2012; Hooper, 2017). Notwithstanding, the main purpose of the feasibility trial was not to power the trial to test inferences about the intervention.

9.3.4 Randomisation and concealment

The aim was to assign participants to one of two conditions using random selection from a sequence of unmarked and opaque envelopes. The experimental group would receive usual care in addition to undertaking the REHIT intervention. The control group would simply receive usual care. Given the nature of the intervention, it would not be possible to conceal the treatment that participants were assigned to. However, due to insufficient recruitment, inclusion of a control group was not feasible. As such, it was not possible to apply randomisation procedures.

9.3.5 Intervention (REHIT)

Participants were required to partake in a total of 15 sessions of REHIT. They were permitted to achieve this by completing two or three sessions per week until the target had been accomplished. Thus, the intervention lasted 5–7 weeks dependent on the frequency of sessions per week. This flexibility within the intervention was used to aid compliance, and to more closely mimic how REHIT might be used in a real-life setting. All exercise sessions were performed on a magnetically braked cycle ergometer (Ergomedic 839E Digital, Monark, Vansbro, Sweden). Saddle height was adjusted for each participant to ensure close to full knee-joint extension (~170°) when the pedal was at the bottom of the cycle. Participants performed a total of 10 minutes cycling, inclusive of 2 (first session only), 4 (sessions 2 and 3), 6 (sessions

4 to 7), or 8 (sessions 8 to 15) × 5 s maximal effort 'sprints' against a braking force proportional to 7.5% of body mass. Exercise intensities in-between sprints were low (~60 W), and a warm-up (3 min at ~60 W) and cool down (2 min at ~30-60 W) were included within the 10-minute session (Figure 9.1). This was the same as the shortened-sprint REHIT protocol used in Chapters 7 & 8.

Affective valence (i.e. pleasure-displeasure) and perceived exertion were assessed using the Feeling Scale (FS) (Hardy & Rejeski, 1989) and Rating of Perceived Exertion (RPE) Borg scale (Borg, 1970), respectively. These were used as per the General Methods (section 6.3.3., pp. 119). These constructs were measured to consider the perceptual response to and acceptability of REHIT, with FS and RPE recorded at 25%, 50%, 75% and 100% of exercise completion (Figure 9.1).

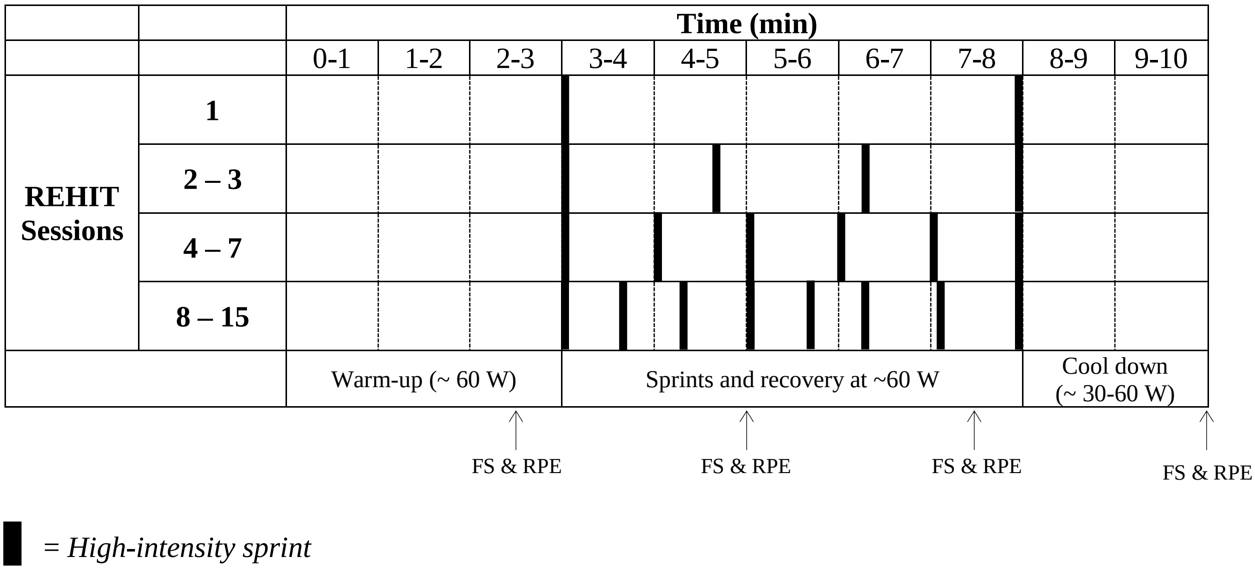

Figure 9.1 Schematic overview of the REHIT training protocol. Abbreviations: REHIT = reduced exertion high-intensity interval training, FS = feeling scale; RPE = rating of perceived exertion.

9.3.6 Usual care

Members of a multi-disciplinary team, including a consultant, diabesity specialist nurse, clinical psychologist, physiotherapist, and dietician worked together to promote patient self-management. Care was tailored to the specific circumstances of each patient after initial assessment and focussed on weight management, dietary education, behavioural therapy, and supported pharmacotherapy initiation as appropriate.

9.3.7 Outcomes to assess feasibility

Screening (eligibility)

The screening rate was defined as the number of patients who had contact with the recruitment team and who were assessed for eligibility using inclusion and exclusion criteria. This included those who decided not to take part, with their permission. Eligibility was determined by dividing the number of people screened by the number who met inclusion criteria.

Recruitment and reasons for not participating in the study

The recruitment team recorded why patients who met the inclusion criteria decided not to participate in the trial. The reason why patients who met the inclusion criteria and verbally consented to having their contact details given to the Chief Investigator and then subsequently decided not to participate were also recorded.

Adverse events

An adverse event was defined as any untoward occurrence that happened during the conduct of the study. All adverse events were recorded in the participant patient notes and were classified as serious or not, and attributable to the study or not, as per the 'Decision Tree for Adverse Event reporting' from the National Institute for Health Research, Clinical Research Network, Introduction to Good Clinical Practice Toolkit (National Institute for Health Research, 2017).

Retention rate

The retention rate was defined as the number of participants who remained in the study and did not drop out.

Completion rate

The completion rate was defined as the number of participants who completed the target number of 15 REHIT sessions.

Intervention adherence

Intervention adherence was calculated by summing the total number of participants and the target number of REHIT sessions (15 per participant), and comparing this against the actual completed sessions. This data was recorded by the Chief Investigator.

Intervention acceptability

Intervention acceptability was measured using the Feeling Scale (FS), Rating of Perceived Exertion (RPE), and Exercise Enjoyment Scale (EES) as surrogate markers. These scales measure various theoretical constructs related to the perceptual response associated with exercise. In hindsight, qualitative methods would have been a useful addition to explore the acceptability of the intervention, although some of these issues were explored informally via patient interaction (all sessions were supervised via the Chief Investigator).

Sample characteristics

With participant consent, socio-demographic (e.g. age, sex, ethnicity) characteristics were recorded by the Chief Investigator for purposes of the study.

Methodological issues of running the trial

Methodological issues of running the trial were explored based around a modified version of common issues that need to be evaluated in feasibility studies, as recommended by Shanyinde *et al*. (2011).

9.3.8 Outcomes to assess clinical effectiveness

Cardiovascular fitness (peak oxygen uptake)

Cardiovascular fitness, or peak oxygen uptake ($\dot{V}O_{2peak}$), was measured at baseline and after the REHIT intervention. Participants cycled on a magnetically braked ergometer (Ergomedic 839E Digital, Monark, Vansbro, Sweden) starting at 20 W, with required power to continue cycling increased by 15 W every 1 min thereafter, until volitional exhaustion or until a pedal cadence of 50–60 rpm could not be maintained. The Monark 839E ergometer provides for a constant rate of work independent of pedal cadence, however a lower threshold cadence was used to minimise risk of over-exertion. Participants respired through a face mask connected via a sample line and volume transducer to an online gas analysis system (Metamax 3B, Cortex, Leipzig, Germany). Respiratory volume, expired oxygen and carbon dioxide, and respiratory exchange ratio were measured with $\dot{V}O_{2peak}$ taken as the highest value averaged over 10 s periods. Several additional criteria were considered to establish if $\dot{V}O_{2peak}$ had been reached: an observed plateau in the oxygen uptake curve, a respiratory exchange ratio of 1.15 or higher, and a Rating of Perceived of Exertion (RPE) of 19-20 on the Borg scale (Borg, 1982).

Glycated haemoglobin (HbA_{1c})

Blood samples were drawn at the beginning and end of the study by a trained phlebotomist using standard venepuncture after an overnight fast. Glycated haemoglobin (HbA_{1c}) was measured by turbidimetric inhibition immunoassay (Roche, Basel, Switzerland) and were reported using the International Federation of Clinical Chemistry (IFCC) reference method (Weykamp *et al*., 2008).

Anthropometry and body composition

Stature and body mass were measured barefoot and wearing light clothes, using a stadiometer and Tanita® MC-180MA Multi-Frequency Body Composition Analyser (Tanita Europe, Netherlands), respectively. Body composition was estimated via whole-body bioelectrical impedance analysis (BIA) using a Bodystat® 1500 (COSMED Deutschland GmbH, Germany). With participants in a supine position, two source electrodes were placed on the dorsal surfaces of the foot and hand, with detector electrodes attached between the radius and ulna (styloid process) and at the ankle between the medial and lateral malleoli. A painless, localised electrical current (~800 μA at a frequency of 50 kHz) was introduced with impedance to current flow between the source and detector electrodes determined based on the relationship between voltage and current (Ohm's law). These relationships are used to quantify volume of body water which is then converted to body density. Along with body mass, stature, gender, age, and ethnicity; body density is used to predict percentage body fat using the Siri equation (Siri, 1961). BIA was selected as a non-invasive, safe, and easy means to predict body composition since other methods were not practical in the hospital clinic. BIA has been shown to underestimate body fat percentage by approximately 2% compared to Bod Pod® (air displacement plethysmography), but has been shown to have excellent reliability under standardised conditions (von Hurst, Walsh, Conlon, Ingram, Kruger & Stonehouse, 2015). Prediction of body fat percentage may be a more useful predictor of morbidity and mortality risk than the commonly used BMI (Yamashita *et al*., 2012; Böhm & Heitmann, 2013).

Blood pressure

Systolic and diastolic blood pressures were measured using an automated digital blood pressure monitor (A&D Medical, USA) with the pressure sensor placed over the brachial artery just above the antecubital fossa. Measurement was taken in a seated position after participants had rested for 5 minutes, with the arm relaxed level with the heart.

9.3.9 Analysis

No probability statistical testing was undertaken because the feasibility study did not aim to make inferences from the data. However, basic descriptive statistics including central tendency (mean) and variability (standard deviation) of scores were recorded to better understand the distribution of primary outcomes. Descriptive statistics were also used to summarise the screening, retention, completion, and adherence data.

9.3.10 Ethical approval and research governance

NHS ethical approval for the study was provided by the National Research Ethics Service Committee Yorkshire & The Humber (REC reference 15/YH/0226; IRAS project ID 167716), in addition to NHS Research Management approval from the relevant NHS Trust Research Committee (R&D ID 15/997).

9.4 Results

9.4.1 Screening (eligibility)

A total of 96 participants were screened by accessing patient records or using direct contact in clinic. Figure 9.2 shows the flow of participants throughout the trial. The eligibility rate was 47%. Of the 96 patients identified, 51 were not eligible to partake in the trial, with two main reasons for this (table 9.1). First, 16 patients were unwilling to be contacted by the Chief Investigator or did not want to receive further information form the recruitment team after being provided with initial verbal information. Second, 26 participants (27% of all the participants screened), since original diagnosis were no longer within the diagnostic range for NDH (i.e. 42–46 mmol·mol) with blood glucose control either having moved into the overt type 2 diabetes range, or returned to euglycaemia (sometimes following lifestyle change). The remaining 45 patients received information about the trial.

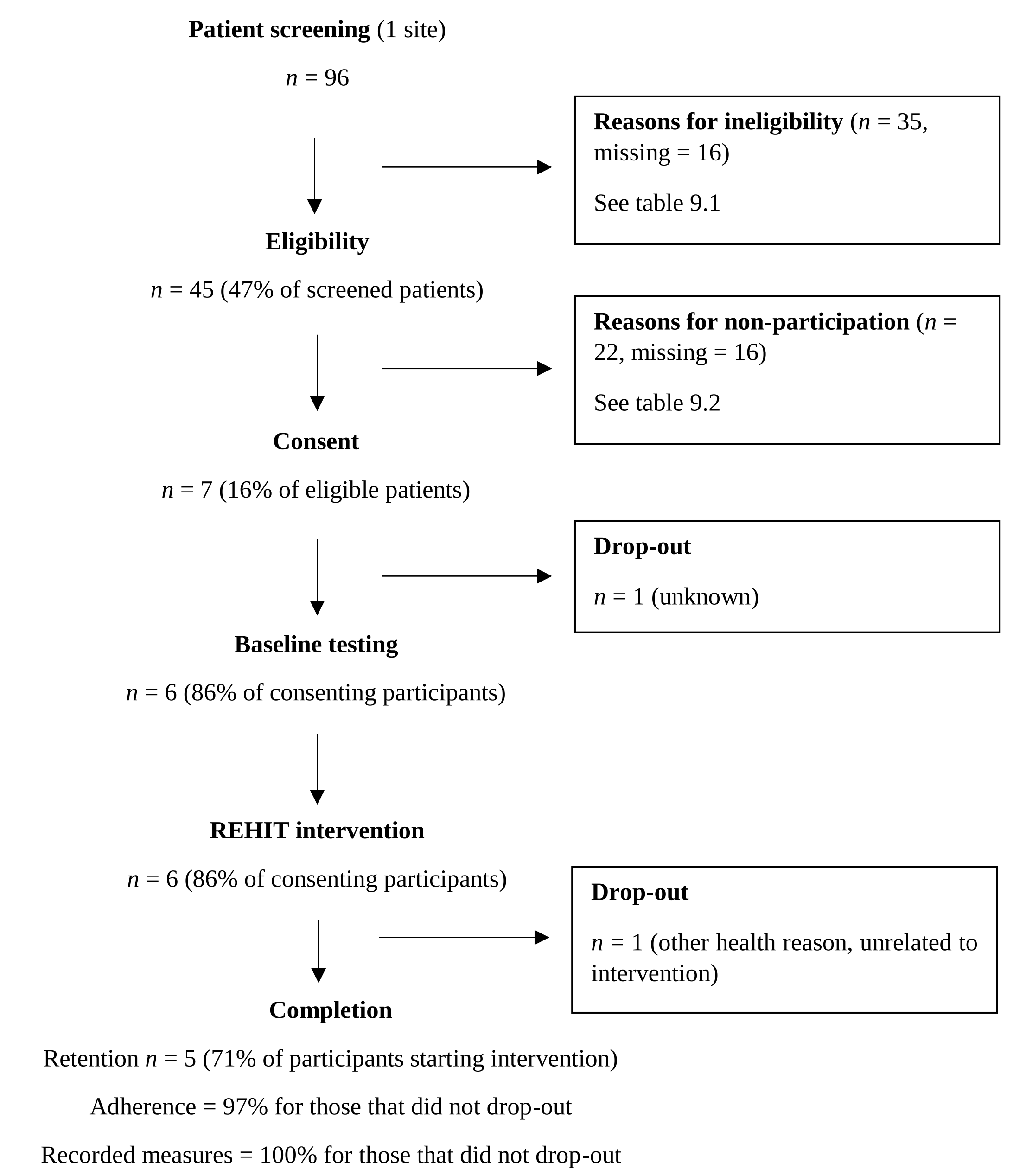

Figure 9.2 Flowchart of participants. Abbreviations: REHIT = reduced-exertion high-intensity interval training

Table 9.1 Reasons for ineligibility (*n* = 51).

Reason	**Number of patients**
No longer meet diagnostic criteria (i.e. 42–46 mmol·mol)	26
Other health reason	8
Unable to understand English instruction	1
Unknown or unwilling to be contacted	16
Total	51

9.4.2 Recruitment and reasons for not participating in the study

During the period from March 2016 to December 2016, recruitment was difficult. The consent rate was 16% (7 out of 45 eligible patients), with 'lack of time' cited as the most common reason for not partaking (15 out of 38, 39%). Sixteen patients did not have a reason for not participating recorded (table 9.2). Explanations for the poor recruitment were numerous. Many patients were reluctant to partake in the trial or were unwilling to be contacted, as mentioned above. Again, the number of eligible patients from those identified through screening was reduced due to patients no longer meeting inclusion criteria. Also, the recruitment team (single site) failed to initiate screening for eligibility at the predicted rate, especially during direct contact. Reasons for this included extremely busy clinics, insufficient frequency with which consultants see patients with chronic illness for lifestyle change advice in primary and secondary care, and the fact that 'pre-diabetes' may not be considered a serious illness by patients. A total of seven participants volunteered to take part in the study (7% of those screened, 16% of eligible patients), with one participant withdrawing before baseline testing (Figure 9.1). Randomisation procedures were not feasible due to low recruitment, with the remaining six participants assigned to the REHIT intervention group.

9.4.3 Adverse events

No adverse events were reported during, or because of, the REHIT intervention.

9.4.4 Retention rate

The retention rate was 71% for patients that consented to partake in the study (2 out of 7 participants dropped out). However, one participant withdrew before baseline testing. The retention rate for participants who started the REHIT intervention was 86% (5 out of 6 participants completed).

Table 9.2 Reasons for not participating (*n* = 38).

Reason	**Number of patients**
Lack of time	15
Distance or travel issues	4
Unable to contact	1
Not interested	2
Unknown	16
Total	38

9.4.5 Completion rate

The completion rate was based on the number of participants who completed the target number of 15 REHIT sessions. Of the five participants who completed the study: three participants managed 15 out of 15 sessions within 5–7 weeks, one completed 15 sessions > 7 weeks, and one participant completed 13 sessions only. Therefore, completion rate was 57% based on the seven participants that provided consent to partake in the study (4 out of 7), and 80% based only on the participants who did not formally drop-out of the study (4 out of 5).

9.4.6 Intervention adherence

Intervention adherence was calculated by summing the total number of participants and the target number of REHIT sessions, and comparing this against the actual completed sessions. Therefore, the maximum number of sessions possible was 105 (seven participants who consented to partake × 15). As such, the completion rate was 72% (76 out of 105 sessions completed). However, the completion rate was much higher based on the five participants that did not drop-out of the trial (73 out of a possible 75 sessions completed, 97%).

9.4.7 Intervention acceptability

Acceptability of the intervention was good, with in-task pleasure and perceived exertion measured during REHIT using the FS and RPE scales, respectively. Enjoyment was also measured after cessation of exercise using the EES. Table 9.3 summarises perceptual responses throughout the intervention. Aggregate peak FS values ranged between 1.4 and 2.6 units, where 1 is 'fairly good' and 3 is 'good'. Similarly, aggregate peak RPE values ranged between 12.7 and 13.9 units, corresponding to 'somewhat hard' and between 'somewhat hard' and 'hard'. Enjoyment was reported as between 5.1 and 6 EES units (between "quite a bit" and "very much"). Taken together, these data suggest that the intensity of the REHIT protocol was tolerable, associated with modest perceived effort, and was enjoyable. These theoretical concepts were used as a proxy for intervention acceptability. For the participant that dropped out of the study prior to baseline testing, it was not identified if the intervention and trial procedures were unacceptable.

9.4.8 Sample characteristics

Sample characteristics are described in table 9.4.

9.4.9 Methodological issues of running the feasibility study

Methodological issues of running the feasibility study are summarised in table 9.5 as per the framework suggested by Shanyinde *et al*. (2011).

Table 9.3 Intervention acceptability. Peak perceptual responses to REHIT throughout the intervention (n = 5).

	Value	Notes
FS		Affective valence (i.e. pleasure-displeasure) was assessed using the single-item, 11-point Feeling Scale (Hardy & Rejeski, 1989). The FS uses a bipolar scale and ranges from –5 'very bad' to + 5 'very good', with anchors designated for 0 (neutral) and all odd integers in-between.
Sessions 1–3	2.6 ± 0.8	
Sessions 4–7	1.7 ± 0.7	
Sessions 8–15	1.4 ± 0.7	
Average	1.9 ± 0.6	
RPE		
Sessions 1–3	12.7 ± 2.1	Exercise exertion was monitored using a rating of perceived exertion using the 15-point Borg scale (Borg, 1970). The scale ranges from 6 'no exertion' to 20 'maximal exertion' with anchors designated for all the odd integers in-between.
Sessions 4–7	13.7 ± 0.9	
Sessions 8–15	13.9 ± 0.7	
Average	13.4 ± 0.6	
EES		
Sessions 1–3	6.0 ± 0.8	Enjoyment was assessed using the single-item, 7-point Exercise Enjoyment Scale (Stanley & Cumming, 2009). Anchors are given at every integer, ranging from 1 'not at all' to 7 'extremely'.
Sessions 4–7	5.2 ± 1.1	
Sessions 8–15	5.1 ± 0.3	
Average	5.4 ± 0.5	

Note: Data are presented as aggregate mean ± standard deviations. Values were recorded at 25%, 50%, 75%, and 100% of REHIT bout completion, with peak values only (at 75%) reported here.
Abbreviations: EES = exercise enjoyment scale, FS = feeling scale, REHIT = reduced-exertion, high-intensity interval training, RPE = rating of perceived exertion.

Table 9.4 Participant characteristics and changes in outcomes to assess clinical effectiveness after the REHIT intervention (female n = 3, male n = 2).

	Pre-intervention	**Post-intervention**
Age (years)	46.4 ± 6.1	-
Mass (kg)	71.2 ± 15.5	71 ± 14.8
BMI (kg·m^2)	26.3 ± 3.9	26.2 ± 3.7
$\dot{V}O_{2peak}$ (ml·kg·min^{-1})	30.6 ± 4.6	33.8 ± 4.3
HbA_{1c} (mmol·mol^{-1})	44 ± 1.6	43.2 ± 0.8
Fat mass (%)	16.2 ± 5.8	16.2 ± 6.1
Systolic BP (mm Hg)	118.4 ± 14.9	118 ± 13.3
Diastolic BP (mm Hg)	75.6 ± 8.9	74.2 ± 8.3

Note: Data are presented as mean ± standard deviations.
Abbreviations: BMI = body mass index, BP = blood pressure, HbA_{1c} = glycated haemoglobin A_{1c}, REHIT = reduced exertion high-intensity interval training, $\dot{V}O_{2peak}$ = peak oxygen uptake.

9.4.10 Outcomes to assess clinical effectiveness

Table 9.4 summarises participant characteristics and outcomes to assess clinical effectiveness, which would be designated as primary outcomes in the conduct of any larger-scale pragmatic trial. The feasibility study was not powered to test the effectiveness hypotheses associated with any planned main large-scale trial, and the sample size was very small. Nevertheless, there appeared to be a trend for increased cardiovascular fitness after the intervention. Mean $\dot{V}O_{2peak}$

increased from 30.6 ± 4.6 $ml \cdot kg \cdot min^{-1}$ to 33.8 ± 4.3 $ml \cdot kg \cdot min^{-1}$ (9% increase). There appeared to be no change in any of the other outcomes, including HbA_{1c}.

Table 9.5 Summary of methodological findings for feasibility research.

Issue	Findings	Comments
Sample size calculation	It was not possible to estimate variability for a formal sample size calculation	Sample size was too small to permit this, although this was not the main aim of the trial
Eligibility	Ineligibility was primary due to two reasons: 1. Participant refusal 2. Participant no longer met diagnostic criteria	Many participants who were identified from patient records as meeting the diagnostic criteria for NDH, no longer had an HbA_{1c} within the diagnostic range 45 out of 96 (47%) patients approached were eligible
Recruitment	Recruitment was very difficult, with issues at clinician and participant levels	Despite initial clinician enthusiasm, they failed to identify necessary participants (other than via patient records) Eligible patients not willing to take part (38/45)
Consent	Low conversion to consent	7 (16%) out of 45 eligible participants
Randomisation procedures	Not applied Some participant bias towards the intervention group was evident	Although planned, randomisation was not applied due to low recruitment. Control arm of the trial was abandoned
Blinding procedures	Not possible given the nature of the intervention	-
Adherence to the intervention	Satisfactory adherence to the intervention Completion was good for those that did not drop-out	76 out of a possible 105 (72%) REHIT sessions were competed (i.e. 7 participants × 15 sessions each) 73/75 (97%) completion for those that did not drop-out: Completed 15/15 sessions with 5–7 weeks, n = 3; Completed 15/15 sessions > 7 weeks, n = 1; Completed < 15 sessions, n = 1
Acceptability of intervention	FS, RPE and EES measures were favourable	See summary of outcomes to assess clinical effectiveness (table 9.3)
Cost and duration of intervention	Not assessed	Difficult to establish cost of CI time and equipment use ECG cost = £45.00 per unit, over standard care HbA_{1c} cost = £2.66 per unit, over standard care
Outcome assessment	Outcome measures assessed the main areas of interest as planned	5/5 (100%) who completed the intervention recorded all measures See summary of outcomes to assess clinical effectiveness (table 9.4)

Selection of most appropriate outcomes	Outcomes measured were the most appropriate for the study aims	Qualitative methods would have been a useful addition to explore the acceptability of the intervention
Retention	Retention rate was acceptable	5/7 (71%) remained in the study
Logistics of multi-centre trial	Not applicable, single centre trial	-
Components of the protocol work together	REHIT protocol and outcome measures worked well. However, eligibility, recruitment and consent were poor	Once recruited, retention was acceptable. However, there were difficulties in communication between the CI and recruitment team, and the ability of the recruitment team to identify participants was poor

Methodological issues based on Shanyinde *et al*. (2011) and Bugge *et al*. (2013). Abbreviations: CI = chief investigator, ECG = electrocardiogram, EES = exercise enjoyment scale, FS = feeling scale, HbA_{1c} = glycated haemoglobin A_{1c}, REHIT = reduced-exertion, high-intensity interval training, RPE = rating of perceived exertion.

9.5 Discussion

The purpose of this feasibility trial was to collect data to improve trial procedures to optimise the design and conduct of any large-scale pragmatic trial. Patients with NDH were recruited to take part in a REHIT intervention delivered in an NHS practice setting, with the aims of any such future trial to improve cardiovascular fitness and blood glucose control. The findings revealed several feasibility issues that would need to be considered in the design and operationalisation of a future trial. Such findings present an opportunity for important learning in relation to participant eligibility, challenges to recruitment, patient consent, and the duration of the study. Given these issues, it is recommended that the trial is not feasible in its current form. However, future studies would benefit from this initial intervention development work, and this underlines the role of feasibility studies undertaken to improve methodological precision and to remove the influence of bias. Some aspects of the trial worked well including adherence to the intervention and general experimental procedures.

The small sample recruited limits interpretation of data. However, it reinforces the purpose of feasibility studies and the need to answer questions relating to whether a study can be done in terms of estimating the rate of eligible people who are willing to participate (Hooper, 2017). Six participants undertook baseline testing and commenced the exercise intervention. This occurred because of a range of challenges related to screening, eligibility, and lack of consent to take part in the study – further compounded by a limited recruitment period (10 months) due to unforeseen delays in acquiring ethical clearance for the study. More than a quarter of the potential participants identified via screening of patient records, were ineligible due to no longer meeting the diagnostic criteria for NDH. That is, since original diagnosis, HbA_{1c} values had increased into the diagnostic range for diabetes, or decreased to normal levels. As such, screening for future diabetes risk using borderline HbA_{1c} values of 42–46 mmol·mol represents a narrow window of opportunity, and patient recruitment needs to occur soon after diagnosis. Anecdotally, the NHS DPP has experienced similar issues using HbA_{1c} as a screening measure (C. Rajeswaran, personal communication, December 2016), which corresponds with the fact that individuals are eligible for inclusion based on HbA_{1c} results taken within the last 12 months (NHS Diabetes Prevention Programme, 2017). Part of the problem lies in the significant biological and assay variability associated with predicting blood glucose excursions. Non-diabetic hyperglycaemia or 'pre-diabetes' are umbrella terms to describe blood glucose concentrations that are higher than normal but below that defined as diabetes. The terms encompass several separate conditions, including impaired glucose tolerance (IGT) and impaired fasting glucose (IFG), which reflect different metabolic abnormalities. A meta-analysis of the progression rates to overt diabetes based on these different measures of glycaemia found that more than 50% of patients with IGT do not progress to diabetes within the next 10 years, compared to around two thirds of patients with IFG (Morris *et al.*, 2013). Similar studies using HbA_{1c} suggest a rate of progression like those for IFG (Edelman, Olsen, Dudley, Harris & Oddone, 2004; Droumaguet *et al*., 2006; Pradhan, Rifai, Buring & Ridker, 2007), whereas the highest risk for developing type 2 diabetes is found in those with both IGT and IFG (Gerstein *et al*., 2007; Zhang *et al*., 2010; Morris *et al*., 2013). Furthermore, the use of ADA or World Health Organisation criteria to define NDH has also been shown to affect the incidence of diabetic states (Forouhi *et al*., 2006; Bansal, 2015), and detecting NDH using HbA_{1c} defines twice as many individuals as the gold standard oral glucose tolerance test (Yudkin & Montori, 2004). Adding to this complex reality, the HbA_{1c} test is neither sensitive nor specific and results in substantial under diagnosis (i.e. false negatives) and over diagnosis (i.e. false positives) (Barry *et al*., 2017). Therefore, despite the simplicity and convenience of using HbA_{1c}, the process of accurately screening and case finding eligible patients is inherently problematic.

Recruitment of participants was difficult which is a valuable finding of the current study. Many participants were reluctant to participate with 'lack of time' cited as the most common reason (33% of those eligible). This is a known issue with physical activity lifestyle interventions (Korkiakangas *et al*., 2009). Sixteen participants (a further 36% of eligible patients) did not provide a clear reason for not participating, or did not have a reason recorded. It is conceivable that these patients also deemed the proposed intervention to be unacceptable because of lack of time. Clinician engagement was problematic as the recruitment team failed to screen and identify eligible patients at the predicted rate, and this was an issue during direct patient contact (as opposed to screening via patient records). Reasons for this included busy clinics and insufficient patient contact time. However, a recent study using exercise in disease-free cancer survivors reported that recruitment staff did not approach people who 'did not look like an exerciser' (Courneya *et al.*, 2014). Although speculative, it is possible that recruiters in the current study, consciously or otherwise, did not recruit patients who they thought were unlikely to agree to take part, or who they thought might find the intervention difficult or even unsafe. Hence, for any future pragmatic trial it would be important to clearly define eligibility criteria, and to provide recruiters with relevant information and training about benefits and contraindications of physical activity (Hubbard *et al.*, 2016). The principle of equitable healthcare is important in feasibility trials (Oliver & Mossialos, 2004), and as such it is important that when exercise interventions are implemented in practice, they are presented to all patients who would benefit from them. Notwithstanding, the safety of HIT in those with a range of diseases is an important consideration in need of further research.

A further general matter related to obtaining consent from patients to take part in the trial could be that patients and healthcare teams did not perceive NDH to be a serious condition. The term 'pre-diabetes' is a misnomer because not everyone diagnosed as NDH will progress to diabetes. Accordingly, it has been argued that current definitions of risk that include diagnosis of pre-diabetes, create unsustainable burdens on healthcare systems and risk unnecessary medicalisation (Yudkin & Montori, 2014). Nevertheless, the rationale behind treatment of NDH includes prevention or delay of development of diabetes, the consequences of diabetes, and the consequences of pre-diabetes itself (Bansal, 2015). A recent meta-analysis of 53 prospective cohort studies (n = 1,611,339) identified that NDH, defined as IGT, IFG, or raised HbA_{1c}, was associated with increased risk of coronary heart disease, stroke, and all-cause mortality (Huang, Cai, Mai, Li & Hu, 2016). Moreover, it was found that health risk might be increased in people with an HbA_{1c} as low as 39 mmol·mol. Long-term intervention studies have demonstrated that lifestyle change which includes physical activity targets, can result in a sustained reduction in the incidence of diabetes for individuals with NDH (Knowler *et al.*, 2002; Li *et al.*, 2008). There also seems to be a consistent reduction in the incidence of retinopathy, although associations with reduction in risk of other microvascular conditions such as neuropathy and nephropathy are less clear (Gong *et al*., 2011). Other reviews suggest the evidence for association with macrovascular disease is conflicted (Hopper, Billah, Skriba & Krum, 2011). Therefore, based on some ambiguity in the evidence base for the risk associated with NDH, and based on the findings of the present feasibility study, dedicated local recruiters should be considered essential for any future trials. This recommendation is based on several lines of reasoning. First, it would allow for improved screening, identification, and recruitment of participants to reach a sample size to sufficiently power the trial to meet the stated research objectives. Second, with appropriate training and support, dedicated recruiters could more accurately inform prospective participants about the benefits and risks of exercise, including the general risks associated with NDH, ensuring equity in access to healthcare. Third, having a dedicated recruiter would ameliorate the burden on busy clinicians.

Several aspects of the trial worked well. Adherence to the exercise intervention was very high, with 97% of sessions completed for the five participants that finished the study. Also, the acceptability of REHIT was good which is important because for REHIT to have any role in public health, the activity must be tolerable and acceptable to those for whom the intervention is intended. Protocols that are overly strenuous are likely to result in negative affective responses which may lead to future avoidance of the activity and resultant poor adherence (Hardcastle *et al*., 2014). This would irrefutably diminish the effectiveness of such interventions, because adherence is a pre-requisite for success. Accordingly, an aim of the current feasibility study, and of any future pragmatic trial, was to use a shortened-sprint REHIT protocol which, as preliminary evidence demonstrates, results in more favourable cognitive and affective responses (see Chapters 7 and 8). FS, RPE, and EES scales were used to quantify pleasure-displeasure, exertion, and enjoyment, respectively. Together with adherence data, these constructs were used as proxy for intervention acceptability. The aggregate peak FS value across the intervention was 1.4 units, which using the nomenclature associated with this numerical rating is somewhat above ‘fairly good’. Importantly, despite a gradual increase in exercise intensity across the intervention, values did not correspond to negative affective states at any point (i.e. displeasure, or < 0 on the FS scale, table 9.3). Hedonistic theories of motivation, such as dual-mode theory, propose that exercise above a certain intensity threshold results in a cascade of physiological responses that negatively influence affective states (Ekkekakis *et al*., 2008). These perturbations were minimised in response to the REHIT protocol used in the current study, which is important because minimising bi-dimensional displeasure could be key to optimising behaviour (Cabanac, 2006), and could in-turn predict long-term exercise adherence (Williams *et al*., 2008; Williams *et al*., 2012). A related assumption within this framework is that people typically choose not to engage in activities that they find aversive (Pollock, 1978). Ratings of enjoyment associated with the intervention were also favourable. It is worth noting that affective valence and enjoyment overlap, but are not identical constructs. An assumption of dual-mode theory is that there exists a distinction between core affect, such as hedonistic pleasure or pain, and more distinct emotional experiences such as enjoyment that require cognitive appraisal and appreciation of the totality of the experience (Wankel, 1993; Russell & Barrett, 1999). Therefore, when taken together, the enjoyment and affective responses suggest the protocol used in this study could be suitable to use in a larger-scale trial, and might be a genuinely time-efficient, yet tolerable and sufficiently enjoyable approach to exercise for people with NDH.

Considering the challenges to feasibility highlighted in this study, a decision should be made as to what changes to make for a future pragmatic trial. Given that the REHIT protocol was well tolerated and generally deemed to be enjoyable, adapting this does not seem to be necessary. Furthermore, the intervention already included an element of flexibility by allowing participants to exercise two or three times per week for a total time commitment of 20–30 min. A minimum volume of exercise is required to improve health outcomes and, considering the design of the current REHIT intervention, it is unlikely that the time commitment could be reduced further. Rather, adjustments to the clinical context, including screening and recruitment strategies, within which the intervention could be delivered, might be beneficial. Inclusion of a dedicated local recruiter should be central to this, as discussed. Considering that a significant number of eligible patients did not provide consent to take part in the study, it is likely that perception of prospective intervention acceptability is an immediate concern. This may relate to perceived lack of time, or other perceived burdens of the intervention such as travel and expense. Despite the finding that REHIT was acceptable for those who completed the trial, others may view the nature, frequency, or intensity of the planned exercise unacceptable. In part, this perception could be assuaged by a knowledgeable recruiter. Furthermore, given the challenges faced in terms of recruitment it will be important to allow a sufficient time frame for recruitment of participants, and to accommodate this in the early stages of planning. This should include gaining ethical permission which may be delayed due to the requirements related to health screening for potential participants (e.g. 12-lead ECG), evaluation of specialist equipment, and development of a delegation log for the health care and research teams.

An alternative option is to use financial incentives to aid with recruitment and retention, as used in other trials, including exercise trials, that aimed to improve health related behaviours (Wilkinson, 2008; Volpp *et al*., 2008; Marteau & Ashcroft, 2009; Mitchell *et al*., 2013). However, the aim of any follow-up trial would be pragmatic in nature, and to achieve this the benefit and feasibility of the intervention must be demonstrated in real-world conditions. Thus, a financial incentive is a confound that may go beyond the confines of what is available in routine practice. As highlighted by Bugge *et al*. (2013), the choice here is to use incentives to increase recruitment and adherence but provide results from an intervention that might be unrealistic in a real-world setting, or not to use incentives and to conduct a pragmatic trial that might show effectiveness if only participants would adhere. A third option also espoused by Bugge *et al*. (2013) is to increase the complexity of the trial to include two components: intervention and incentive versus intervention alone. A separate consideration is that many eligible patients might have found the location of the intervention (i.e. a hospital based clinic) to be inconvenient or unacceptable. The rationale for running the intervention at the hospital was to co-locate clinical facilities with exercise prescription. By allowing clinical consultation and then commencement of exercise prescription to take place at the same place, it was hoped that patient care would be more seamless and that this might improve patient engagement. Conceivably, the intervention could be located at community or even home settings to improve the convenience for many patients. However, these considerations were beyond the scope of the current feasibility study. Other strategies to improve the clinical context include systematic recruitment plans that incorporate both active and passive strategies, technology-supported visit reminders, up-front scheduling, and using a study coordinator who has a strong relationship among the healthcare team and patients (Page & Persch, 2015). In the current study, the Chief Investigator (exercise physiologist) performed this role, but this was on a part-time basis, which meant it was challenging to be the primary contact for the study.

Long-term diabetes prevention trials incorporating physical activity as part of supported lifestyle change have been shown to reduce the incidence of diabetes in individuals with NDH by 58% (Knowler *et al*., 2002). However, it is not clear if interventions lacking individual and group support would be similarly effective. Exploring ways of minimising physical inactivity and improving cardiovascular fitness in those most at risk of disease remains a demanding priority. Accordingly, studies addressing the effectiveness of REHIT in real-world settings remains important to further this research agenda. Several studies have considered affective response to HIT (e.g. Jung *et al*., 2014; Decker & Ekkekakis, 2017), but few have been conducted outside of a laboratory environment. Since conception of the current feasibility study, two trials have considered HIT or REHIT in patients with type 2 diabetes (Redval *et al*., 2016; Ruffino *et al*., 2016). Both studies compared the effects of REHIT intervention against an alternative exercise programme in patients with diabetes. Although participants were recruited from hospitals (in Norway and the UK, respectively), the interventions nevertheless took place in a laboratory environment. Increases in $\dot{V}O_{2max}$ (~7–10%) following REHIT were found, although oral glucose tolerance test derived measures of insulin sensitivity and HbA_{1c} were not improved. However, changes in HbA_{1c} are expected to be small. A meta-analysis demonstrated that in patients with type 2 diabetes, structured aerobic, resistance, or combined exercise training is associated with an HbA_{1c} decline of just −0.67% (Umpierre *et al*., 2011). The trend in results in the current feasibility study are in-line with these results, hence any future trial would need to be sufficiently powered to detect small, but meaningful, changes in HbA_{1c}. The need to perform further studies examining the efficacy, acceptability, and longer-term adherence to REHIT as a practical 'real-life' intervention remains (Ruffino *et al*., 2016).

Sample and research design limitations should be considered alongside the findings of this feasibility study. As mentioned, by carrying out the REHIT intervention within a hospital practice setting, this study co-located clinical facilities with exercise prescription. The Chief Investigator for the study performed the exercise specialist role, yet it is not clear who could carry out this role within routine practice. It has been proposed that a range of healthcare professionals, such as specialist diabesity nurses or physiotherapists, could have an important role to play in treating physical inactivity related disease through exercise interventions (Haines *et al*., 2012), and this could include administering REHIT since protocols are straightforward to communicate, require minimal equipment, and could be incorporated into a multidisciplinary diabesity clinic. Nevertheless, this would need to be considered alongside competing demands, and staff would need appropriate training and organisational support to do so (Brown, 2006; Haines *et al*., 2012). In the present study, further practical issues were evident when locating a suitable space within the hospital to deliver the exercise intervention, because specialist facilities for this purpose do not routinely exist. From a sampling perspective, due to the issues faced regarding screening and recruitment, it is difficult to determine if participants recruited to any future trials would be typical of the target population. Comparing the characteristics of eligible consenting and non-consenting patients can be used as an indicator to assess if participants are representative of the target population. This information was not systematically recorded in the current study, and should be for future trials. Similarly, a greater understanding of reasons for non-participation is needed because this information can be used to improve consent rate in future studies (Hubbard *et al*., 2016). With hindsight, qualitative methods would have been a useful addition to explore some of these issues, and the general acceptability of the intervention. A measure of exercise intentions to predict future exercise behaviour would also be a valuable additional measure for subsequent studies. Finally, it was not possible to determine if the processes for achieving randomisation would work smoothly. It is likely that some bias would be evident towards the REHIT intervention group, as participants would perceive this to be good for them. This could be lessened by including an active control group, rather than solely standard care. This would be appropriate as the effects of the intervention should be considered alongside those associated with current physical activity recommendations.

In conclusion, this study describes the feasibility and acceptability of a REHIT intervention in NDH patients, with the intention of improving cardiovascular fitness and blood glucose control. In its current form, the study is not feasible. However, the findings form the basis for important learning in relation to the potential for transfer of exercise interventions into real-life scenarios with specific populations. Future interventions need to be sensitive to features of the local context such as the built environment, socioeconomic status, and the specific needs of individuals with chronic disease. Some aspects of the study worked well, such as the adherence to and the acceptability of the REHIT intervention. The findings highlighted several changes that would be required before progress to a larger-scale pragmatic trial is appropriate. These changes must address issues related to screening, recruitment, and consent of eligible patients. Use of a dedicated local recruiter, participation incentives, and training of the healthcare team must be balanced against broader considerations around the realities of building a pragmatic study into routine practice. It was not possible, based on the data collected, to estimate variability and to use this in a formal sample size calculation for a full-scale trial. Recruiting a sample sufficiently large to power the trial to meet the stated research objectives will be important, especially considering that clinical changes in HbA_{1c} are small. As discussed, allowing a longer period for recruitment will be essential for achieving this. Underpowered studies limit the ability to draw conclusions about the effect of interventions on health outcomes, and are more likely to be abandoned. Therefore, in-line with the MRC's complex interventions framework, it is recommended that the process of intervention development continue post-feasibility. This is warranted because REHIT may be a genuinely time-efficient and acceptable exercise intervention to counter the burden of physical inactivity, and may result in physiological benefit without overly compromising perceptual response.

PART FOUR: SYNTHESIS

Chapter 10 Conclusion, Recommendations and Summary

10.1 Concluding discussion

Time efficiency is frequently lauded as one of the practical benefits of HIT. However, it is intellectually dishonest to suggest this is true based solely on the minimal amount of time spent completing high-intensity 'sprints'. If the total duration of a HIT session is not appreciably different to current exercise guidelines – necessitated by the inclusion of warm-up, cool down, and recovery in-between sprints – it is no more likely to appeal to individuals who do not engage in regular exercise due to perceived 'lack of time'. Furthermore, the increased intensity may be a separate barrier, resulting in an avoidance response and poor exercise adherence. As highlighted in the review of literature in this thesis (Chapter 5), much of the evidence supporting the efficacy of HIT is in fact based on protocols that are not appreciably more time-efficient than current exercise guidelines, when considered on a per session basis. However, a minority of studies suggest REHIT may be a genuinely time-efficient alternative (e.g. Metcalfe *et al*., 2011; Revdal, Hollekim-Strand & Ingul, 2016; Ruffino *et al*., 2016). It is not clear if this iteration of HIT attenuates some of the benefits of higher-volume or more strenuous HIT (i.e. Metcalfe *et al*., 2016a), although evidence suggests it is associated with meaningful improvements in $\dot{V}O_{2max}$ and some of the molecular skeletal muscle responses akin to other types of HIT (Metcalfe *et al*., 2011, 2015; Ruffino *et al*., 2016). The acceptability and tolerability of this type of HIT among sedentary or insufficiently active individuals is likely to be more favourable. As such, REHIT could be adopted alongside broader lifestyle change, as a public health strategy to counter the deleterious effects of low fitness and physical inactivity, including some populations with chronic disease (Ruffino *et al*., 2016).

The aims of the research studies included in this thesis, although distinct in their application and focus, were bound by the theme of exploring an approach to REHIT that, despite including maximal-effort cycling sprints, would not overly compromise perceptual response. The original contribution to knowledge is that a shortened-sprint protocol can improve $\dot{V}O_{2peak}$ whilst minimising large negative peaks in affective response. A hedonistic theory of motivation, based on dual-mode theory, was used to consider how sensations of affect (pleasure-displeasure), enjoyment, and perceived effort may in-turn predict future exercise adherence, and was in advance of very recent suggestions to focus on protocols with fewer or shorter sprints (Vollard & Metcalfe, 2017). The main findings were that both traditional REHIT and shortened-sprint REHIT resulted in affective responses that were neutral or positive. Importantly, the protocols did not result in large negative peaks for most participants, although some heterogeneity in results was evident. This was observed in response to a single exercise bout (Chapter 7) and a longitudinal intervention (Chapter 8). Additionally, affective responses and perceived effort were more favourable for shortened-sprint REHIT. Given that both protocols resulted in small but clinically significant increases in $\dot{V}O_{2peak}$, the 20-s sprints used for traditional REHIT may be unnecessarily strenuous. This is important because longer duration maximal-effort sprints are more likely to be associated with negative affective states, since a greater deviation from homeostasis is likely to occur, which was evident in the studies included in this thesis. There was however a trend for greater increase in $\dot{V}O_{2peak}$ after traditional REHIT and significant heterogeneity in training response was evident for both protocols.

To maintain study fidelity and minimise error interpreting outcomes, various methodological strategies were used to monitor and ensure reliability and validity of the exercise interventions used throughout this thesis. All interventions were administered by the same qualified exercise scientist, to ensure they were delivered as prescribed (content fidelity) and with consistency across participants (process fidelity). Research was based on established underling theory and a degree of control over known confounding variables was applied (e.g. diet and other physical activity). Furthermore, all equipment was calibrated to minimise measurement variation. These strategies focus on internal validity and contribute to the quality of the research, although blinding of assessors who measured outcome variables and allocation concealment were not possible. Studies 1 and 2 were sufficiently powered to detect significant differences, and this is necessary to make inferences about populations based on data collected from a sample. Deductive reasoning was justified for the studies in this thesis on the basis that the theoretical constructs are well established (e.g. hedonistic theories of motivation and mechanistic responses to HIT). As such, the methodology justifies the methods used which have been widely used by others (e.g. Allison *et al.*, 2017; Decker & Ekkekakis, 2017) and are reproducible (e.g. test-retest reliability for $\dot{V}O_{2peak}$ testing is known to be ~2%; Gore, Tanner, Fuller & Stanef, 2013). Study one used a randomised counterbalanced crossover design to minimise the chance of order effects influencing the results, which is a common issue with repeated measures designs. Study 2 used a randomised positive-controlled design to eliminate selection bias. Furthermore, comparing shortened-sprint REHIT against a previously tested intervention (i.e. traditional REHIT), rather than a control group receiving no treatment, is appropriate since REHIT has so far been shown to be the minimal amount of exercise to induce improvements in cardiovascular fitness, and hence new iterations should be compared against this.

Since the time commitment per session was 10 minutes, inclusive of a warm-up and cool down, shortened-sprint REHIT could be a genuinely time-efficient approach to exercise for those who otherwise would not engage with higher volume exercise recommendations. However, compared to traditional REHIT, shortened-sprint REHIT is relatively complex using a more structured exercise regime requiring greater self-regulation. Therefore, it is possible that shortened-sprint REHIT could be deemed less practically manageable. Similarly, both protocols use specialist cycle ergometers that allow very rapid transition from unloaded pedalling to a high mechanical or electromagnetic braking force which permits generation of high peak power within the first few seconds of high-intensity intervals. This characteristic may be required to elicit the metabolic benefits associated with REHIT, and it is not known if this could be replicated on more widely available cycling machines in commercial gyms, or with cycle machines purchased for home use. Nevertheless, the principle of time-efficient exercise such as REHIT is relevant to a wide range of individuals and thus has practical application within public health strategy. It could flexibly be applied in a range of scenarios for individuals who perceive themselves to be time poor, and it is important for REHIT to be an accessible form of exercise that could be easily adopted into daily routine. For this to work, research on the efficacy of REHIT outside the laboratory setting and without the use of specialised exercise equipment is required. At present, based on the overall quality of the scientific evidence (see Chapter 5) we should be cautious extrapolating current evidence to public health settings or practical exercise guidelines. There is also insufficient evidence to suggest that HIT or REHIT can be adopted by everyone. Furthermore, it would be inappropriate to dismiss traditional, higher volume approaches to exercise or to suggest they are passé. Rather, HIT should be one of many physical activity and exercise options (Biddle & Batterham, 2015). If REHIT can encourage those who are sedentary to increase their activity even marginally, it could prove to be a practical approach to improving public health. Emphasising fitness and healthy lifestyles for their own sake, rather than a preoccupation losing body mass, will allow exercise to be used to its full potential. Pragmatically, the focus need not be on optimal exercise prescription, but on one we might deem to be ‘good enough’.

The dual-mode theory is a conceptual framework developed to understand the exercise dose-response relationship, and to explain interindividual variability in affective responses to various exercise intensities (Ekkekakis & Acevedo, 2006). According to this theory, HIT is likely to result in affective responses that are predominantly of displeasure since the ‘all-out’ nature of the sprints is carried out in the *severe* exercise domain (Gaesser & Poole, 1996), which is above the ventilatory threshold and associated with substantial homeostatic disturbance. The peak-end rule suggests that even though individuals may experience varying intensities of affect during exercise, retrospective evaluations tend to be related to the moment a distinct peak affective response is experienced (Redelmeier & Kahneman 1996; Kahneman, 1999; Fredrickson, 2000). As such, the application of the dual-mode theory to the peak-end rule suggests that individuals who exercise at severe intensities would record a high negative peak affective valence during HIT, and would therefore be reluctant to repeat the exercise (Parfitt & Hughes, 1996). These negative affective responses are likely to occur in response to the high exercise intensity during the sprints. Notwithstanding this premise, research on the dual-mode theory has primarily focused on continuous exercise at ~85% of VO_2 reserve (e.g. Ekkekakis, Parfitt & Petruzzello, 2011). Hence, this theoretical framework may be unsuitable for HIT because the intermittent nature of the activity fundamentally alters the exercise experience. Oliveira *et al*. (2013) observed greater ratings of perceived exertion during HIT compared to moderate-intensity continuous exercise, but no difference in physical activity enjoyment between the two types of exercise. The studies included in this thesis contribute to original knowledge by being the first to consider affective valence responses to REHIT.

Ratings of perceived exertion were lower for shortened-sprint REHIT (8 × 5 s sprints) compared to traditional REHIT (2 × 20 s sprints) in studies 1 and 2. For study 1 (Chapter 7), shortened-sprint REHIT was also associated with greater enjoyment (see Figure 7.4, p. 159), which supports the notion that higher intensities and perception of effort are associated with less enjoyment. However, the results of study 2 (Chapter 8) contradicted this finding since there was no difference in enjoyment despite traditional REHIT being associated with greater perceived exertion (table 8.2, p. 180). Although it is not clear what could have caused the discordance in results between the two present studies, these findings nevertheless provide support to suggest that dose-response effects for affective states may be different for intermittent exercise compared to continuous exercise. REHIT within the severe exercise intensity domain seems to avoid the equivalent quadratic decrease in negative affect as per continuous exercise. Pragmatically, this could increase the physical activity options for some people because exercising below the ventilatory threshold, to prevent diminishing affective states, can be very limiting for unfit individuals. Ventilatory threshold variably occurs at ~55% of $\dot{V}O_{2max}$ in sedentary, but otherwise healthy, populations (Gaskill *et al.*, 2001). Hence, for those with a low $\dot{V}O_{2max}$, exercising around half of their maximum severely restricts the range of viable activities, or else they are likely to exceed their threshold. In this way, REHIT could help to circumvent the negative peaks associated with exercise above the ventilatory threshold, as outlined by the dual-mode theory. The DMT may need further elaboration to consider the fundamentally different nature of intermittent exercise. Future research should systematically explore dose-response relationships for REHIT with dual-mode theory in mind, but emphasis should be placed on inter-individual response and the notion that a single, global dose-response or intensity-affect curve is unobtainable (Ekkekakis *et al.*, 2005).

An assumption of dual-mode theory is that there exists a distinction between core affect, such as hedonistic pleasure or pain, and more distinct emotional experiences such as enjoyment that require cognitive appraisal and appreciation of the totality of the exercise experience (Wankel, 1993; Russell & Barrett, 1999). Accordingly, although affective valence and enjoyment overlap, they are not identical constructs. Affective states in response to exercise intensity have a mediational role to enjoyment (Ekkekakis, Parfitt & Petruzzello, 2011). The time point at which measures of perceptual response are recorded significantly impacts results. Affective responses taken during activity are likely to be lower than ones taken at the end because there is a unanimous shift toward pleasure on cessation of exercise. Perceptions of effort may dissipate before they are recorded if they are not recorded during exercise. In the present studies, affect varied throughout REHIT sessions, and peak values were markedly different to average values. Peak FS values were closer to negative affective states, and peak RPE values were higher, compared with mean values (see tables 7.1, p. 157; and 8.2, p. 180). Therefore, relying on average values may disguise true affective responses, and distort interpretation of results. These exhortations highlight the need for future research to carefully consider the nature and timing of measures related to perceptual responses to exercise. Recording of peak responses rather than average values seems most appropriate, since memory and evaluation of exercise is associated with peak affective states.

It is generally assumed that individuals with greater fitness will invariably find HIT type exercise to be easier than those with lower fitness. However, a serendipitous and preliminary finding of the studies included in this thesis was that fitter individuals who are more familiar with exercise might perceive REHIT to be more strenuous. During pilot work (Chapter 6), it was observed that participants with higher mean $\dot{V}O_{2max}$ values, compared to those of Metcalfe *et al*. (2011), reported higher perceived exertion for the same REHIT protocol (17 ± 1, 'very hard' vs ~13 ± 1, 'somewhat hard', respectively). Again, during study 3 (Chapter 9) using relatively inactive NDH patients, aggregate mean peak RPE values were lower than for study 2 (Chapter 8) which used participants who were younger, fitter, and more physically active (13.9 ± 0.7 vs 14.4 ± 0.9 RPE units, respectively). These findings are in-line with those of Ruffino *et al*. (2016), who observed mean RPE values of 13.6 ± 1.1 units in patients with type 2 diabetes, which are lower than the values recorded using the same protocol with fitter participants within this thesis. A plausible explanation for this seemingly paradoxical finding could be that fitter individuals can achieve higher levels of anaerobic substrate phosphorylation during the 'all-out' sprints, which subsequently causes a cascade of biochemical, neuroendocrine, autonomic, cardiovascular, and respiratory changes that dramatically transform the internal environment resulting in higher perceived effort. Furthermore, it is possible that molecular responses that govern the beneficial physiological adaptations associated with HIT, are dependent on the metabolic status of skeletal muscle. Therefore, although entirely speculative, less fit individuals may be unable to exercise at the intensity required to cause the dramatic changes to the *rate* at which energy is depleted, and consequently may not signal the mechanisms that lead to improvements in $\dot{V}O_{2max}$ and glucose uptake.

Increases in $\dot{V}O_{2max}$ following HIT are strongly evidenced (Weston, Taylor & Batterham, 2014a; Milanović, Sporiš & Weston, 2015). Likewise, increases in $\dot{V}O_{2max}$ of ~10–15% have been reported after REHIT (Metcalfe *et al*., 2011; 2016b). Findings from the current studies support this observation, with increases of 9% for traditional REHIT and 6% for shortened-sprint REHIT. The discrepancy in the magnitude of increase may be accounted for by the shorter duration interventions, or the reduced number of REHIT sessions included in the present studies. The importance of adequate $\dot{V}O_{2max}$ in reducing the risk of all-cause mortality and disease risk has been a unifying theme throughout this thesis. The reason is simple: researchers, clinicians, and public health officials have been encouraged to focus on physical activity and fitness-based interventions rather than weight-loss driven approaches to reduce mortality risk (Barry *et al*., 2014). In study 2, although magnitude based inferences suggested that increases in $\dot{V}O_{2peak}$ were small following traditional REHIT and shortened-sprint REHIT (Cohen's d = -0.53 and -0.36, respectively), they are nonetheless clinically important. Observational research variably defines 'fit' and 'unfit' using population quintiles, or a metabolic equivalent (MET) (a multiple of the resting metabolic rate approximating 3.5

$mL \cdot kg^{-1} \cdot min^{-1}$). A cardiovascular fitness level of < 5 METs (~17.5 $mL \cdot kg^{-1} \cdot min^{-1}$) is associated with high risk for mortality, whereas levels > 8 to 10 METs (up to 35 $mL \cdot kg^{-1} \cdot min^{-1}$) are associated with increased survival (Myers *et al.*, 2002; Ross *et al.*, 2016). Furthermore, health benefits are most apparent at the low end of the fitness continuum, with the largest benefits (more than half of risk reduction) occurring between the least fit and the next least fit group of individuals. Accordingly, small increases in $\dot{V}O_{2peak}$ (i.e. 1–2 METs or 3.5–7 $mL \cdot kg^{-1} \cdot min^{-1}$) are associated with considerably (10% to 30%) lower adverse cardiovascular event rates (Ross *et al.*, 2016). Therefore, as observed in the current studies in this thesis, the potential for REHIT to improve fitness by ~1 MET after a relatively short intervention is significant.

Mechanistic links between exercise capacity, or $\dot{V}O_{2max}$, and health outcomes are poorly understood. Animal studies have shown that metabolic differences during exercise between fit and unfit individuals, including fatty acid and branched-chain amino acid utilization, contribute to high intrinsic exercise capacity and the health and longevity benefits associated with enhanced fitness (Overmyer *et al.*, 2015). It has also been suggested that impairment of mitochondrial function may link reduced fitness to cardiovascular and metabolic disease (Wisløff *et al.*, 2005). Yet, despite our nascent comprehension of this phenomena, and the fact that training response is highly variable (Bouchard *et al.*, 1999; Vollard *et al.*, 2009), $\dot{V}O_{2max}$ is arguably one of the most important physiological properties that can be manipulated to prevent cardiovascular disease (Wei *et al.*, 1999). However, for REHIT to be optimally valuable as an exercise therapy, it must also improve other health outcomes. For example, skeletal muscle insulin sensitivity is an important biomarker in the development of type 2 diabetes and metabolic syndrome, and is a principal target for preventative strategies. Currently, the effects of REHIT on insulin sensitivity in healthy participants have been conflicting (Metcalfe *et al.*, 2011; 2016a), and recent studies employing REHIT with type 2 diabetes patients failed to show improvements in insulin sensitivity or glycaemic control (Revdal, Hollekim-Strand & Ingul, 2016; Ruffino *et al.*, 2016). These remain key challenges for furtherance of the research agenda around REHIT using fewer or shorter sprints.

The safety of HIT and REHIT is an important and potentially contentious matter, particularly for patients with chronic disease. For exercise in general, the relative risk of an acute cardiac event increases during exercise, but the absolute risk remains low. This has been reported in prospective research as one death per 1.51 million episodes of exercise in apparently healthy people (Albert *et al.*, 2000). Whilst higher intensity exercise, such as HIT, may increase risk, people who experience an exercise-related cardiac event generally have underlying structural cardiac disease (Thompson *et al*., 2007). According to Ruffino *et al*. (2016), the expected increase in blood flow and blood pressure during sprints presents the main *potential* risk of HIT. Therefore, appropriate screening for high-risk individuals should be carried out before commencing HIT. This inevitably has resource implications in real-world settings, and the benefit-to-risk ratio for high-risk exercisers might be more favourable with moderate-intensity exercise. Furthermore, caution should be used in people with diabetes using insulin therapy because of the risk of hypoglycaemia caused by exercise-induced increase in the rate of glucose clearance into skeletal muscles. However, no adverse events have been reported in research using HIT with individuals with type 2 diabetes (Little *et al*, 2011b; Ruffino *et al*., 2016). People with NDH may not have many of the disease complications associated with type 2 diabetes because of the relatively early state of disease progression (Wright & Swan, 2001). Consequently, the prescription of HIT to this population group should be acceptable if other co-morbidities have been appropriately screened for. In this thesis, no severe adverse events were observed in any of the studies, but since lack of evidence is not evidence for absence, this does not ‘prove’ that REHIT can be safely adopted by everyone. However, the studies provide some additional support for the safety of REHIT. Further detailed studies are required to investigate the safety of HIT, although this is a difficult concept to demonstrate experimentally.

Under supervised and controlled laboratory settings, REHIT appears to be a potent and time-efficient approach to exercise for increasing fitness. At the same time, in terms of perceived effort, affective response and enjoyment, it seems to be tolerable and acceptable. The challenge remains however, to translate existing research into interventions that can be delivered in real-world settings, particularly for sedentary individuals with limited exercise experience, and who may have disease related contraindications to exercise. The aim of study 3 (Chapter 9) included in this thesis was to explore the feasibility and acceptability of a REHIT intervention in NDH patients in an NHS practice setting. The study was not feasible in its current form although several findings were valuable for the design and conduct of any future trials. A salient issue was the use of HbA_{1c} for screening eligible patients. Part of the problem relates to inherent biological and assay variability, in addition to poor reliability and sensitivity (Barry *et al*., 2016). Furthermore, HbA_{1c} diagnosed NDH consists two conditions which have a heterogeneous pathogenesis. Isolated IFG relates primarily to hepatic insulin resistance, whereas isolated IGT is caused by skeletal muscle insulin resistance (Nathan *et al*., 2007). Again, small but important differences in diagnostic criteria may contribute to international inconsistency in how individuals at risk of diabetes are identified (Borch-Johnsen & Colagiuri, 2009). These issues obscure the fact that some people with HbA_{1c} values in the NDH range will return to a normal glucose range, and others with normal glycaemia will subsequently develop type 2 diabetes. Indeed, the natural history of both IFG and IGT is variable, with ~25% progressing to diabetes, ~50% remaining in their abnormal glycaemic state, and ~25% reverting to normal glucose tolerance over an observational period of 3–5 years (Shaw *et al*., 1999; Gabir *et al*., 2000; Stern, Williams & Haffner, 2002). A finding from the current feasibility study was that recruitment can be problematic when using HbA_{1c} defined NDH as inclusion criterion for future risk of diabetes.

The small sample size of study 3 means it is difficult to make assumptions about the value of any future main evaluation study. However, the UK's NHS Diabetes Prevention Programme (DPP) is based on pragmatic interventions and provides some context from which to draw perspective. Currently, the NHS DPP places emphasis on a 'screen and treat' approach. This aims to identify subpopulations as 'high risk' and offer individual evidence-based behaviour change programmes. Barry and colleagues (2017) recently questioned the efficacy and effectiveness of this approach, highlighting that because screening – based on HbA_{1c} and fasting glucose – is inaccurate, many people will receive a false positive diagnosis and be referred to an intervention, while others will receive a false negative and be wrongly reassured of their level of risk without receiving intervention support. It has been suggested that screen and treat policies alone are unlikely to have substantial impact on the worsening epidemic of diabetes, and that such individualised policy is removed from the multi-level, community-wide, and politically engaged prevention plans recommended by the World Health Organisation (WHO, 2014; Barry *et al*., 2015, 2017). Others have stressed the need to review inclusion criteria for the programme (Guess, 2017), and the need for further diabetes prevention trials in people with HbA_{1c} defined NDH (Færch & Vistisen, 2017). The evidence base for the DPP is based on a Public Health England systematic review and meta-analysis assessing the effectiveness of pragmatic lifestyle interventions for the prevention of type 2 diabetes in routine practice (Ashra *et al*., 2015). Data from 36 studies were included in the review, and the pooled incidence rate of diabetes was 26% lower in those receiving a diabetes prevention programme compared with usual care (95% Confidence Interval: 7% to 42%). This value is much lower than the 58% reduction observed in the influential Finnish (Tuomilehto *et al*., 2001) and US (Knowler *et al*., 2002) Diabetes Prevention Programme trials. However, this may be explained by the inclusion of studies that used pragmatic lifestyle interventions. Similarly, a meta-analysis of 22 DPP's reported a mean reduction in mass of 2.1 kg (Dunkley *et al*., 2014), which is less than the 5.6 kg reported in the US DPP (Knowler *et al*., 2002). Accordingly, these lower reductions of incidence might more accurately reflect 'real-world' results.

A distinct option is to focus on a population-wide approach, whereby everyone is targeted via public health policies on environmental moderators (Swinburn *et al*., 2011). Indeed, Barry *et al*. (2017) advocated supplementing screen and treat policies with approaches such as protection of green spaces, increased walkability of the environment, affordable leisure activities, and improved regulation of food nutritional standards, labelling, and advertising. The balance between the medical model of screen and treat, and the public health model is a challenging one. As Waugh (2017) recently pointed out: individuals with HbA_{1c} values in the NDH range (42–46 mmol·mol) are at increased risk of diabetes, but others who develop diabetes come from the largest proportion of the population with baseline HbA_{1c} within the normal range. Indeed, in one prospective cohort study, two thirds of participants who developed diabetes had baseline HbA_{1c} lower than 42 mmol·mol (Chamnan *et al*., 2011). Thus, if we exclusively focus on 'at risk' patients with NDH, we fail to acknowledge the remainder of the healthy population who would benefit from the same advice. This shift in perspective, could avoid undue medicalisation of patients and, in its place, focus on reversing the drivers of the diabetes epidemic (Yudkin & Montori, 2014).

As part of the feasibility study included in Chapter 9, a REHIT intervention was implemented in practice using a screen and treat approach. However, the broader recommendations from this thesis support a population-wide approach to public health. Although interventions for people who are diagnostically considered to have NDH should remain a priority, advice to engage in more regular physical activity and structured exercise are applicable to the general population. The fundamental prospect for tolerable approaches to low-volume exercise, such as REHIT, is that they can contribute to wider strategies that counter the negative effects of physical inactivity, by motivating people to engage in activity that might be more consistent with the practicalities of building the activity into everyday life. Future research needs to address the scope for this, yet several other feasibility issues apparent from study 3 should be considered. Recruitment, consent, and clinician engagement all posed challenges. Solutions to these issues revolve around using a dedicated local recruiter with a strong relationship among the healthcare team and patients, and participant incentives to take part. However, it follows that a compromise must be made between scientific robustness and generalisability to routine real-world contexts, otherwise thought of as the inverse relationship between internal and external validity. Such issues relating to design and delivery of interventions, and the organisational and logistical difficulty of applying experimental methods in routine service are common to complex interventions.

Sample and research design limitations in this thesis are evident. An important factor to consider is whether the results of studies 1 and 2 are externally valid. They were carried out under ‘ideal’ circumstances with experimental control and were fully supervised. The presence of a supervisor during REHIT is likely to improve concordance with the protocol including facilitation of motivation to complete each high-intensity sprint. The appeals of Grossman (2005) highlight that behavioural variables may confound results of human physiology research. This relates to lack of control over physical activity and exercise outside the experimental intervention. Although participants were instructed to maintain their normal levels of daily activity during the study period, physical activity (or diet) diaries were not used. Ambulatory accelerometery data would address the issue further, but was not feasible. Furthermore, samples (for studies 1 and 2) were derived from a convenient pool of interested sport and exercise science students, who may have had knowledge of the hypotheses of the study which could have influenced their response to REHIT (e.g. the placebo or Hawthorne effect). Experimenter bias can also be revealed, explicitly or implicitly, when discussing the purpose of research. Although discussion of this nature between participants and researcher was consciously restricted, it is likely that several participants were aware that the aim of the shortened-sprint REHIT protocol was to be less strenuous than other protocols. Thus, behavioural and psychological effects are potential confounds which may have exerted influence on psychological and physiological outcomes. Therefore, whether these results can be replicated in other populations, and whether the intervention is sustainable in the context of broader demographic, cultural, and socioeconomic factors is not known. Although study 3 implemented a REHIT intervention in an NHS practise setting, with participants who were more representative of the general population, many of the same issues apply. Sessions were fully supervised, and it would have been unethical to proscribe other healthy behaviours throughout the duration of the study.

Other theoretical considerations should be considered alongside the wider findings within this thesis, and relate to the scales used to measure psychometric information. Research on the 15-point Borg RPE scale has revealed inconsistencies in the strength of the relationship between ratings of perceived exertion and various physiological criterion measures, such as heart rate, blood lactate concentration, percent $\dot{V}O_{2max}$, and respiration rate (e.g. Russell, 1997). Findings from a meta-analysis revealed RPE to be a valid measure of exercise intensity (*r* = 0.80 to 0.90), although fitness and type of exercise were found to account for variation across studies (Chen, Fan & Moe, 2010). Thus, exercise history and level of fitness are likely to influence accuracy of response (Parfitt, Markland & Holmes, 1994; Parfitt, Eston & Connolly, 1996; Russell, 1997). The 15-point scale was originally constructed to increase linearly with the intensity of exercise during cycle ergometery, with the scale value range from 6 to 20 denoting heart rates ranging from 60 to 200 beats·min^{-1} (Borg, 1970, 1982). Accordingly, the scale is not necessarily suited to reflecting the intensity of intermittent exercise which can fluctuate rapidly, particularly during HIT. Nevertheless, moderate correlations have been reported for RPE and heart rate during high-intensity interval cycling for interval periods (*r* = 0.63) and recovery periods (*r* = 0.44) (Green *et al*., 2005). However, correlations between RPE and lactate were lower (*r* = 0.34 to 0.43). Other studies have reported weak to moderate correlation (*r* = 0.4) between RPE, average heart rate, and percent heart rate reserve during prolonged indoor cycling with varying intensities (Muyor, 2013). Psychological variables, such as mood or affect may undermine the relationship between ratings of perceived exertion and physiological indicators of exercise intensity (Parfitt & Eston, 1995; Parfitt *et al*., 1996). Consequently, the use of RPE as a proxy indicator of perceived exertion or exercise intensity is not straightforward.

Similarly, the study of affect presents a substantial challenge for exercise research because it is not possible to establish affect as a narrowly defined state. Measuring affective valence (pleasure-displeasure) requires a dimensional approach, for which the FS aims to measure core affect as the main construct. Core affect is a neurophysiological state consciously accessible as a simple primitive non-reflective feeling (Russell & Feldman Barrett, 2009). Both interoceptive factors (awareness of stimuli within the body) and cognitive cues effect affective states. Therefore, the FS cannot be implemented with the assumption that a single causal factor will influence behaviour change. Recordings of affective response throughout REHIT are likely to be derived from a blend of contributing factors. An outcome such as affect is a theoretical construct rather than a direct observable, and is measured along a conceptual continuum that is not a true account (Tickle-Degnen, 2013). Accordingly, quantification of affect relies heavily on human interpretative processes in assessing the dimension of interest. Consequently, any numerical value assigned to a response is not a pure reflection of the construct, but only an indirect estimate that has been obtained by the mediating influence of language and interpretation, and the arbitrary nature of the measurement scale (Brustad, 2002).

Although the FS has been used in an ecological setting to successfully regulate exercise intensity (Hamlyn-Williams, Tempest, Coombs & Parfitt, 2015), criteria for evaluating reliability and convergent or discriminant validity are lacking. Hardy & Rejeski (1989) reported that RPE and FS were moderately inversely correlated (r = -0.33 to -0.55) during cycle ergometery, but observed greater variability as metabolic demands increased. Also, RPE was more strongly related to physiological cues than responses to the FS. Hence, FS and RPE measured during REHIT are not the same construct. The FS was designed to be easy to use and easily understandable (Haile, Gallagher & Robertson, 2015). It was used in the studies in this thesis because single-item measures are quick to administer, reducing interruption during activity – and thus are ideally suited for use during REHIT. However, scores on single-item measures depend entirely on one response, which could be erroneous if the measure is misunderstood. Therefore, single-item responses tend to be less reliable than multi-item measures of the same constructs (Ekkekakis, 2012). It has also been suggested that typical understanding of affective response may be overly simplified or mistaken (Russell, 1980). A final consideration related to the challenge of measuring affective response during exercise was emphasised by Ekkekakis *et al*. (2011). Group level responses might subsume psychologically important individual variation. Inter-individual differences in response may not reflect random error but could reflect systematic sources of variability. Variance in affective response was observed for the studies in this thesis, as it has been for other forms of exercise (Van Landuyt, Ekkekakis, Hall & Petruzzello, 2000; Ekkekakis *et al*., 2005; Backhouse, Ekkekakis, Biddle, Foskett & Williams, 2007). The magnitude and causes of inter-individual variation in affective response may be important for predicting future engagement with exercise but the reality may be that *some* people find REHIT to be acceptable, whereas others do not. The use of psychometrics to establish affect as a causal factor in future exercise behaviour decisions is not without challenge.

In conclusion, improving health outcomes for the general population requires effective measures to motivate people to protect their own health. Regular physical activity is an essential part of this, but approaches to exercise must be tolerable and avoid adverse negative affective states, elsewise they are unlikely to be adhered to which is a prerequisite for the success of any intervention. REHIT is a genuinely time-efficient approach to exercise which may have a role in parrying the negative consequences of a physically inactive lifestyle. The original contribution to knowledge presented in this thesis, based on three related studies, provide preliminary evidence to suggest that REHIT is enjoyable whilst minimally effecting displeasure and perceived exertion associated with the exercise. At the same time, it can also result in clinically meaningful increases in $\dot{V}O_{2peak}$, although heterogeneity in training response is evident. The challenge remains to translate this evidence to real-world scenarios. Any future trials which aim to consider the effectiveness of REHIT as a pragmatic intervention for patients with NDH would need to carefully consider feasibility issues such as recruitment, consent, and patient eligibility, in addition to broader issues related to identifying at risk populations using a criterion such as HbA_{1c}. The dose-response relationship between the intensity of REHIT and the associated affective response will be important for the acceptability of such protocols with sedentary populations and those with chronic disease. Yet, given that health benefits associated with improvement in $\dot{V}O_{2max}$ are most apparent at the low end of the fitness continuum, the potential for REHIT to induce rapid increases in a time-efficient manner should not go unnoticed.

10.2 Recommendations for future research

Several lines of investigation are required to expand knowledge on the effects of low-volume, high-intensity exercise; and will be explored using further research:

- The dose-response to various iterations of HIT and REHIT remains important and largely unexplored. The optimal intensity, frequency, and duration of sprints to bring about clinically significant health benefits in an acceptable and time-efficient manner is not known. This will be explored using randomised, positive-controlled, experimental studies whilst isolating the influence of dose, intensity, and mode. The emphasis on the minimal amount of exercise required to improve health should remain. Alongside this, studies are required to elucidate the physiological and molecular responses to HIT and REHIT using fewer or shorter sprints. Some of the signalling mechanisms that follow higher-volume or more strenuous HIT seem to occur in response to traditional REHIT (e.g. Metcalfe *et al*., 2015); however, this needs further exploration including protocols with fewer or shorter sprints, such as shortened-sprint REHIT. Such mechanistic studies require muscle biopsy samples and quantification of skeletal muscle oxidative capacity as reflected by the maximal activity or protein content of mitochondrial enzymes such as PGC-1α and citrate synthase. Understanding the effect of REHIT on activation of upstream signals such as AMPK and p38 mitogen-activated protein kinase (MAPK) is also needed. Since change in skeletal muscle glycogen content may be the signal that leads to exercise-induced molecular adaptations, this should also be measured. Systematically exploring the exercise stimulus and subsequent cellular responses and adaptations for diverse protocols will allow a greater understanding of the potential for this type of exercise to benefit health markers and health outcomes.

- Similarly, it is essential to understand the dose-response relationship for affective responses to HIT and REHIT, as this may be related to exercise adherence. Future experimental studies will compare perceptual responses for a range of approaches to low-volume, time-efficient exercise. Psychometrics such as those used in this thesis (i.e. FS, RPE, and EES) are adequate for quantifying such constructs. Future research will measure affective response *during* exercise, rather than before and after activity. The time points at which recordings are taken should accurately depict the nature of the exercise bout, capturing periods during and after high-intensity sprints. Furthermore, future research studying affect, RPE, and enjoyment in relation to REHIT, with aims of predicting future intentions, will use qualitative or a mixed-method approach as this would be a worthwhile addition to further explore such phenomena, and may facilitate further practical research investigations. As per Rose & Parfitt (2007), asking participants how they feel during and after various iterations of REHIT could explain factors that influence the affective response and which contribute to individual differences in quantitative data. This will be valuable since there is a need for future research on HIT to explore the heterogeneity in training response and adaptation. Focussing only on average responses obfuscates the inherent variability in these measures, thus there is a need to evaluate the magnitude and causes of inter-individual differences in physiological and psychological (affective) responses. Theoretical considerations outlined by the DMT and peak-end rule should guide these research efforts. It may be necessary to revise the DMT, if affective responses to intermittent activity are reliably observed to be different to those of continuous exercise above the ventilatory threshold.
- A related area of future research should focus on the effects of intermittent exercise, including REHIT, on the sense of fatigue and fatigue symptoms. Fatigue is related to many diseases, so this is of great societal importance. Such research will use an interdisciplinary perspective focusing on psychophysiological mechanisms that may be associated with fatigue. In relation to this, it may be beneficial to explore self-monitoring and self-regulation skills based on the principles of biofeedback, to guide affective responses to HIT. Within-participant experimental research will focus on cognitive-behavioural intervention strategies that aim to change cognitions, resulting in suppression of large

negative peaks in affective response and associated maladaptive behavioural consequences. These strategies, such as breathing techniques and imagery, will be applied using a randomised crossover approach to compare the intervention against a control condition to reduce the order of exercise conditions from adversely influencing results.

- In-line with broader research on affective response and exercise (Ekkekakis & Lind, 2006), it would be valuable to systematically investigate if 'self-selected' or 'preferred' exercise intensity, as opposed to imposed (or prescribed) exercise dose, could be used during REHIT to elicit more favourable cognitive and behavioural responses. Using a within-participant crossover design, measurement of physiological and psychological changes such as heart rate, oxygen uptake, perceived exertion, and affect will be assessed throughout exercise to compare responses to REHIT when the intensity is imposed by the experimenters, and in a separate condition during which intensity is self-selected. For example, participants may self-select the duration and frequency of sprints. This is important because imposing intensities that are higher than what would be self-selected could diminish the enjoyment of and intrinsic motivation for physical activity, reducing adherence (Ekkekakis & Lind, 2006). For REHIT to be effective, we must consider not only what is safe and effective from a physiological standpoint but also what is tolerable and enjoyable from a psychological perspective (Biddle & Fox, 1998).
- The effect of low-volume exercise on appetite and energy intake needs to be systematically explored. Preliminary research suggests that REHIT may decrease acylated ghrelin (Metcalfe *et al.*, 2015). However, the potential contribution of diverse approaches to REHIT on weight loss, via direct energy expenditure or via effects on appetite, should be investigated. Assessment of blood analyses for concentration of acylated ghrelin, peptide YY, and glucagon-like peptide-1 in addition to subjective measures of appetite, using validated 100-mm visual analogue scales, can be used to measure suppression of appetite. Participants can also be presented with an *ad libitum* meal to assess post-exercise food consumption. To achieve this, randomised crossover studies are needed to compare responses to various protocols against a control condition. Twenty-four-hour food records will be required to standardise diet before each condition. There are challenges when researching the effects of exercise on appetite control and energy intake. Post-exercise compensatory eating behaviour is known to be highly heterogeneous (Hopkins, Blundell & King, 2013), and a single bout of exercise does not reflect the cumulative effects of regular exercise on energy balance in the medium- or long-term (Broom, Hopkins, Stensel, King

& Blundell, 2014). Nevertheless, the physiological and behavioural mechanisms that mediate appetite and energy intake are important to gain a greater understanding of how REHIT influences appetite control and body weight regulation.

- A significant challenge remains to translate current evidence supporting the use of HIT and REHIT into less ideal real-world environments. For example, willingness to exercise at maximal capacity during sprints may diminish in the absence of a supervisor, and affective responses may be different for unsupervised sessions. As per Jung *et al*. (2015), further research should consider adherence to REHIT following initial supervised sessions. A combination of self-reported and objective measures of physical activity behaviour (e.g. log books and accelerometery) will be used after a specified period of independent exercise. This might be especially relevant for individuals with chronic disease as adherence to exercise is known to be very low. Also, the majority of HIT and REHIT research has used cycle ergometry. Future research needs to consider if other exercise modalities (e.g. running, whole-body floor based exercises) can be used to produce the same effects. Using cycle ergometery allows for more precise control of exercise intensity, and provides optimal resistance for peak power generation. This characteristic may be required to elicit the metabolic adaptations associated with REHIT. It may be more challenging to simulate this with other types of exercise. Nevertheless, alternative approaches to HIT may be more appropriate for adoption in a home environment. Likewise, most research has used specialist laboratory cycle ergometers. It is not clear if cycle machines more commonly found in commercial gym environments, or cycle machines purchased for home use, could be used to replicate current findings. Further research investigating REHIT performed in a real-world gym setting is warranted, since limited research has explored group-based community exercise. Other researchers have used higher-volume HIT in such environments and demonstrated improvements in cardio-metabolic risk factors and psychological health in physically inactive adults (Shepherd *et al*., 2015).
- A broad research challenge for furtherance of research on REHIT, is implementation of practical and acceptable protocols in individuals with chronic disease. In practice many patients present with co-morbidities that may make prescription of REHIT more problematic. A wide range of metabolic or other ‘mismatch’ diseases might be improved by REHIT, such as diabetes, cardiovascular disease, chronic obstructive pulmonary disease, and cancer. The tolerability and acceptability of REHIT for these populations should be explored using longitudinal studies to assess the impact on important health

outcomes. Additionally, the idea of co-locating clinical and exercise prescription in one location, such as hospital clinics as used in this thesis, needs further attention. In theory, this could accelerate transition of research discoveries into clinical practice via greater communication and involvement of clinical consultants. It would also allow patients to receive clinical guidance and then start their exercise prescription at the same time and place. However, delivering interventions in primary care within a busy practice setting may be very challenging requiring considerable time and demanding skills for which the healthcare team may not have specialist training. The broad purpose of the National Centre for Sport and Exercise Medicine (NCSEM) aims to accelerate the translation of research on physical activity in all its forms into changes in frontline medical and public health policy and practice (Harris, 2017). Co-locating clinical consultation with exercise provision simplifies the patient journey and may improve exercise adherence via this alternative care pathway. Having consultants based in a sports facility may facilitate more frequent prescription of exercise as medicine. As such, the NCSEM may be well placed to investigate the effects of REHIT on patients with a wide range of chronic diseases, and to bring such research discoveries to the NHS.

10.3 Summary

The original contribution to knowledge presented in this thesis is that REHIT can improve $\dot{V}O_{2peak}$ without overly compromising cognitive responses to exercise. For the samples in this thesis, these responses included avoidance of large peaks in displeasure, a tolerable perception of exercise exertion, and acceptable levels of enjoyment associated with task completion. Increases in $\dot{V}O_{2peak}$ were small but clinically important and could reduce mortality risk. Additionally, shortened-sprint REHIT resulted in more favourable responses compared to traditional REHIT which suggests that longer duration sprints may be unnecessarily strenuous. These findings suggest that such responses could influence future exercise behaviour. This contribution to knowledge is based on the presentation of original data collected in the three studies included in this thesis. These were based on a critical appraisal of current HIT literature, and the underlying evolutionary perspective that regular exercise or physical activity is essential for optimal health outcomes. The theoretical foundation of the thesis was based on applying the peak-end rule to the dual-mode theory. Hedonistic theories may explain or predict exercise behaviour, and this was operationalised for REHIT by hypothesising that high-intensity exercise is likely to result in displeasure and an aversive response with the prospect of future exercise engagement. As such, the theoretical framework was predicated on an intensity-affect-adherence series of events. The findings of this thesis suggest that by manipulating intensity using shorter duration sprints, it is possible to modulate affective states during REHIT.

Physical activity has been an integral part of human existence throughout evolutionary history. Accordingly, from an evolutionary perspective we require regular physical activity for optimal health. The Agricultural, Industrial and Technological Revolutions have transformed our environment to such an extent that the rate of cultural evolution vastly exceeds the rate of biological evolution. The requirement for physical exertion is now negligible, thus we live in an environment for which our genome is maladapted. Frequently, chronic diseases, including obesity and diabetes, are caused by deficient exercise stimulus. Therefore, if we remain physically inactive, we fail to deal with the cause of such diseases. Despite strong evidence for the efficacy of exercise in preventing, delaying, or treating mismatch diseases, levels of activity remain low among the general population. The most commonly cited barrier to physical activity is internally perceived ‘lack of time’. This is juxtaposed with government advice to be active on most days of the week accumulating at least 150 minutes of moderate-intensity activity or exercise. Approximately half of individuals who start an exercise programme stop within the first six months. As such, the challenge of prescribing exercise as medicine remains a challenge because of poor adherence. The advent, and current popularity of HIT has been proposed as a means of circumventing this barrier, because it is popularly believed to be less time intensive than traditional exercise recommendations. Proponents highlight the rapid physiological benefits this type of exercise induces, including increased $\dot{V}O_{2max}$ and insulin sensitivity. Regrettably, as demonstrated in Chapter 5 much of the evidence supporting the efficacy of HIT is based on protocols that are not appreciably more time-efficient than other types of exercise. This is necessitated by the inclusion of a warm-up, recovery in-between periods of high-intensity sprints, and a cool down. Moreover, if the intensity of protocols is too severe it is likely to be associated with large negative affective states, which may variably mediate an aversive response towards future exercise sessions.

REHIT was developed with the aims of being genuinely time-efficient, less strenuous, and more applicable to a sedentary population. Through the work of Metcalfe and colleagues (e.g. Metcalfe *et al.*, 2011), the minimum amount of exercise that so far has been shown to improve $\dot{V}O_{2max}$ incorporates two 20 s cycle sprints at maximal exercise capacity within an otherwise low-intensity 10-minute exercise session. This is inclusive of a warm-up and cool down, with a total weekly time commitment of just 30 minutes. $\dot{V}O_{2max}$ is increased following REHIT interventions, induced via activation of adaptive cellular signalling pathways as per higher-volume or more strenuous HIT. These adaptations include increased gene expression of PGC-1α which regulates mitochondria biogenesis. This was once considered exclusive to longer duration aerobic exercise, and may be particularly important because mitochondria biogenesis plays a role in energy metabolism under conditions of both health and disease. Furthermore, increases in $\dot{V}O_{2max}$ protect against evolutionary mismatch diseases, as evidenced by several large-scale epidemiological studies.

Currently, there is a dearth of literature investigating the affective response to REHIT. It is plausible that 20 s sprints, regardless of their brevity, may induce negative affective states since energy flux relies heavily on anaerobic glycogenolysis which causes rapid alterations in the metabolic status of cells. Application of the dual-mode theory to the peak-end rule suggests that individuals exercising at maximal capacity (in the severe exercise domain, and above the ventilatory threshold) will experience negative affect during REHIT, and that retrospective memory and evaluation of the exercise will be related to the moment a distinct peak response is experienced. Therefore, individuals may experience a prospective avoidance response for future sessions. It is thought that skeletal muscle glycogen content is an important acute regulator of metabolism and that the dramatic rate of glycogenolysis during maximal sprints may be the signal that induces molecular adaptations. Glycogen phosphorylase (which catalyses the rate-limiting step in glycogenolysis) is known to be rapidly activated within the first 6 s of maximal-intensity cycling, before rapidly declining as the sprint continues beyond this duration (Parolin *et al.*, 1999). Therefore, it is plausible that the 20 s sprints used in REHIT are longer than required, and that shorter sprints could provide the necessary stimulus for beneficial adaptation to occur. It is also plausible that shorter sprints could do this without overly compromising cognitive and affective responses to exercise. Hence, the preceding rationale emphasises the aims of the studies included within this thesis.

The three studies included in this thesis are distinct in their application, but were bound by the theme of using a novel, shortened-sprint REHIT protocol (8 × 5 s sprints) as a time-efficient and tolerable approach to exercise. Results provide preliminary evidence to suggest that this protocol results in more favourable FS and RPE responses than traditional REHIT (i.e. 2 × 20 s sprints). However, both protocols resulted in affective responses that remained positive during activity, so both may be tolerable approaches to exercise. Statistical inferences revealed significant main effects for time which reflected fluctuations in affect throughout exercise, with peak values higher than mean values. This reinforces the pleas of others (e.g. Ekkekakis *et al*., 2005) to record responses *during* exercise, rather than after cessation of activity, to more accurately depict affective responses. These results were observed in response to a single bout of REHIT, and for a longitudinal (5–7-week) intervention. In study 1, shortened-sprint REHIT was deemed to be more enjoyable than traditional REHIT. However, results from study 2 contradicted this finding with no difference in enjoyment between protocols, despite higher RPE reported for traditional REHIT. $\dot{V}O_{2peak}$ was significantly increased after shortened-sprint and traditional REHIT (6% and 9% increase from baseline, respectively). Magnitude based inferences suggested that increases were small, but these are nonetheless clinically important. These increases of ~1 MET (~3.5 $mL \cdot kg^{-1} \cdot min^{-1}$) are sufficient to reduce cardiovascular disease and all-cause mortality risk (Myers *et al*., 2002; Ross *et al*., 2016). Training response in $\dot{V}O_{2max}$ is known to be highly variable for aerobic exercise, with similar findings reported for REHIT (Metcalfe *et al*., 2016b). Observations from this thesis corroborate this finding with heterogeneity in the range of -2% to 20%.

These findings suggest that, REHIT is an enjoyable and efficacious means of improving $\dot{V}O_{2peak}$, whilst minimising negative affect associated with the activity. However, it should be noted that samples were not representative of sedentary populations or those with chronic disease. The feasibility study (study 3, Chapter 9) aimed to describe and report data relevant to the acceptability of shortened-sprint REHIT with NDH patients in an NHS practice setting. Several issues including eligibility, recruitment, and patient consent led to the recommendation that the trial was not feasible in its current form. However, this preparatory stage of trial design was successful in pre-empting problems with the exercise intervention that could be remedied to optimise the design and conduct of a larger-scale pragmatic trial, to improve transferability into real-world practice. The ability for REHIT to improve other biomarkers of health is important to optimise the therapeutic potential of this approach to exercise. Compared to more intense HIT, it remains to be seen if improvements in insulin sensitivity are attenuated following REHIT.

Theoretical issues have been highlighted for the psychometric scales used to measure affect, perceived exertion, and enjoyment. It is inherently difficult to establish affect as a causal factor in future exercise behaviour decisions. This is due to the complex interaction of psychobiological and environmental mediators which make measurement challenging. Nevertheless, the dose-response relationship between intensity of REHIT and the accompanying affective response is important for furtherance of research on low-volume, time-efficient exercise. Although the volume-intensity relationship for REHIT could be considered *ad infinitum*, future research should focus on the optimal combination of sprint frequency, sprint duration, and sprint intensity that is necessary to induce adaptations in a genuinely practical, time-efficient, and tolerable manner. Exploring the physiological and molecular responses to shortened-sprint REHIT will be valuable.

Finally, accumulating evidence supports the use of REHIT to improve health. This thesis presents an argument that a shortened-sprint protocol can induce improvements in health whilst simultaneously avoiding large negative peaks in displeasure and perceived exertion, which may in-turn be related to exercise adherence. It might therefore be prudent to suggest we should move away from a global, high-volume exercise prescription for all. The combination of time-efficiency, efficacy, and acceptability mean that REHIT could be a practical adjunct to other lifestyle changes and may help motivate some people to increase physical activity and fitness, to improve their own health. Research is required to translate current findings into effective real-world strategies. The decisive factor may be the acceptability and accessibility of the activity for whom the intervention is intended, and the practicalities of building the activity into everyday life. Yet, if REHIT can encourage those who are sedentary to increase their activity even marginally, it could prove valuable in improving public health. Fundamentally, as an exercise-dependent species we need to find ways to engineer physical activity back into our lives. Simply, advocating time-efficient REHIT should be part of the solution, when safe to do so. To underline the notable attempts of two experts in exercise physiology to draw attention to the matter more than 10 years ago: “We must respect our genes and the circumstances which selected them, or accept the consequences” (Spurway & Wackerhage, 2006).

11.4 Disseminated findings and future dissemination strategy

Publications

Haines, M., Gillibrand, W. & Garbutt, G. (2012). High-intensity interval training (HIT): A time-efficient exercise prescription for pre-diabetes? *Diabesity in Practice,* 1(4), 133 – 140.

Haines, M. (2015). Assessing the feasibility of a reduced-exertion, low-volume, high-intensity interval training (HIT) protocol: a pilot study. *Journal of Sports Sciences,* 33(S1), S25–S31.

Oral presentations

Haines, M. (2017). *What exercise should we be doing?* Accepted to the Engage Research Festival, University of Huddersfield, April 2017.

Haines M. (2017). *Time-efficient exercise for health*. Accepted to the Postgraduate Research Festival, University of Huddersfield, November 2017.

Haines, M. (2017). *The effects of a shortened-sprint, reduced exertion high-intensity interval training (REHIT) protocol on peak oxygen uptake and peak affective response.* Accepted to the BASES Annual Conference, November 2017, Free communication session.

Poster presentations

Haines, M. (2015). *Assessing the feasibility of a reduced exertion, low-volume, high-intensity interval training (HIT) protocol: A pilot study*. Poster presented at the BASES Annual Conference, December 2015.

Intended publications

Chapter 7 will be submitted to the *Journal of Sport and Exercise Psychology*.

Chapter 8 will be submitted to the *Journal of Science and Medicine in Sport*.

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Appendices

Appendix 1. Further critical appraisal of evolutionary perspectives of exercise, obesity, and diabetes

The obesogenic environment

The term 'obesogenic environment' refers to an environment that promotes adiposity and by association is not conducive to weight loss (Swinburn, Eggar & Raza, 1999). In broad terms, the environment promotes low energy expenditure as physical activity is seldom required. Simultaneously, the environment encourages overeating through an abundant food supply that is often energy dense, easily available, relatively inexpensive, good tasting and served in large quantities (Hill & Peters, 1998). This environment is virtually the opposite of the one in which our genome was 'designed' by natural selection. The phenotypic expression of our genotype is a complex interaction between our genes, behaviour and environment, and while the environmental influences have yet to be fully explored and understood (Jackson, 2004), the recent increased incidence and prevalence of obesity points to social and environmental causes (Swinburn *et al*., 1999; Booth, Pinkston & Poston, 2005).

Human adiposity is ultimately determined by laws of thermodynamics; that is, energy balance. This is determined mainly by energy intake from food and energy expenditure associated with movement and basal cellular metabolic processes. The premise of the obesogenic environment is that dietary behaviour may be influenced by access to different foods through various types of outlets and services. Similarly, movement (physical activity) levels may be influenced by access to recreational or sports facilities, green spaces or parks, as well as transport infrastructure and land use. The discussion in this section focusses on how environmental factors may operate by determining the levels of physical activity undertaken by populations. However, it is acknowledged that the Western diet has been implicated as a significant factor in the prevalence of chronic disease (Lindeberg, Cordain & Eaton, 2003; Lindeberg, 2010; Cerrara-Bastos *et al*., 2011). Environmental determinants of food provision have been summarised elsewhere (White, 2008).

A 2007 evidence review from Foresight (Jones, Bentham, Foster, Hillsdon & Panter, 2007) suggested that the environment influences levels of physical activity and obesity. Studies examining *perceptions* of the environment and physical activity were grouped into seven attributes: safety, availability and access, convenience, local knowledge and satisfaction, urban form, aesthetics, and supportiveness of neighbourhoods. However, it was not possible to elucidate the mechanisms by which environmental components operate and the most important components of the obesogenic environment that promote inactivity remain unclear. Studies examining the relationship between *objective* measures of the environment and physical activity were less common. Nevertheless, deprivation and poverty were found to be associated with low levels of physical activity (Jones *et al*., 2007).

Lake and Townsend (2006) specifically explored the relationship between the built environment and physical activity. The built environment – consisting physical design, land use patterns (residential, commercial, office, industrial), and transportation systems – was found to be linked to physical activity, obesity and chronic disease. There was a consistent link between urban design, walking and cycling. In contrast, a recent systematic review of 92 studies (Mackenbach *et al*., 2014) concluded that available research does not allow robust identification of ways in which the physical environment influences obesity. However, two environmental variables appear to be more consistently associated with obesity than other factors: 'urban sprawl' (based on population density) is positively associated with obesity, whereas 'land use mix' (where the built environment blends a combination of residential, commercial, cultural and industrial uses) was negatively associated with obesity. However, these factors have only been widely studied in North America, not in the UK. The cultural and physical differences between the USA and UK environments mean that research is often not directly comparable (Lake & Townsend, 2006).

A main limitation of research that has linked the obesogenic environment with physical inactivity and obesity is the cross-sectional nature of the studies, meaning direct causal pathways between environments, physical inactivity and obesity are difficult to establish. Furthermore, research often depends on simplistic data collection methods such as recollection and self-report, which produce notoriously unreliable data. As such, because of bias and imprecision, self-reported information should be interpreted with caution. Notwithstanding, the fact that extensive reviews (e.g. Mackenback *et al*., 2014) have showed minimal evidence for an association between the environment and obesity indicates that we still do not fully understand the complex interactions involved. Simply put, lack of evidence is not evidence for lack of effect. The heterogeneity in methods and measures reported in research, or differences in context or location, might have contributed to inconsistent results. What is clear is that modern human environments are enormously complex (Stokols, Grzywacz, McMahan & Phillips, 2003) and that they differ markedly from the environments of our ancestors. The adoption of a lifestyle that has very different evolutionary pressures compared to the one that shaped our genome – in terms of time, space, social relationships, culture and nature – is an important factor in determining our energy balance, and by extension our fitness, health and wellbeing – including the likelihood of developing obesity and type 2 diabetes. It is admissible to label the modern environment as 'diabesogenic' considering the dramatic increase in the prevalence of type 2 diabetes across the developed world.

Evolution, exercise and type 2 diabetes

If we have evolved as an exercise-dependent species, the inactive lifestyle afforded by modern environments is detrimental. Our current genome is therefore maladapted, and may result in abnormal gene expression, which in turn frequently manifests as clinically overt disease (Booth, Chakravarthy & Spagenburg, 2002a). By association exercise is the natural treatment for diseases which are caused by lack of physical activity. It can be hypothesised that humans have evolved genes that 'expect' physical activity – because a hunter-gatherer lifestyle dictates obligatory physical activity for survival – and that because of sedentary lifestyle, normal physiological gene expression is threatened, providing a causal link to disease such as type 2 diabetes. Evolutionary pressures associated with type 2 diabetes can be explained via human endurance exercise capacity.

Based on fossil finds and anatomical studies, Bramble and Lieberman (2004) have described the endurance running capabilities of extinct human ancestors. They suggested that striding bipedalism is a key derived behaviour of hominids that possibly originated soon after the divergence of the chimpanzee and human lineages. Humans perform remarkably well at endurance running activities, compared to other apes and other species such as quadrupeds, due to a diverse array of features. These include legs with long spring-like tendons attached to short muscle fascicles that generate force economically (e.g. the calcaneal tendon); a spring-like medial longitudinal arch of the foot; musculoskeletal adaptations that ensure stabilisation and balance (e.g. enlarged *gluteus maximus* muscle); and many derived features related to heat dissipation (e.g. elaboration and multiplication of eccrine sweat glands and reduced body hair which increases convection rates) (Bramble and Lieberman, 2004). Biochemical (Scholz, D'Aout, Bobbert & Aerts, 2006) and histochemical (Myatt, Schilling & Thorpe, 2011) adaptations also support the hypothesis that humans have evolved as a low-muscle-power, high-endurance species compared to other apes.

The endurance capabilities of humans also require specific cellular mechanisms to regulate energy provision, and this relates to the precise mechanistic basis underlying how exercise increases insulin sensitivity. Exercising skeletal muscles undergoing concentric, eccentric or isometric actions either in isolation or in combination, increase their glucose uptake. Molecular signalling studies demonstrate that the mechanisms leading to the insulin- and exercise-induced stimulation of glucose uptake in skeletal muscle are distinct (Goodyear & Kahn, 1998; Booth *et al*., 2002). As such, during exercise intracellular changes are mediated in response to the metabolic status of the muscle caused specifically by muscle action, and therefore bypass insulin resistance conditions – thus they are 'insulin independent' (Hawley & Lessard, 2008; Haines, Gillibrand & Garbutt, 2012). The evolutionary pressures that have shaped human physiology, including the molecular machinery of myocytes adapted for endurance activity, reinforces the notion that exercise is important for normal glucose metabolism and by association, reducing the incidence of hyperglycaemic states and type 2 diabetes.

Furthermore, evolutionary considerations suggest that skeletal muscle deficiency relative to adipose tissue may also be an important risk for type 2 diabetes. Rode & Shephard (1994) assessed physical fitness and body composition among adult Inuit living in Igloolik, Northwest Territories, Canada, during a 20-year period of rapid acculturation to a sedentary lifestyle. Fitness of the community deteriorated markedly and body fat, estimated by skinfold thickness, increased which increases insulin resistance and the risk of diabetes. Furthermore, skeletal remains from the Late Palaeolithic Era (≈100,000 to 50,000 years ago) indicate average muscularity like that of today's athletes (Eaton & Eaton, 2003). This trend towards sarcopenia (reduced muscle mass) and hyper-adiposity is significant because it distorts the genetically selected milieu for insulin action. Myocytes represent one of the bodies most significant glucose and insulin sensitive cells. An evolution-based prediction is that insulin resistance is proportional to fat mass, but inversely proportional to the mass and metabolic activity of skeletal muscle (Eaton *et al*., 2002). This relationship might reflect competition between the insulin receptors of myocytes and adipocytes for available insulin molecules, resulting in episodes of hyperglycaemia and hyperinsulinemia (*ibid*.). In turn, further metabolic deterioration could result from down-regulation of insulin receptors, glucose transporters, and intracellular enzymatic sequences, leading to type 2 diabetes (Eaton & Eaton, 1999).

Two further evolutionary theories link physical inactivity, obesity and type 2 diabetes. First, Neel's 'thrifty' genotype hypothesis (Neel, 1962; 1999) emphasises the irrefutable periods of feast and famine that would have characterised the availability of food for much of our ancestral past. Those with ‘thrifty’ metabolic adaptations, which favoured more economical storage of excess energy as adipose tissue, would have been more likely to survive and pass on their genes, because during periods of famine, the ability to hold on to stored fat would have been advantageous. Furthermore, recent research (Sumithran *et al.*, 2011) shows that following weight loss, levels of circulating hormones which affect our appetite tend to promote over-eating and weight regain. These adaptations which were once useful, are now causing unprecedented levels of obesity across all populations that lead a lifestyle characterised by physical inactivity and an abundance of food (i.e. an obesogenic environment). It is possible in our evolutionary past that our physiology relied on external events, such as famine or high volumes of obligatory physical activity, to regulate adiposity. Given the exertional requirements of hunter-gatherer existence, obesity would have been very unlikely for most humans.

Second, Wendorf & Goldfine (1991) suggested an evolutionary basis for development of type 2 diabetes by exercise deficiency. They hypothesised that selective insulin resistance in skeletal muscle could be beneficial by blunting the hypoglycaemia that occurs during fasting. Concomitantly, normal energy storage in liver and adipose tissue during feeding would afford hunter-gatherers survival advantages. Once again, when placed in an obesogenic environment this genotype appears maladapted; individuals with virtually unlimited access to calorie dense food are likely to become obese with secondary insulin resistance in liver and adipose tissue (Wendord & Goldfine, 1991). Our physiology has been shaped over millennia by evolutionary processes which make us suited to a hunter-gather lifestyle – which necessitates high levels of physical activity and likely periods of famine and feast. The dramatically different way in which we interact with our modern environment inadvertently leads to changes to the metabolic milieu of muscle, which can result in insulin resistance and type 2 diabetes for a great number of people.

The hypothesis that humans have evolved as endurance runners is consistent with data showing that a sedentary lifestyle is a risk factor for type 2 diabetes (Hu, Li, Colditz, Willett & Manson, 2003) and explains why exercise is an effective treatment to prevent and treat the disease (Goh *et al.*, 2014). Strong intervention and observational research further supports this by showing that exercise interventions and lifestyle modification are able to reduce the risk of developing type 2 diabetes. Nevertheless, for obvious reasons it is impossible to collect data directly from our ancestors. Human skeletal remains amenable to gross anatomical, microscopic and biomechanical evaluation provide some clues, but surviving hunter-gather groups minimally affected by Western civilisation have also been studied. Their subsistence patterns, obligatory physical activity and various biomarkers act as the best, yet imperfect, surrogate for Palaeolithic humans (Eaton *et al*., 2007).

Hunter-gatherer groups

Modern hunter-gatherer groups who continue critical aspects of Palaeolithic lifestyle have been studied extensively. Although few groups exist today who remain completely uninfluenced by Western lifestyle, they nevertheless provide a key insight into our ancestral physiological response to the environment. Overall health patterns are quite different for these groups and suggest many chronic degenerative diseases of modern life are not inevitable concomitants of aging, but rather are conditions that develop when behavioural and environmental circumstances differ from those under which our ancestors evolved (Eaton *et al*. 2002). In relation to diabetes and obesity, seminal research has studied a range of groups across five continents (Miller, Rubenstein & Åstrand, 1968; Joffe *et al*., 1971; Kuroshima, Itoh, Azuma & Agashi, 1972; O'Dea, Spargo & Akerman, 1980; Spielman *et al*., 1982; King *et al*., 1984; Rode & Shephard, 1994).

Spielman *et al*. (1982) measured blood plasma glucose and insulin in response to a standard oral glucose load in the Yanomama and the Marubo, two relatively unacculturated Amerindian groups of the Brazilian Amazon. Compared to age- and sex-matched Caucasian controls in the USA, both groups had favourable responses to glucose. They did however differ significantly from each other and in the degree of deviation from the control group. Of the two groups, the Marubo, the more acculturated group, resembled the controls more closely. The Yanomama differed significantly from the control group with respect to plasma concentrations of glucose and insulin at all time points (fasting, 1 h and 2 h post glucose load). Similarly, Kuroshima *et al*. (1972) compared carbohydrate metabolism in Japanese controls to those of the Ainu, an indigenous people of Japan (Hokkaido, and formerly north-eastern Honshu) and Russia (Sakhalin and the Kuril Islands). No differences were observed in blood plasma glucose, immune-reactive insulin and human growth hormone levels following a glucose tolerance test. However, fasting levels of plasma free fatty acids (FFAs), and fluctuation in FFA after glucose load, were significantly lower in the Ainu compared to the control group. FFAs are an important biomarker for risk of insulin resistance and type 2 diabetes. They have been shown to produce a defect in insulin stimulated glucose transport and to cause both insulin resistance and inflammation in the major insulin target tissues (i.e. skeletal muscle, liver, and adipose cells), and thus are an important link between obesity, insulin resistance, inflammation, the development of type 2 diabetes and other metabolic disorders (Boden, 2008).

The results of these studies differ from research conducted with a group of !Kung San (Kalahari region of Southern Africa) (Joffe *et al*., 1971) who live by hunting wild animals and collecting wild vegetation. Plasma glucose, immune-reactive insulin, and growth hormone levels following a 50 g oral glucose load were measured in 15 adult !Kung San. They showed relative glucose intolerance and significantly impaired insulin secretion compared with 10 non-obese Caucasian controls, although values were within the normal range by current standards (e.g. mean plasma glucose concentration of 121 mg·dL 2 hours after the glucose load). Factors such as inadequate or unusual nutrition and stress were considered but do not account completely for the values in carbohydrate metabolism observed in the !Kung San. These results were unexpected considering previous research found that plasma cholesterol, phospholipid and triglyceride content were extremely low, and are probably accounted for by low dietary fat content and high physical activity in this group (Miller *et al*., 1968).

Epidemiologic studies have shown that relatively recent acculturated groups – for example: Australian Aborigines; American Dakota Siox, Oklahoma and Pima Indians; and New Zealand Polynesian and Pacific Islanders – have a high prevalence of diabetes and associated complications (Naqshbandi, Harris, Esler & Antwi-Nsiah, 2008). Furthermore, the transition from urban, back to traditional hunter-gatherer lifestyle improves a range of biomarkers related to glucose control. O'Dea *et al*. (1980) found that Australian Aborigines (Mowanjum Community, Derby, Western Australia) who spent 12 weeks reverting to a traditional lifestyle improved insulin response to a starch tolerance test. Similar research in overweight and diabetic Australian Aborigines living an urban lifestyle, demonstrated improvements in carbohydrate and lipid metabolism after a temporary (7 week) reversion to a hunter-gatherer lifestyle. Improvements in fasting plasma glucose, triglycerides and very-low density lipoprotein were reported, in addition to improved postprandial glucose clearance (O'Dea, 1984).

The relationship between modifying a traditional lifestyle for a Western lifestyle, and the associated deterioration in glucose tolerance and subsequent risk for type 2 diabetes, is epitomised in a series of studies carried out in the highlands of Papua New Guinea. Groups with Melanesian ancestry were studied over time following a period of acculturation. King *et al*. (1984) surveyed 308 participants across two villages and found a total absence of type 2 diabetes in these communities. The prevalence of impaired glucose tolerance was just 2%. At the time the results supported a theory that Melanesians were relatively resistant to the deleterious influence of acculturation upon glucose tolerance as seen in other Pacific groups. However, the authors concluded with a cautionary note that the population cultural change may have been insufficient, or of too recent onset, for deterioration in glucose tolerance to manifest. Follow-up surveys showed an unexpectedly high insulin response to glucose tests and it was suggested that the highland communities living in non-traditional circumstances in Papua New Guinea might be in a 'metabolic transition' towards diabetes (King *et al*., 1989). By the mid 1990's a further study (Dowse *et al*., 1994) found one of the highest prevalence's of abnormal glucose tolerance in the world with 27.5% of men and 33% of women reported as having type 2 diabetes, with a further 20.5% of men and 22% of women having impaired glucose tolerance. It was concluded that the Melanesian people had an extraordinary susceptibility to glucose intolerance which was exposed after adoption of modern lifestyle habits, and is a powerful example of how phenotypic expression of our genome can manifest in disease because of environmental change and physical inactivity.

Finally, Lindeberg, Eliasson, Lindahl & Ahrén (1999) performed a health survey of 164 subsistence horticulturists aged 20 to 86 years in the tropical islands of Kitava, Trobriand Islands, Papua New Guinea. Compared to 472 randomly selected age-matched Swedish controls, Kitavans had lower serum fasting insulin levels for all ages in addition to decreasing serum insulin with age. The mean insulin concentration in 50- to 74-year-old Kitavans was only 50% of that in Swedish participants. Kitavans also had low blood pressure and BMI; 87% of men and 93% of women aged 40-60 years had a BMI below 22 $kg{\cdot}m^2$ and not a single individual in this age group was overweight or obese (Lindeberg, 2010). These findings may explain why ischemic heart disease and stoke were rare or absent. This study is important as it provided one of the last opportunities to study humans who were uninfluenced by Western lifestyle and dietary habits. There is little reason to suspect genetics as a major explanation for the remarkable health of the Kitavan population. Compared with populations of northern European ancestry, traditional ethnic groups in general and Pacific Islanders especially seem more prone, not less, to develop diabetes after adopting a Western lifestyle (Lindeberg *et al*., 1999). Rather it is likely that the lifestyle afforded by the 'non-Westernised' environment, in terms of moderate to high physical activity and diet, is more in-line with the environment for which our genome was selected, reducing the manifestation of overt disease.

The idea that modern *Homo sapiens* are still adapted to an ancestral environment is reinforced by data showing that populations minimally affected by modern habits, or still living hunter-gather lifestyles, exhibit superior health markers, body composition, and physical fitness compared to industrialised populations. Although global studies of groups who live traditional lifestyles are an imperfect surrogate for our hominid ancestors, and despite the fact that most studies are observational surveys with small samples (with the exception of Lindeberg *et al*., [1999]); all groups show remarkable insulin sensitivity. It therefore seems reasonable to assume that pre-agricultural human ancestors would have shared this desirable metabolic characteristic and that the rise of insulin resistance and type 2 diabetes are driven by a changed environment in terms of physical activity and diet.

Summary

Nearly every aspect of the modern environment and our behavioural lifestyle choices inadvertently promotes obesity and diabetes. Although the evidence is imperfect, studies of fossils and human skeletal remains; anatomical, biochemical and histochemical comparison with other apes; and observations of modern acculturated and unacculturated hunter-gatherer groups, suggests that *Homo sapiens* are adapted for an environment where a large amount of energy expenditure is required to survive. This differs vastly from the modern ‘diabesogenic’ environment, to which we are now maladapted, and results in a wide range of physiological, cellular and metabolic responses and adaptations that predispose us to obesity, insulin resistance, hyperglycaemia, and diabetes.

Solutions to obesity and diabetes must include physical activity, but also consider what is socially and culturally acceptable. We must accept that cognitive effort is required to achieve this. An appreciation of the evolutionary pressures that are the driving force behind metabolism and physiology furthers understanding of pathophysiology. In attempting to promote lifestyle change that includes exercise to prevent, delay or treat obesity and diabetes, we need to understand that we have been shaped by evolution for a life of physical activity, but at the same time were have evolved to avoid unnecessary and metabolically ‘expensive’ movement. Aptly, “We must respect our genes and the circumstances which selected them, or accept the consequences” (Spurway & Wackerhage, 2006).

Appendix 2. Further critical discussion of the evidence for HIT as an exercise therapy for a range of populations

Introduction

Many chronic diseases are triggered by discordance between our genomes, which have been selected for high physical activity, and our lifestyles which are marked by inactivity. Thus, physical inactivity is an endemic problem in the United Kingdom and has been described as the greatest public health problem of our time (Sallis, 2009). The 2008 Health Survey for England (Craig, Mindell & Hirani, 2009) was the first-time objective measures of physical activity were used in a national general population survey and the results were alarming. It was estimated subjectively, via self-report, that 61% of men and 71% of women measured did not meet minimum physical activity recommendations for health. However, this figure increased to 94% for men and 96% for women when measured objectively using accelerometery.

The benefits of regular exercise in the prevention and treatment of disease is strongly evidenced (Booth, Chakravarthy, Gordon & Spangenburg, 2002b; Jones *et al*., 2011). Traditional exercise guidelines for health have focussed on relatively high-volumes of moderate-intensity exercise on most or all days of the week. Current guidelines from the ACSM (Haskell *et al*., 2007), BASES (O'Donovan *et al*., 2010) and the Department of Health (DoH, 2011) recommend 150 minutes per week of moderate-intensity aerobic exercise or 75 minutes of vigorous-intensity aerobic exercise. For adults at risk of cardiovascular disease or type 2 diabetes it is recommended to effectively double these durations (O'Donovan *et al*., 2010). However, perceived lack of time is the most commonly cited barrier to exercise (Reichart, Barros, Dominigues & Hallal, 2007; Korkiakangas, Alahuhta & Laitinen, 2009). Therefore, the use of exercise as a preventative or therapeutic treatment is conceptually problematic and the challenge of encouraging individuals and populations to lead a more active lifestyle remains.

The advent, and current popularity (Thompson, 2013), of high-intensity interval training (HIT) could offer some solution. HIT is characterised by an alternating low-intensity, high-intensity interval based approach to exercise. Total duration of exercise is usually lower than traditional guidelines and most of the exercise time is spent at a low-intensity, with the caveat that a series of high-intensity (often described as 'maximal' or 'all-out') periods of exercise are included. Proponents of HIT highlight the physiological benefits this type of exercise offers and suggest it has the potential to reduce time burden and therefore appeal to people who otherwise would not engage with exercise (Gibala & McGee, 2008; Gibala, Little, MacDonald & Hawley, 2012). Whether the general population could safely and effectively adopt HIT is not clear, and is an important consideration because the acceptability and accessibility of the activity to those for whom the intervention is intended, and the practicalities of building the activity into everyday life, need to be considered (Haines, Gillibrand & Garbutt, 2012). Thus, this critical review aims to: (1) consider issues of practicality by describing a low-volume approach to HIT, and (2) evaluate the current evidence for low-volume HIT as an exercise treatment for a range of populations.

Current evidence for low-volume, HIT

Research using healthy participants

Most studies on low-volume (≤ 30 min) HIT have used active or sedentary participants, primarily males, free from chronic disease (see Table 1). Low-volume HIT has been shown to induce rapid skeletal muscle remodelling towards a more oxidative phenotype, as reflected by intracellular signalling, and the maximal activity and protein content of mitochondrial enzymes. Perhaps most notably is the effect of HIT on peroxisome proliferator-activated receptor-γ coactivator (PGC)-1α, which is a transcription coactivator that interacts with a broad range of transcription factors involved in many biological responses; including mitochondria biogenesis, glucose and fatty acid metabolism, and fibre type switching in skeletal muscle (Liang & Ward, 2006). Evidence suggests PGC-1α is a powerful regulator of energy metabolism under conditions of both health and disease (Finck & Kelly, 2006) and is considered the 'master regulator' of mitochondria biogenesis (Wu *et al*., 1999). Several studies using low-volume HIT have demonstrated significant increases in PGC-1α. Little, Safdar, Wilkin, Taropolsky & Gibala (2010) used cycling efforts at 100% of peak power (8-12 × 60 s) determined during a maximal graded exercise test, interspersed with 75 s of rest, three times per week. After just two weeks the nuclear abundance of PGC-1α was ~25% higher. Similarly, Hood *et al*. (2011) found PGC-1α protein content increased by ~56% using a very similar protocol. Other studies using Wingate-based HIT have found increases in PGC-1α following 3 hours of recovery after a single bout of low-volume HIT (Gibala *et al*., 2009; Little, Safdar, Bishop, Tarnopolsky & Gibala, 2011a). Furthermore, Burgomaster *et al*. (2008) compared six weeks of low-volume HIT to continuous endurance exercise (40–60 min cycling at ~65% $\dot{V}O_{2peak}$) and found similar increases in PGC-1α protein content across groups despite significantly different total training volumes (~225 *vs*. ~2250 kJ·week^{-1} for HIT and endurance exercise, respectively).

Several studies have also found increases in 'upstream signals' that activate PGC-1α and mitochondria biogenesis (Gibala *et al*., 2009; Little *et al*., 2010, 2011a; Cochran *et al*., 2014). These include 5'-adenosine monophosphate-activated protein kinase (AMPK) and p38 mitogen-activated protein kinase (MAPK), which increase in response to the metabolic status of the muscle, most likely the intramuscular ATP:ADP/AMP ratio during and after exercise (Chen *et al*., 2000). Other studies have reported increases in key enzymes such as citrate synthase (CS), and cytochrome c oxidase (COX). CS is a rate limiting enzyme in the first step of the citric acid cycle, and increases in maximal activity of ~11–38% have been reported following low-volume HIT (Burgomaster, Hughes, Heigenhauser, Bradwell & Gibala, 2005; Burgomaster, Heigenhauser & Gibala, 2006; Gibala *et al*., 2006). COX is a large transmembrane protein complex and the last enzyme in the respiratory electron transport chain. Increased activity of ~35% has been reported in several studies (Gibala *et al*., 2006; Burgomaster *et al*., 2007; Hood *et al*., 2011). Taken together this evidence suggests that low-volume HIT is an effective strategy for improving oxidative metabolism and, as pointed out by Gibala *et al*. (2012), may highlight potential widespread health benefits.

Low aerobic capacity is an independent risk factor for type 2 diabetes and cardiovascular disease (Lee, Blair & Jackson, 1999; Wei *et al*., 1999; Church *et al*., 2004; Katzmarzyk, Church, Janssen, Ross & Blair, 2005; Lee *et al*., 2005). As such it is an important indicator for the potential health benefits of low-volume HIT. Increases in $\dot{V}O_{2max}$ of ~7–22.5% have been reported for studies ranging from 2 to 12 weeks (Rakobowchuk *et al*., 2008; Nybo *et al*., 2010; Dunham & Harms, 2012; Heydari *et al*., 2012; Jacobs *et al*., 2013; Matsuo *et al*., 2013). The large range of values are likely a result of heterogeneity in terms of the specific HIT protocol used, the intervention duration and baseline $\dot{V}O_{2max}$. The total session duration used in these studies is typically in the region of 20–30 min and of an intensity that might make them impractical, although Metcalfe *et al*. (2011) used a reduced-exertion HIT protocol with a total duration of just 10 min, inclusive of a warm-up and cool down, over a 6-week period and found $\dot{V}O_{2peak}$ improved by 12–15%. Participants also reported relatively low ratings of perceived exertion (RPE 13 ± 1) in this study. However, these findings were not supported by Haines (2015) who used a very similar protocol for a 4-week pilot study and found higher perceived exertion (RPE 17 ± 1) and smaller increases in $\dot{V}O_{2max}$ (~2%).

Skeletal muscle is a major site for glucose disposal, and high-intensity exercise places greater reliance on intramuscular glycogen as fuel, so it is not surprising that HIT has been speculatively linked to improving risk factors for insulin resistance and type 2 diabetes. Babraj *et al*. (2009) showed improvements in plasma glucose, insulin, and non-esterified fatty acid concentrations in response to an oral glucose tolerance test (12%, 37% and 26%, respectively) after just 2 weeks of HIT (repeated Wingate tests). Peripheral insulin sensitivity and muscle glucose uptake were improved by 23%. Others have found increases in insulin sensitivity of ~28–35% (Nybo *et al*., 2010; Richards *et al*., 2010; Hood *et al*., 2011; Metcalfe *et al.*, 2011) and increases in glycogen content of ~26–50% (Burgomaster *et al*., 2005; Burgomaster *et al*., 2006). Importantly low-volume HIT has also demonstrated rapid increases in glucose transporter (GLUT)-4 proteins. GLUT-4 allows facilitated diffusion of glucose into the muscle cells where it can be polymerised and stored as glycogen. Using similar protocols over a 2-week period, Little *et al*. (2010) and Hood, Little, Tarnopolsky, Myslik & Gibala (2011) found an increase of ~119–260% in GLUT-4 protein content. Since HIT depletes stored glycogen, muscle cells must recover during the post-exercise period and often overcompensate in a process known as muscle glycogen super compensation (Wojtaszewski *et al*., 2003). This is caused by up-regulation of glycogen synthase and via translocation of GLUT-4 to the muscle sarcolemma followed by an increase in the intrinsic activity of the transporters (Furtad, Poon & Klip, 2003) improving glucose transport post-exercise. Furthermore, there is a close relationship between PGC-1α function, insulin sensitivity and type 2 diabetes, which is likely related to the role of PGC-1α in mitochondria biogenesis (Liang & Ward, 2006). Therefore, a link between low-volume HIT and the prevention of metabolic and cardiovascular disease could be important.

The efficacy of low-volume HIT for inducing beneficial physiological changes is not in doubt. However, it should be noted that the majority of the research has used protocols and associated intensities that are likely too severe and thus intolerable for most people, although current research is starting to address the exercise intensity-affective response continuum for low-volume HIT (e.g. Jung *et al*., 2014). Also, in reiterating the recommendation in this review, that the terms ‘time-efficient’ and ‘low-volume’ should be the preserve of protocols that are less than 30 min per session, it is apparent that most low-volume HIT studies are only minimally under this recommendation (i.e. most protocols are of a duration of 20–30 min). Therefore, a greater focus on genuinely time-efficient approaches to HIT, using less severe intensities, is required. Such protocols would increase the likelihood that individuals will engage with and adhere to HIT. Whether such protocols could elicit similar skeletal muscle remodelling is not clear.

Table A1 Summary of studies that have used HIT with a total session duration of ≤ 30 min.

Authors	*n* [a]	Population	Age (years) (mean ± *s*)	BMI (kg·m^2) (mean ± *s*)	Low-volume HIT Protocol	Session Duration (min) [b]	Intervention Period	Main Outcomes
Adamson *et al.* *(2014)*	6	Elderly	65 ± 4	-	6-10 × 6 s cycle sprints (6-7% BM), 1 min recovery, 2 × per week	~7 – 11	6 weeks	↑ $\dot{V}O_{2max}$ (8%), ↓ blood pressure (9%), improved functional test scores
Babraj *et al. (2009)*	16	Sedentary or active, healthy men	21 ± 2	23.7 ± 3.1	4-6 × 30 s cycle sprints (7.5% BW), 4 min recovery, 3 × per week	~18 – 27	2 weeks	Improvements in plasma glucose (12%), insulin (37%) and NEFA (26%) concentration-time curves in response to OGTT, ↑ insulin sensitivity (23%)
Bond *et al.* (2015)	13	Adolescents	13 – 14 (range)	-	8-10 × 60 s cycling sprints (at 90% of peak power [c]), 75 s recovery, 3 × per week		2 weeks	↑ endothelial function and heart rate variability, no difference in triglycerides, cholesterol, glucose, insulin & blood pressure), most adaptation diminished at 72-h
Boutcher *et al.* (2013)	16	Sedentary, healthy overweight women	23 ± 4.0	27.7 ± 3.2	60 × 8 s cycle sprints (80 – 85% HRpeak [c]), 12 s recovery, 3 × per week	30	12 weeks	↑ $\dot{V}O_{2max}$ (19%), cardiac vagal modulation of heart rate was associated with aerobic training response
Boyd *et al. (2013)*	9	Overweight/ obese men	22.7 ± 3.8	32.3 ± 2.1	8-10 × 60 s cycling sprints (80 rpm at 100% of maximal power [c]), 60 s recovery, 3 × per week	26 – 30	3 weeks	↑ $\dot{V}O_{2max}$ (28%), ↑ COX and PGC-1α, no difference in perceived enjoyment or self-efficacy compared to a lower intensity exercise group
Buchan *et al.* (2013)	42	Adolescents	16.7 ± 0.6		4-6 × 30 s running sprints (maximal effort), 20–30 s recovery, 3 × per week	~4 – 6	7 weeks	↑ in vertical jump performance, 10 m sprint, predicted aerobic fitness, ↓ systolic blood pressure (4%), no change in biochemical markers
Burgomaster *et al.* *(2005)*	8	Healthy	22.1 ± 1	-	4-7 × 30 s cycle sprints (7.5% BW), 4 min recovery, 3 × per week	~18 – 27.5	2 weeks	↑ CS maximal activity (38%), ↑ resting muscle glycogen content (26%), improved exercise test scores

Burgomaster *et al.* *(2006)*	8	Active, healthy men	21 ± 1	-	4-7 × 30 s cycle sprints (7.5% BW), 4 min recovery, 3 x per week	~18 – 27.5	2 weeks	↑ PDH, ↑ CS maximal activity (11%), ↑ resting muscle glycogen content (50%), ↓ glycogenolysis and lactate production, improved exercise test scores
Burgomaster *et al.* *(2007)*	8	Active, healthy men	22 ± 1	-	4-6 × 30 s cycle sprints (7.5% BW), 4 min recovery, 3 x per week	~18 – 27	6 weeks (followed by 6 weeks detraining)	↑ COX-4 (~35%) and GLUT-4 (~25%) after 1 week and remained higher than baseline after 6 weeks of detraining
Burgomaster *et al.* *(2008)*	10	Healthy	24 ± 1	-	4-6 × 30 s cycle sprints (7.5% BW), 4.5 min recovery, 3 x per week	~20 – 30	6 weeks	↑ protein content of PGC-1α, ↑ markers of carbohydrate and lipid oxidation (similar responses compared to endurance exercise group)
Cochran *et al.* *(2014)*	17	Active, healthy	~22	-	Various – study was composed of two sub-studies, 3 × per week	~18	6 weeks	↑ markers of oxidative phenotype (AMPK, p38 MAPK, PGC-1α) to the same extent as isocaloric continuous training
Coppoolse *et al.* *(1999)*	11	COPD patients	63.8 ± 8	25. ± 10	9 × 60 s cycling (90% peak power [c]), 2 min recovery, 3 × per week (+ 2 days of continuous exercise)	30	8 weeks	↑ peak work load (17%), ↓ leg pain at peak power, no changes in VO_2, minute ventilation or CO_2 production
de Araujo *et al.* *(2012)*	15	Obese children	10.7 ± 0.7	30.8 ± 0.7	3-6 × 60 s treadmill efforts (100% peak velocity [c]), 3 min recovery, 2 × per week	~12 – 24	6 weeks	↑ $\dot{V}O_{2peak}$ (14.6%), ↓ insulinaemia (30.5%), ↓ body mass (2.6%), improved exercise test scores
Dunham & Harms *(2012)*	8	Active, healthy	20.2 ± 2.1	24.2 ± 2.2	5 × 60 s cycle bouts (90% of final intensity [c]), 3 min recovery, 3 × per week	23	4 weeks	↑ $\dot{V}O_{2max}$ (~8-10%), ↑ maximum inspiratory pressure (inspiratory muscle strength), improved exercise test scores
Eskelinen *et al*. (2015)	14	Inactive, healthy men	47	25.9	4-6 × 30 s cycle sprints (0.088 kp/kg FFM), 4 min recovery, 3 x per week	~18 – 27	2 weeks	↑ $\dot{V}O_{2peak}$ (6%), ↑ glucose uptake in main working muscles (12%), no difference in FFA uptake, similar to endurance training group
Freese *et al*. (2011)	12	Active, healthy	~21	≤ 30	4 × 30 s cycle sprints (7.5% BW), 4 min recovery	27	Three bouts (two days)	↓ postprandial TG after HIT with energy deficit (21%) and energy balance (10%) compared to

								control, no difference in responses of insulin, glucose or NEFA
Freese *et al*. (2014)	23	Women at risk of metabolic syndrome	51.7 ± 10.4	31.5 ± 7.1	4-8 × 30 s cycle sprints (9% FFM), 4 min recovery, 3 × per week	23 – 41	6 weeks	Improvements in role-physical (performing daily activities) and vitality (feelings of energy and fatigue)
Freese *et al*. (2015)	22	Women at risk of metabolic syndrome	52 ± 10.6	31.4 ± 7.1	4-8 × 30 s cycle sprints (9% FFM), 4 min recovery, 3 × per week	23 – 41	6 weeks	↓ fasted (12%) and postprandial TG (10%), six weeks of HIT did not magnify the attenuation in postprandial TG
Gibala *et al. (2006)*	8	Active, healthy men	24 ± 1	-	4-6 × 30 s cycle sprints (7.5% BW), 4 min recovery, 3 × per week	~ 18 – 27	2 weeks	↑ maximal activity of COX, improved muscle buffering capacity, ↑ glycogen content, improved exercise test scores (all similar to endurance training exercise group)
Gibala *et al. (2009)*	6	Active, healthy men	23 ± 2	-	4 × 30 s cycle sprints (7.5% BW), 4 min recovery	~18	Single bout	↑ phosphorylation of AMPK and p38 MAPK immediately after exercise, ↑ PGC-1α mRNA after 3 h recovery, PGC-1α protein content unchanged
Gillen *et al. (2012)*	7	Type 2 diabetes patients	62 ± 3	30.5 ± 1.9	10 × 60 s cycle bouts (~ 90% maximum intensity [c]), 1 min recovery	25	Single bout	↓ postprandial hyperglycaemia (65 ± 40%), ↓ peak glucose (~16%), ↓ average blood glucose (~14%)
Haines (2015)	11	Active, healthy	22.3 ± 7.3	23.8 ± 2.2	2 × 10-20 s cycle sprints (7.5% BW), ~3.5 min recovery, 2-3 × per week	10	4 weeks	↑ $\dot{V}O_{2max}$ (~2%), fasting glucose and body composition were unchanged, significant RPE associated with protocol (17 ± 1)
Harris *et al*. (2014)	6	Active, healthy females	22 ± 2	23.6 ± 1.8	4 × 30 s cycle sprints (7.5% BW), 4.5 min recovery, 3 x per week	~20	4 weeks	↑ $\dot{V}O_{2max}$ (~15%), ↑ number and mobilisation of circulating angiogenic cells which may enhance vascular repair, work-matched sprint continuous training was just as effective as traditional HIT
Heydari *et al. (2012)*	20	Inactive, healthy men	24.9 ± 4.3	28.4 ± 2.4	60 × 8 s cycle sprints (80 – 90% HR_{max} [c]), 12 s recovery, 3 × per week	30	12 weeks	↑ $\dot{V}O_{2max}$ (~15%), ↓ body mass (1.7%), ↓ in heart rate, ↑ stroke volume, improved forearm vasodilatory capacity, improved arterial stiffness, ↑ baroreceptor sensitivity

Hood *et al. (2011)*	7	Sedentary healthy men	45 ± 5	27 ± 5	10 × 60 s cycle efforts (60% of peak power [c]), 1 min recovery, 3 × per week	28	2 weeks	↑ CS and COX-4 (~35%), ↑ PGC-1α (56%), ↑ GLUT protein (~260%), improved insulin sensitivity (~35%)
Jung *et al.* (2014)	44	Inactive, healthy	-	-	10 × 60 s cycle efforts (~90% HR_{max} [c]), 1 min recovery	~25	Single bout	↑ enjoyment compared to CMI and CVI exercise (> 50% preferred HIT), ↑ pleasure after exercise compared to CVI exercise, but ↓ pleasure compared to CMI at these times, confidence to engage with HIT = CMI, and ↑ than CVI
Jung *et al.* (2015)	15	Inactive with pre-diabetes	51 ± 11	33.1 ± 7.7	10 × 60 s cycle efforts (~90% HR_{peak} [c]), 1 min recovery, 3 × per week	25	4 weeks (unsupervised, at home)	Compared to a moderate-intensity continuous training group: greater adherence to prescribed protocol (89 ± 11% *vs*. 71 ± 31%), more time spent in vigorous physical activity per week measured by accelerometer (24 ± 18 min *vs*. 11 ± 10 min)
Kilpatrick *et al*. (2014)	20	Inactive overweight/ obese	22 ± 4	29 ± 3	Various – study compared different HIT intervals against continuous exercise	28	Single bouts	Performing more intervals of shorter duration produces lower post-exercise RPE compared to fewer intervals of longer duration
Kilpatrick *et al*. (2015)	24	Active, healthy	22 ± 3	24 ± 4	Various – study compared different HIT intervals against continuous exercise	24	Single bouts	Interval protocol produced affective and enjoyment responses similar to moderate continuous exercise and more positive than heavy continuous exercise
Knowles *et al*. (2015)	39	Sedentary and active ageing males	≥ 55	-	6 × 30 s cycle sprints (40% PPO [c]), 3 min recovery, 1 × every 5 days	~21	6 weeks	↑ $\dot{V}O_{2max}$ (~8.5-10%), ↑ perceptions of health-related quality of life and exercise motives (especially appearance and weight management)
Jacobs *et al. (2013)*	16	Inactive, healthy men	23 ± 2	-	8-12 × 60 s cycle efforts (100% of peak power [c]), 75 s recovery, 3 × per week	21 – 30	2 weeks	↑ $\dot{V}O_{2peak}$ (~8%), expansion of skeletal muscle mitochondria (~20%) as assessed via COX, improved exercise test scores, no change to cardiac output, total haemoglobin, plasma volume or peripheral fatigue resistance

Little *et al. (2010)*	7	Active, healthy men	24 ± 0.4	-	8-12 × 60 s cycle efforts (100% of peak power [c]), 75 s recovery, 3 × per week	20 – 29	2 weeks	↑ maximal activity and protein content of CS and COX, ↑ PGC-1α (~25%), ↑ SIRT1 (~56%), ↑ muscle glycogen (17%), ↑ GLUT-4 (119%), improved exercise test scores
Little *et al. (2011a)*	8	Active, healthy men	24 ± 1	-	4 × 30 s cycle sprints (7.5% BW), 4 min recovery	~18	Single bout	↑ p38 MAPK and AMPK in muscle cytosol, ↑ nuclear PGC-1α protein
Little *et al. (2011b)*	8	Type 2 diabetes patients	62.5 ± 7.6	31.7 ± 5.8	10 × 60 s cycle efforts (~ 90% HR_{max}), 1 min recovery, 3 × per week	25	2 weeks	↑ markers of mitochondrial biogenesis (including CS, ~20%), ↑ GLUT-4 protein content (~369%), ↓ average 24 h blood glucose concentration (~14%), improved 3 h postprandial glucose control (~42%)
Little *et al*. (2014)	10	Inactive overweight/ obese	41 ± 11	36 ± 7	10 × 60 s cycle efforts (~ 90% HR_{peak}), 1 min recovery	25	Single bout	Greater and more lasting effects on reducing incremental postprandial glucose compared with continuous moderate intensity exercise
Martinez *et al*. (2014)	20	Inactive overweight/ obese	22 ± 4	29 ± 3	Various – study compared different HIT intervals against continuous exercise	28	Single bouts	Higher pleasure and enjoyment for shorter interval trials
Matsuo *et al. (2013)*	28	Sedentary, healthy men	26.5 ± 6.2	< 25	Various – study included more than one HIT group, 5 × per week	10 – 18	8 weeks	↑ $\dot{V}O_{2max}$ (16.7-22.5%), ↑ left ventricular mass, stroke volume and resting heart rate
Metcalfe *et al. (2011)*	14	Sedentary, healthy men	26 ± 3	-	1-2 × 10-20 s cycle sprints (7.5% BW), ~3.5 min recovery, 3 × per week	10	6 weeks	↑ $\dot{V}O_{2peak}$ (12-15%), ↑ insulin sensitivity (28%)
Nybo *et al. (2010)*	8	Active, healthy men	37 ± 3	-	5 × 120 s treadmill running (> 95% HR_{max}), recovery not specified, 3 × per week	20	12 weeks	↑ $\dot{V}O_{2max}$ (14%), ↑ insulin sensitivity (28%), improved response to OGTT
Oliveira *et al*. (2013)	15	Healthy men	24 ± 4	24.2 ± 2.5	~6-7 × 120 s treadmill efforts (at 100% VO_{2peak} [c]), ~1 min recovery	~19	Single bout	Compared to continuous training HIT resulted in: ↑ felt arousal, ↑ RPE, ↓ pleasure, no difference in enjoyment

Parolin *et al. (1999)*	6	Sedentary healthy men	28.5 ± 1.8	-	3 × 30 s isokinetic cycle sprint (7.5% BW), 4 min recovery	~9.5	Single bout	Large ↑ in GP for sprint 1 at 6 s, ↓ in GP and ↑ in PDH after 15 s of sprint 1 and during sprint 3
Rakobowchuk *et al. (2008)*	10	Inactive, healthy	23.6 ± 3.2	23.6 ± 3	4-6 × 30 s cycle sprints (7.5% BW), 4 min recovery, 3 × per week	~20 - 29	6 weeks	↑ $\dot{V}O_{2peak}$ (~7%), improved popliteal endothelial function and artery distensibility, ↑ anaerobic peak power
Richards *et al. (2010)*	21 19	Sedentary or active, healthy	- -	- -	(Dual study) 4-7 × 30 s cycle sprints (7.5% BW), 4 min recovery, 3 x per week	18 – 31.5	2 weeks	↑ insulin sensitivity, no change in resting energy expenditure or thermogenic response
Sevits *et al. (2005)*	15 12	Active, healthy men	23 ± 1 26 ± 2	24.4 ± 0.8 23.6 ± 0.5	(Dual study) 4 × 30 s cycle sprints (7.5% BW), 4 min recovery	~18	Single bout	↑ TDEE by ~950 kJ, no change in RMR
Skleryk *et al*. (2013)	8	Sedentary, obese men	40.2 ± 2.3	32.2 ± 2.1	8-12 × 10 s cycle sprints (5% BW), 80 s recovery, 3 x per week	~18 – 21	2 weeks	No changes in metabolic or skeletal muscle adaptations in the HIT group or the traditional exercise recommendations comparison group
Trilk *et al. (2010)*	14	Sedentary overweight/ obese women	30.1 ± 6.8	35.7 ± 6.3	4-7 × 30 s cycle sprints (5% BW), 4 min recovery, 3 x per week	~22 – 31.5	4 weeks	↑ $\dot{V}O_{2max}$ (12%), ↑ stroke volume (11.4%), ↓ resting heart rate (-8.1%)
Whyte *et al. (2010)*	10	Sedentary overweight/ obese men	32.1 ± 8.7	31 ± 3.7	4-6 × 30 s cycle sprints (6.5% BW), 4.5 min recovery, 3 × per week	~20 – 30	2 weeks	↑ $\dot{V}O_{2max}$ (9.5%), ↑ anaerobic mean power (3.6%), improved insulin sensitivity index (23.3%) and fasting fat oxidation, ↓ systolic blood pressure and fasting carbohydrate oxidation (not apparent after 72 h), ↓ waist and hip circumference
Whyte *et al*. (2013)	10	Sedentary overweight/ obese men	26.9 ± 6.2	29.9 ± 9.1	4 × 30 s cycle sprints (6.5% FFM), 4.5 min recovery, 3 × per week	24	Single bout	↑ insulin sensitivity (~45%) compared to control (but no difference compared to matched-work extended sprint group), ↑ fat oxidation in the fasted state (63%) 24-h post exercise

Zelt *et al*. (2014)	11	Active, healthy men	23 ± 5	25 ± 3	(Multiple HIT groups)	~25 – 30	4 weeks	↑ $\dot{V}O_{2peak}$ (4–8%), ↑ lactate threshold (8–16%), critical power (5–7%) and Wingate peak power (6%) (with no significant difference between HIT groups or endurance training comparison group)
	12		22 ± 2	26 ± 3	4–6 × 30 s *or* 15 s cycle sprints (6.5% FFM), 4.5 min *or* 4.75 min recovery, 3 × per week			

Abbreviations: AMPK = 5'-adenosine monophosphate-activated protein kinase; BM = body mass; COPD = chronic obstructive pulmonary disease; CMI = continuous moderate-intensity; CVI = continuous vigorous-intensity; COX = cytochrome c oxidase; CS = citrate synthase; FFA = free fatty acid; FFM = fat free mass; GLUT = glucose transporter; GP = glycogen phosphorylase; HR_{max} = maximum heart rate; MAPK = mitogen-activate protein kinase; NEFA = non-esterified fatty acids; OGTT = oral glucose tolerance test; PDH = pyruvate dehydrogenase; PGC-1α = peroxisome proliferator-activated receptor-γ coactivator-1α; RMR = resting metabolic rate; RPE = rating of perceived exertion; SIRT = sirtuin; TDEE = total daily energy expenditure; TG = triglyceride; $\dot{V}O_{2max}$ = maximal volume of oxygen consumed per minute; $\dot{V}O_{2peak}$ = peak volume of oxygen consumed per minute

[a] Number of participants in HIT group; [b] Values are conservative (several studies do not adequately detail warm-up and cool down procedures); [c] Intensity determined during a maximal graded exercise test

Research using participants with chronic disease

Low-volume HIT studies investigating physiological response and adaptation using participants with chronic disease are limited. Two studies have considered patients with type 2 diabetes and one study has used patients with chronic obstructive pulmonary disease. A further five studies have used overweight or obese participants. Little *et al*. (2011b) used eight patients with type 2 diabetes (haemoglobin A_{1C} [HbA_{1c}] 6.9 ± 0.7%) who undertook cycling intervals at ~90% maximum heart rate (10 × 60 s intervals with a 1:1 work to rest ratio) three times per week for two weeks. Patients were diagnosed with diabetes at least three months prior to the start of the study, were not taking insulin and had no long-term diabetic complications (e.g. retinopathy, neuropathy or nephropathy). Six of the patients were however using standard blood glucose lowering medications (e.g. metformin). Average 24 h blood glucose concentration was lowered (~24%) and 3 h postprandial glucose control was improved (~42%) after the HIT intervention. Furthermore, GLUT-4 protein content increased by ~369%. Similarly, the same research group (Gillen *et al*., 2012) used this sample and reported decreases in postprandial hyperglycaemia (~65%), peak glucose (~16%) and average blood glucose (~14%). Little, Jung, Wright, Wright & Manders (2014) also found greater and more lasting effects on reducing postprandial glucose compared to continuous moderate-intensity exercise. Reducing post meal glucose excursions is important for the treatment of type 2 diabetes as they are associated with comorbidities such as cardiovascular disease (Ceriello *et al*., 2004). It is also important for achieving targeted HbA_{1c} levels, which is a relatively new method of diagnosing diabetes preferred in the UK (Woerle *et al*., 2007; John, 2012).

PGC-1α is implicated in insulin resistance and type 2 diabetes as it is downregulated in skeletal muscle of diabetic patients (Mootha *et al*., 2003), and a common polymorphism of the PGC-1α gene has been linked to an increased risk of type 2 diabetes (Hara *et al*., 2002). PGC-1α has also been reported to activate the expression of insulin-sensitive GLUT-4 in skeletal muscle (Michael *et al*., 2001). Therefore, PGC-1α has a likely role in preventing type 2 diabetes, possibly through an association with mitochondria biogenesis and energy metabolism. As previously discussed, it is clear that low-volume HIT is a potent means of activating PGC-1α-mediated mitochondria biogenesis in healthy individuals. The study by Little *et al*. (2011b) provides preliminary evidence that this is also the case for patients with type 2 diabetes, evidenced by increased citrate synthase activity.

Research with overweight or obese participants has used both Wingate-based HIT (Trilk, Singhal, Bigelman & Cureton, 2010; Whyte, Gill & Cathcart, 2010) and less intense protocols (Hood *et al*., 2011; Boyd, Simpson, Jung & Gurd, 2013). Whyte *et al*. (2010) used six sessions of sprint interval training over two weeks with overweight and obese men (BMI 31 ± 3.7) and found improved $\dot{V}O_{2max}$, improved insulin sensitivity, increased resting lipid oxidation and reduced systolic blood pressure. The change to insulin sensitivity diminished by 72 h post-intervention so it is possible improvements might simply reflect a temporal response – rather than a lasting adaptation. However, using a similar study, Richards *et al*. (2010) measured insulin sensitivity using the gold-standard hyperinsulinaemic euglycaemic clamp technique and concluded improvement was not due to the acute effects of the most recent exercise bout. Boyd *et al*. (2013) compared two low-volume HIT protocols with differing intensities in obese men (BMI 32.3 ± 2.1 $kg{\cdot}m^2$) and found skeletal muscle remodelling toward a more oxidative phenotype, as assessed via increased activity of COX, CS and PGC-1α, occurred irrespective of intensity – strengthening the notion that lower intensity HIT can also be efficacious. Improvements in $\dot{V}O_{2peak}$ and exercise test scores were also reported for both groups, although this was significantly higher for the high-intensity group.

Of note, more recent research has started to address psychological constructs related to the tolerability and adherence of HIT in patients with chronic disease. Boyd *et al*. (2013) reported similar levels of enjoyment regardless of intensity, in addition to high confidence to successfully complete HIT and schedule sessions into the lives of people with obesity. This occurred despite high-intensity exercise being perceived to be less pleasurable and suggests that participants perceived HIT as manageable. Jung, Bourne, Beauchamp, Robinson & Little (2015) compared HIT to moderate-intensity continuous training in patients with pre-diabetes. Patients were asked to maintain unsupervised exercise at home for a period of four-weeks. Exercise adherence was monitored via accelerometery and activity logs and was greater in the HIT group (89%) compared to the moderate-intensity continuous group (71%). Other studies have reported higher pleasure and enjoyment for low-volume HIT compared to continuous exercise in obese patients (Martinez, Kilpatrick, Salomon, Jung & Little, 2014) and improvements in perceived ability to perform daily activities and feelings of 'energy' and 'fatigue' in women at risk of metabolic disease (Freese *et al*., 2014). Although we do not know if these perceptions can translate into acceptable long-term adherence to HIT, taken together with physiological data, it seems that this type of exercise might be an appropriate exercise choice to improve vascular and metabolic health in overweight and obese individuals.

Research in older adults and young people

Two preliminary studies have specifically considered low-volume HIT in the elderly population. Adamson, Lorimer, Cobley & Babraj (2014) randomly allocated 12 participants to a control group or HIT group (collective mean age of 64.3 years) who performed 6–10 six second 'all-out' cycling efforts against 6.5–7% body weight over a six-week period. $\dot{V}O_{2max}$ increased by 8%, systolic blood pressure decreased by 9% and functional fitness test scores improved. Knowles, Herbert, Easton, Sculthorpe & Grace (2015) found similar increases in $\dot{V}O_{2max}$ (~8.5-10%) following a reduced exertion Wingate-based HIT protocol and improved perceptions of health-related quality of life and exercise motives (especially appearance and weight management) in ageing men. Whether low-volume HIT can be a safe and effective strategy for counteracting age-related functional decline, reducing disease risk and promoting further engagement in physical activity requires more detailed consideration.

Similarly, research using children is sparse. de Araujo *et al*. (2012) suggestes HIT is a promising strategy for promoting health adaptations in children because it more closely resembles their spontaneous exercise patterns, including both physiological and psychological predilections. They randomly assigned thirty obese (BMI 30.8 ± 0.7 $kg \cdot m^2$) children aged between 8 and 12 years, into a low-volume HIT or endurance training group. Children in the HIT group performed repeated 60 s efforts at 100% of the peak velocity determined during a maximal graded test, interspersed with 3 min of active recovery. This was performed 3-6 times per week for 12 weeks. $\dot{V}O_{2peak}$, exercise tests scores and insulinaemia were improved by a similar amount in both groups. Finally, improvements in endothelial and autonomic function, measured non-invasively via flow mediated dilation and heart rate variability respectively, may result in lowered cardiovascular disease risk in adolescents after just two-weeks (6 sessions) of low-volume, HIT (Bond *et al*., 2015). Although the study is limited by a small sample size and lack of control group, this finding is important because the effect of exercise usually focuses on traditional cardiovascular disease risk factors (e.g. blood pressure, blood lipid profile, insulin sensitivity), whereas changes in endothelial function have rarely been explored, yet it is a sentient event in the atherosclerotic process (Bond, Williams & Barker, 2016).

Conclusions

The general efficacy of HIT as a potent means of inducing adaptations beneficial for health is not in question (Biddle & Batterham, 2015). It is clear in this review that this is also the case for low-volume HIT of less than 30 min duration per session. However, what has not been considered so well is the effectiveness to clinical practice and public health, for those with chronic disease. At present most research has focused on protocols that are exclusively or in combination, too intense and not particularly time-efficient compared to traditional exercise guidelines. Although proponents of HIT are not proposing Wingate-based HIT as a strategy to improve public health, the fact remains that a great deal of the research in this field is based around these protocols. In addressing concerns related to tolerability of such protocols some researchers have adopted more practical approaches to HIT (e.g. Little *et al*., 2010), but even these are near-maximal with a 1:1 work-to-rest ratio. Furthermore, most HIT research is only minimally under the current guideline of 30 min for moderate-intensity exercise per session. Future studies need to work on refining low-volume HIT protocols to investigate if genuinely time-efficient, practical and tolerable approaches can provide similar physiological benefits. How intensity influences cognitive and affective responses such as pleasure and displeasure will be important as they might predict adherence.

The commonly prescribed dose of 150 min per week of moderate-intensity exercise may be the result of a self-fulfilling prophecy whereby, based primarily on epidemiological data, 150 min was identified as a good recommendation, and subsequent research has used this threshold to define intervention goals (Church & Blair, 2009). From an evolutionary behavioural standpoint, we should accept that we are unlikely to engineer significant volumes of exercise into our current 'diabesogenic' environment. Therefore, research focussing on alternative forms of exercise such as low-volume HIT, which could be more time-efficient, is warranted. However, this should not blind us to two things. First, the overall quality of the scientific evidence at present is limited and even fulfils criteria which could mark it as 'bad science': namely small and unrepresentative samples, lack of control groups, lack of randomisation and excessive speculation. We should be cautious extrapolating current evidence to public health settings or exercise guidelines. Second, currently there is insufficient evidence to suggest that HIT can be adopted by everyone and the approach could be hazardous for high-risk individuals. Although difficult to achieve for most people, traditional exercise guidelines are not passé. Rather they should be considered an activity target that can be complemented by other types of activity, such as HIT. And as eloquently argued by Professor Alan Batterham, "HIT deserves a prominent place among a smörgåsbord of physical activity and exercise options" (Biddle & Batterham, 2015). Emphasising healthy lifestyles for their own sake, rather than a preoccupation with body weight, will allow exercise to be used to its full potential. In a spirit of pragmatism, the choice is not the optimal exercise prescription but one we might deem to be ‘good enough’.

Appendix 3. **AHA/ACSM Health/Fitness Preparticipation Screening Questionnaire.**

AHA/ACSM Health/Fitness Facility Preparticipation Screening Questionnaire

Assess your health status by marking all *true* statements

History

You have had:

___ a heart attack
___ heart surgery
___ cardiac catheterization
___ coronary angioplasty (PTCA)
___ pacemaker/implantable cardiac
___ defibrillator/rhythm disturbance
___ heart valve disease
___ heart failure
___ heart transplantation
___ congenital heart disease

Symptoms

___ You experience chest discomfort with exertion.
___ You experience unreasonable breathlessness.
___ You experience dizziness, fainting, or blackouts.
___ You take heart medications.

Other health issues

___ You have diabetes.
___ You have asthma or other lung disease.
___ You have burning or cramping sensation in your lower legs when walking short distances.
___ You have musculoskeletal problems that limit your physical activity.
___ You have concerns about the safety of exercise.
___ You take prescription medication(s).
___ You are pregnant.

If you marked any of these statements in this section, consult your physician or other appropriate health care provider before engaging in exercise. You may need to use a facility with a **medically qualified staff.**

Cardiovascular risk factors

___ You are a man older than 45 years.
___ You are a woman older than 55 years, have had a hysterectomy, or are postmenopausal.
___ You smoke, or quit smoking within the previous 6 months.
___ Your blood pressure is >140/90 mm Hg.
___ You do not know your blood pressure.
___ You take blood pressure medication.
___ Your blood cholesterol level is > 200 mg/dL.
___ You do not know your cholesterol level.
___ You have a close blood relative who had a heart attack or heart surgery before age 55 (father or brother) or age 65 (mother or sister).
___ You are physically inactive (i.e., you get <30 minutes of physical activity on at least 3 days per week).
___ You are > 20 pounds overweight.

If you marked two or more of the statements in this section you should consult your physician or other appropriate health care provider before engaging in exercise. You might benefit from using a facility with a professionally qualified exercise staff to guide your exercise program.

___ None of the above

You should be able to exercise safely without consulting your physician or other appropriate health care provider in a self-guided program or almost any facility that meets your exercise program needs.

Appendix 4. **ACSM logic model for classification of risk.**

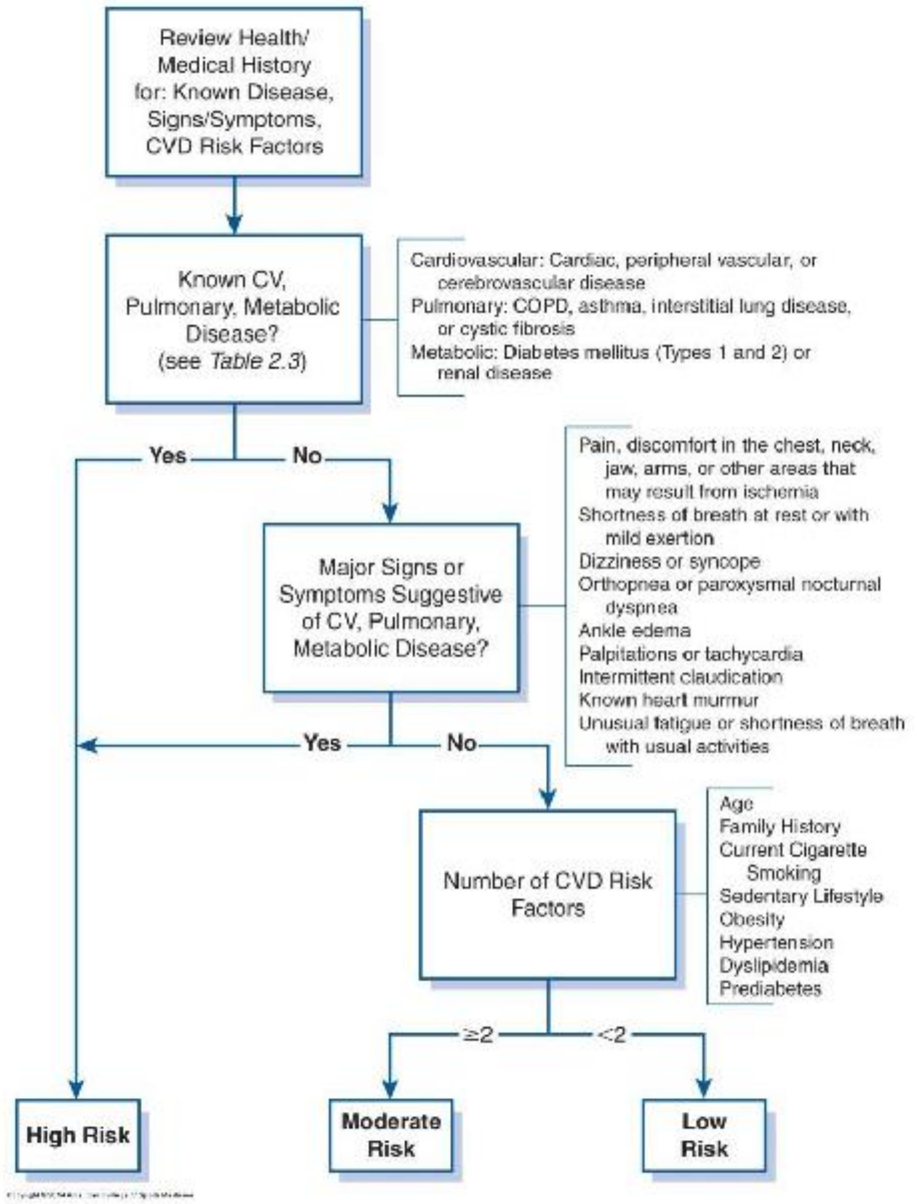

FIGURE 2.3. Logic model for classification of risk. CV, cardiovascular; CVD, cardiovascular disease.

TABLE 2.3. **New ACSM Recommendations for Exercise Testing Prior to Exercise-Diagnosed Cardiovascular Disease**

Unstable or new or possible symptoms of cardiovascular disease (see *Table 2.2*)
Diabetes mellitus and at least one of the following:
Age >35 yr OR
Type 2 diabetes mellitus >10-yr duration OR
Type 1 diabetes mellitus >15-yr duration OR
Hypercholesterolemia (total cholesterol ≥240 mg · L^{-1}) (6.62 mmol · L^{-1}) OR
Hypertension (systolic blood pressure ≥140 or diastolic ≥90 mm Hg) OR
Smoking OR
Family history of CAD in first-degree relative <60 yr OR
Presence of microvascular disease OR
Peripheral artery disease OR
Autonomic neuropathy
End-stage renal disease
Patients with symptomatic or diagnosed pulmonary disease including chronic obstructive pulmonary disease (COPD), asthma, interstitial lung disease, or cystic fibrosis.

ACSM, American College of Sports Medicine; CAD, coronary artery disease.

***Appendix 5*. The Feeling Scale (FS) (Hardy & Rejeski, 1989).**

Feeling Scale

PLEASURE – DISPLEASURE

+ 5	Very good
+ 4	
+ 3	Good
+ 2	
+ 1	Fairly good
0	Neutral
- 1	Fairly bad
- 2	
- 3	Bad
- 4	
- 5	Very bad

***Appendix 6*. 15-point Rating of Perceived Exertion (RPE) Borg scale (Borg, 1970).**

Rating of Perceived Exertion (RPE)

EFFORT

6	No exertion at all
7	Extremely light
8	
9	Very light
10	
11	Light
12	
13	Somewhat hard
14	
15	Hard (heavy)
16	
17	Very hard
18	
19	Extremely hard
20	Maximal exertion

*Appendix 7***. Exercise Enjoyment Scale (EES) (Stanley & Cumming, 2009).**

Exercise Enjoyment Scale

ENJOYMENT

7	Extremely
6	Very much
5	Quite a bit
4	Moderately
3	Slightly
2	Very little
1	Not at all

Appendix 8. **Confirmation of School Research Ethics Panel (SREP) approval.**

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26 February 2015

TO WHOM IT MAY CONCERN

Name:	**Mr Matthew Haines - University of Huddersfield**
Research Project Title:	**"The effects of modified High-intensity Interval Training (HIT) on glucose homeostasis in impaired fasting"**

Mr Matthew Haines, the holder of this letter, is a PhD Student at the University of Huddersfield, where he is currently pursuing a doctorate on the above topic within the Centre for Applied Psychological and Health Research.

Mr Haines' research has been through the School Research Ethics Panel (SREP) and his project was approved on 20 July 2012 (with a further revision approved 26 February 2015).

I confirm that:

1. This research proposal has been discussed with the Chief Investigator and agreement in principle to sponsor the research is in place.
2. An appropriate process of scientific critique has demonstrated that this research proposal is worthwhile and of high scientific quality.
3. Any necessary indemnity or insurance arrangements will be in place before this research starts. Insurance or indemnity policies will be renewed for the duration of the study where necessary.
4. Arrangements will be in place before the study starts for the research team to access resources and support to deliver the research as proposed.
5. Arrangements to allocate responsibilities for the management, monitoring and reporting of the research will be in place before the research starts.
6. The duties of sponsors set out in the Research Governance Framework for Health and Social Care will be undertaken in relation to this research.
7. I understand that the summary of this study will be published on the website of the National Research Ethics Service (NRES), together with the contact point for enquiries named in this application. Publication will take place no earlier than 3 months after issue of the ethics committee's final opinion or the withdrawal of the application.

If you require any further information in relation to this letter, please to not hesitate to contact me.

Yours faithfully

Prof Rachel Armitage
Chair, School Research Ethics Panel (SREP)
School of Human and Health Sciences
[redacted]

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Appendix 9. **Confirmation of National Research Ethics Service (NRES) approval.**

NHS
Health Research Authority

NRES Committee Yorkshire & The Humber - Sheffield

Jarrow Business Centre
Viking Business Park
Rolling Mill Road
Jarrow
Tyne and Wear
NE32 3DT

Telephone: 0191 4283564

18 June 2015

Mr Matthew Haines
University of Huddersfield
Queensgate Campus
Huddersfield
HD1 3DH

Dear Mr Haines

Study title:	**The effect of low-volume, high-intensity training on intermediate hyperglycaemia in service users of an NHS Specialist Diabesity Service**
REC reference:	**15/YH/0226**
IRAS project ID:	**167716**

Thank you for your correspondence of 16 June 2015, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this favourable opinion letter. The expectation is that this information will be published for all studies that receive an ethical opinion but should you wish to provide a substitute contact point, wish to make a request to defer, or require further information, please contact the REC Manager, Miss Kathryn Murray, nrescommittee.yorkandhumber-sheffield@nhs.net. Under very limited circumstances (e.g. for student research which has received an unfavourable opinion), it may be possible to grant an exemption to the publication of the study.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

A Research Ethics Committee established by the Health Research Authority

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations

Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publicly accessible database. This should be before the first participant is recruited but no later than 6 weeks after recruitment of the first participant.

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g. when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non-clinical trials this is not currently mandatory.

If a sponsor wishes to request a deferral for study registration within the required timeframe, they should contact hra.studyregistration@nhs.net. The expectation is that all clinical trials will be registered, however, in exceptional circumstances non registration may be permissible with prior agreement from NRES. Guidance on where to register is provided on the HRA website.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Ethical review of research sites

NHS sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see

"Conditions of the favourable opinion" below).

Non-NHS sites

The Committee has not yet completed any site-specific assessment (SSA) for the non-NHS research site(s) taking part in this study. The favourable opinion does not therefore apply to any non-NHS site at present. We will write to you again as soon as an SSA application(s) has been reviewed. In the meantime no study procedures should be initiated at non-NHS sites.

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
Covering letter on headed paper [Cover letter]	1.0	11 March 2015
Covering letter on headed paper [Cover letter for provisional]	1.0	16 June 2015
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Evidence of sponsor indemnity from 01.08.14 to 31.07.15]	1.0	11 March 2015
GP/consultant information sheets or letters [GP information letter]	1.0	24 April 2015
Letter from sponsor [Letter from sponsor]	1.0	26 February 2015
Letters of invitation to participant [Letter of invitation]	2.0	10 June 2015
Participant consent form [Consent form]	1.0	24 April 2015
Participant information sheet (PIS) [PIS - control group]	1.0	25 February 2015
Participant information sheet (PIS) [Participant Information Sheet]	2.0	10 June 2015
REC Application Form [REC_Form_12062015]		12 June 2015
Research protocol or project proposal [Project overview]	2.0	10 June 2015
Summary CV for Chief Investigator (CI) [CI CV summary]		06 February 2015
Summary CV for supervisor (student research) [Summary CV for supervisors]	1.0	24 April 2015

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

<u>Reporting requirements</u>

The attached document *"After ethical review – guidance for researchers"* gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports

- Notifying the end of the study

The HRA website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website:
http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/

HRA Training

We are pleased to welcome researchers and R&D staff at our training days – see details at http://www.hra.nhs.uk/hra-training/

15/YH/0226	**Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project.

Yours sincerely

pp.
Professor Basil Sharrack
Chair

Email:nrescommittee.yorkandhumber-sheffield@nhs.net

Enclosures: "After ethical review – guidance for researchers" *[SL-AR2]*

Copy to: *Prof Rachel Armitage, University of Huddersfield*
Ms Judith Holliday, Mid Yorkshire Hospitals NHS Trust

Appendix 10. **Letter of access for research.**

The Mid Yorkshire Hospitals NHS
NHS Trust

Bringing together community and hospital services

If you need this correspondence in a larger font size please contact: 01924 543175

Research Office
Rowan House
Pinderfields Hospital
Aberford Road
Wakefield
WF1 4DG
Tel:01924 543174
Fax:01924 543766
MY.Research@midyorks.nhs.uk

Mr M Haines
[redacted]

JH/CSC/N:R&D

9 November 2015

Dear Mr Haines

Re: The effect of low volume, high intensity exercise on pre-diabetes

Letter of access for research

This letter should be presented to each participating organisation before you commence your research at that site. The participating organisation is: **Mid Yorkshire Hospitals NHS Trust.**

In accepting this letter, each participating organisation confirms your right of access to conduct research through their organisation for the purpose and on the terms and conditions set out below. This right of access commences on 9 November 2015 and ends on 8 November 2016 unless terminated earlier in accordance with the clauses below.

You have a right of access to conduct such research as confirmed in writing in the letter of permission for research **Mid Yorkshire Hospitals NHS Trust.** Please note that you cannot start the research until the Principal Investigator for the research project has received a letter from us giving confirmation from the individual organisation of their agreement to conduct the research.

The information supplied about your role in research at the organisation(s) has been reviewed and you do not require an honorary research contract with the organisation(s). We are satisfied that such pre-engagement checks as we consider necessary have been carried out, however the final decision rests with The University of Huddersfield. Evidence of checks should be available on request to the organisation.

You are considered to be a legal visitor to the organisations premises. You are not entitled to any form of payment or access to other benefits provided by the organisation or this organisation to employees and this letter does not give rise to any other relationship between you and the organisation, in particular that of an employee.

While undertaking research through the organisation you will remain accountable to your substantive employer but you are required to follow the reasonable instructions of the organisation or those instructions given on their behalf in relation to the terms of this right of access.

Where any third party claim is made, whether or not legal proceedings are issued, arising out of or in connection with your right of access, you are required to co-operate fully with any investigation by the organisation in connection with any such claim and to give all such assistance as may reasonably be required regarding the conduct of any legal proceedings.

You must act in accordance with the organisations policies and procedures, which are available to you upon request, and the Research Governance Framework.

You are required to co-operate with the organisation in discharging its duties under the Health and Safety at Work etc Act 1974 and other health and safety legislation and to take reasonable care for the health and safety of yourself and others while on the organisations premises. You must observe the same standards of care and propriety in dealing with patients, staff, visitors, equipment and premises as is expected of any other contract holder and you must act appropriately, responsibly and professionally at all times.

If you have a physical or mental health condition or disability which may affect your research role and which might require special adjustments to your role, if you have not already done so, you must notify your employer and each organisation prior to commencing your research role at that organisation.

You are required to ensure that all information regarding patients or staff remains secure and *strictly confidential* at all times. You must ensure that you understand and comply with the requirements of the NHS Confidentiality Code of Practice and the Data Protection Act 1998. Furthermore you should be aware that under the Act, unauthorised disclosure of information is an offence and such disclosures may lead to prosecution.

You should ensure that, where you are issued with an identity or security card, a bleep number, email or library account, keys or protective clothing, these are returned upon termination of this arrangement. Please also ensure that while on the organisations premises you wear your ID badge at all times, or are able to prove your identity if challenged. Please note that the organisation does not accept responsibility for damage to or loss of personal property.

This organisation may revoke this letter and any organisation may terminate your right to attend at any time either by giving seven days' written notice to you or immediately without any notice if you are in breach of any of the terms or conditions described in this letter or if you commit any act that we reasonably consider to amount to serious misconduct or to be disruptive and/or prejudicial to the interests and/or business of the organisation or if you are convicted of any criminal offence. You must not undertake regulated activity if you are barred from such work. If you are barred from working with adults or children this letter of access is immediately terminated. Your employer will immediately withdraw you from undertaking this or any other regulated activity and you MUST stop undertaking any regulated activity immediately.

Your substantive employer is responsible for your conduct during this research project and may in the circumstances described above instigate disciplinary action against you.

No organisation will indemnify you against any liability incurred as a result of any breach of confidentiality or breach of the Data Protection Act 1998. Any breach of the Data Protection Act 1998 may result in legal action against you and/or your substantive employer.

If your current role or involvement in research changes, or any of the information provided in your Research Passport changes, you must inform your employer through their normal procedures. You must also inform your nominated manager in each participating organisation and the R&D office in this organisation.

Yours sincerely

Judith Holliday
RESEARCH MANAGER

cc [redacted]

Appendix 11. **Confirmation of NHS Trust Research Committee approval.**

The Mid Yorkshire Hospitals **NHS**
NHS Trust

Bringing together community and hospital services

If you need this correspondence in a larger font size please contact: 01924 543175

Research Office
Rowan House
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Fax:01924 543766
MY.Research@midyorks.nhs.uk

Mr Matthew Haines
Senior Lecturer
School of Human and Health Sciences
University of Huddersfield
Queensgate Campus
HD1 3DH

JH/CSC/N:R&D(15/997)

21 March 2016

Dear Mr Haines

The effect of low volume, high intensity exercise on pre-diabetes V1
The effect of low volume, high intensity training on Intermediate hyperglycaemia in service users of an NHS Specialist Diabesity Service
REC 15/YH/0226 R&D 15/997

Your research study has been approved by the Trust's Research Committee.

Your SSI form states that you plan to recruit 40 in total.

To meet the national target of recruiting your first patient into this study within 30 days of this permission letter, your first patient should be recruited by 20 April 2016. Please let us know if you believe you will be unable to meet this target and provide any reasons for this.

There are some conditions to this approval:

- The study may only begin after appropriate Research Ethics Committee approval has been received. **I can confirm receipt of the latest REC approval letter dated 18 June 2015.**
- To comply with the Research Governance Framework (DOH, 2001), the Local Investigator/Researcher should ensure that the study is conducted in accordance with the approved protocol. Informed consent must be obtained in accordance with the protocol and a copy given to the participant, a copy kept in the medical record, where appropriate, and a copy kept by the Investigator in their research file. The Trust may audit these requirements.
- Research activity must be monitored by the Trust. A copy of letters or reports received following monitoring visits or inspections relating to the conduct of this study, at this site, must be sent to this office.

- Research involving radiation exposures must comply with local Trust policies and procedures, including authorisation by a named local Practitioner.

- Annual progress reports will be required, and a copy of the final report. We will contact you annually to ensure we have up to date contact details and to confirm the status of the project.

- Any researchers not employed by this organisation who will be conducting research on Trust premises may require a research passport, an honorary contract, or a letter of access. If you require help with this, in the first instance, contact myself.

- For research within the scope of the Medicines for Human Use (Clinical Trials) Regulations 2004, investigators must provide evidence of appropriate ICH-GCP training. The Trust may audit this requirement.

- You have specified that this study will close to recruitment on 01 April 2017. The trial will be completed on 30 June 2017. If you require an extension to the recruitment or follow up period this must be submitted to R&D for approval.

If you agree with the terms stated, please will you sign a copy of this letter and return it to this office.

May I take this opportunity to wish you every success with your research.

Yours sincerely

Judith Holliday
RESEARCH MANAGER

cc: [redacted]

Document	Version Number	Date
REC approval letter		18 June 2015
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Evidence of sponsor indemnity from 01.08.14 to 31.07.15]	1.0	11 March 2015
GP/consultant information sheets or letters [GP information letter]	1.0	24 April 2015
Letter from sponsor [Letter from sponsor]	1.0	26 February 2015
Letters of invitation to participant [Letter of invitation]	2.0	10 June 2015
Participant consent form [Consent form]	1.0	24 April 2015
Participant information sheet (PIS) [PIS - control group]	1.0	25 February 2015
Participant information sheet (PIS) [Participant Information Sheet]	2.0	10 June 2015
Research protocol or project proposal [Project overview]	2.0	10 June 2015

Appendix 12. **Example letter of invitation.**

University of HUDDERSFIELD

NHS
The Mid Yorkshire Hospitals
NHS Trust

INVITATION LETTER

Study title: The effect of low-volume, high-intensity exercise on pre-diabetes

Dear Sir or Madam:

My name is Matthew Haines. I am a Senior Lecturer and doctoral candidate at the University of Huddersfield. I am conducting a research study and would like to invite you to participate. The study will take place at Dewsbury and District Hospital as part of the Specialist Diabesity Service.

I am studying if low-volume, high-intensity exercise – where you do harder exercise but for much shorter periods of time – is beneficial for patients with pre-diabetes. Pre-diabetes is a term used to describe a condition that comes before diabetes and most people with pre-diabetes will eventually develop diabetes if left untreated. Diabetes is a serious disease and results in personal suffering and financial strain on the NHS. Regular exercise is one important lifestyle choice we can make that might prevent or delay progression to diabetes. The type of exercise I am interested in is less of a time burden compared to other types of exercise and it is possible that people are more likely to stick to this type of exercise. Therefore, the aim of my research is to see if this type of exercise will be beneficial in patients with pre-diabetes.

You have been asked to participate because your doctor has referred you for pre-diabetes checks. Taking part in the study is your decision. If you decide to take part and later decide to withdraw, you can do so at any time, without prejudice and if you choose without giving a reason.

If you agree to take part in the research you will be asked to attend a familiarisation session at Dewsbury and District Hospital. All of the procedures that will be used will be explained to you in full and you will have the opportunity to ask questions. If you agree to take part in the research you will be asked to sign a consent form and you will then be randomly assigned to one of two groups after consenting to take part – an 'exercise group' or a 'control group'.

It is important that you are prepared to be allocated to either group.

Unfortnately it is not possible to reimburse you for your time and travel expenses. However, the aim of the exercise is to improve health risk factors in relation to diabetes and it is expected that the extra support, supervision and advice offered throughout the study may encourage positive behaviour change. Therefore taking part may be of great benefit to you.

All information collected from you during this study will be kept secure and any identifying material, such as names will be removed in order to ensure anonymity. It is anticipated that the research will be published in a journal and report. However, your anonymity will be ensured. All information disclosed within the research will be kept confidential.

If you would like to take part please inform your healthcare team who will pass your contact details to me. I will contact you within one week and arrange for your involvement in the study to begin. Alternatively, if you have any questions or require any further information about the study, please contact me directly. A 'Participant Information Sheet' is also attached for further information.

With kind regards

Matthew Haines
E-mail: m.haines@hud.ac.uk | Tel: [redacted]
Senior Lecturer, University of Huddersfield

Version 2.0, 10th Jun. 2015

Appendix 13. **Example participant information sheet.**

University of HUDDERSFIELD

NHS
The Mid Yorkshire Hospitals
NHS Trust

PARTICIPANT INFORMATION SHEET

Study title: The effect of low-volume, high-intensity exercise on pre-diabetes

Thank-you for showing interest in this research

Before you decide to take part it is important that you understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with me if you wish. Please do not hesitate to ask if there is anything that is not clear or if you would like more information. **Reading this information sheet should take about 5–10 minutes.**

What is the purpose of the study?
Regular exercise is one important lifestyle choice we can make that might prevent or delay progression to diabetes. In particular low-volume, high intensity exercise – where you do harder exercise but for much shorter periods of time – might be a particularly good form of exercise for this purpose. The Invitation Letter provides further information.

Why I have been invited?
You have been asked to participate because your doctor has referred you for pre-diabetes checks, and therefore we would like to take this opportunity of inviting you to take part in this research. It is important for volunteers to use this exercise to see if it is an effective treatment for pre-diabetes.

Do I have to take part?
It is entirely your decision whether or not you take part. If you decide to take part you will be asked to sign a consent form. You will be free to withdraw from the research at any time, without giving a reason and without prejudice.

What will happen to me if I take part?
You will be asked to attend a familiarisation session at Dewsbury and District Hospital. All of the procedures that will be used will be explained to you in full and you will have the opportunity to ask questions. If you agree to take part in the research you will be asked to sign a consent form and to complete a Physical Activity Readiness Questionnaire.

- The study period will last 5–7 weeks
- You will be asked to have a standard electrocardigram, or ECG, to check the rhythm and elecrical acivity of your heart. This is a very simpe procedure, is completely painless and cannot be harmful
- You will be asked to complete a range of physical measures before the study starts. These will include an exercise test on a stationary bike (relative to your current fitness), a blood sample to check for blood glucose control, blood pressure and level of body fat (using a non-invasive method)
- **You will then be randomly allocated to an 'exercise group' or a 'control (non-exercise) group'**
- **If you are randomised to the exercise group**: during the study you will undergo 2–3 short exercise sessions per week on non-consecutive days at Dewsbury and District Hospital (20-30 minutes total weekly time commitment). A range of sessions will be offered across the week. In total you will need to complete 24 sessions of exercise. This can be achieved by completing either 2 sessions per week for 12 weeks, or 3 sessions per week for 8 weeks
- The exercise will include:
    - Steady cycling on a stationary bike for a total of 10 minutes

Version 2.0, 10th June 2015

- However, you will be asked to complete periods of harder cycling for 5 seconds (called sprints) at intervals during this period
  - The number of sprints will increase form 2 to 8 across the study period.
  - The 10 minute exercise session also includes a 3 minute warm-up and 2 minute cool down
  - Please note the level of difficulty will be determined before you start exercising and will be relative to you based on your fitness. The overall difficulty of each session will be low to moderate
- **If you are randomised to the 'control group'**: you will act as a control, therefore you will **not** take part in an exercise intervention
- At the end of the study you will be asked to repeat the range of physial measures taken before the study started

You may suffer some discomfort (e.g. fatigued muscles) as a result of the exercise although this will not be excessive.

Expenses and payments
There is no payment for taking part in this research and reimbursement for travel expenses cannot be provided.

What are the possible benefits of taking part?
The exercise should provide a range of physical and mental health benefits. For example, regular exercise reduces the likelihood of cardiovascular disease, diabetes, some cancers; in addition to improved mood and reduced risk of depression. Specifically, the aim of the exercise is to improve health risk factors in relation to diabetes. It is also expected that the extra support, supervision, and advice throughout the study may encourage positive behaviour change. At the end of the study you will be offered a final consultation and free exercise and lifestyle consultation (both 'exercise' and 'control' groups).

What are the possible disadvantages and risks of taking part?
You will be asked to refrain from partaking in any 'new' forms of structured exercise (for example, using the gym) if you are assigned to the 'exercise group'. However, your treatment will be otherwise unaffected. Injury or illness as a result of taking part in this research is unlikely.

Will my taking part in the study be kep confidential?
All information (data) collected from you during this research will be kept secure and any identifying material, such as names will be removed in order to ensure anonymity. It is anticipated that the research may, at some point, be published in a journal or report. However, should this happen, your anonymity will be ensured. All information disclosed within the research will be kept confidential.

Who has reviewed the study?
All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by NRES Committee Yorkshire & The Humber – Sheffield, in addition to the University of Huddersfield.

What if there is a problem?
Should you feel that the information here is being infringed or that your interests are otherwise being ignored, neglected or denied, you can also inform the School of Human and Health Sciences, School Research Ethics Panel [redacted] who will undertake to investigate any complaint.

Who can I contact for further information?
If you require any further information about the research, please contact me on:

Name: **Matthew Haines**
E-mail: [redacted]
Telephone:

Version 2.0, 10th June 2015

Appendix 14. **Example consent form.**

University of
HUDDERSFIELD

NHS
The Mid Yorkshire Hospitals
NHS Trust

CONSENT FORM

Title of study: The effect of low-volume, high-intensity exercise on pre-diabetes

It is important that you read, understand and sign the consent form. Your contribution to this research is entirely voluntary and you are not obliged in any way to participate, if you require any further details please contact the researcher.

- I have been fully informed of the nature and aims of this research
- I consent to taking part in it
- I understand that I have the right to withdraw from the research at any time, up to the point of final data analysis, without giving any reason
- I understand that the information collected (person identifiable data) will be kept in secure conditions for a period of five years at The University of Huddersfield
- I understand that no person other than the researchers and facilitators (e.g. audit/monitoring by regulatory authorities or Research and Development) will have access to the information provided
- I understand that my identity will be protected by the use of number in the report and that no written information that could lead to my person being identified will be included in any report
- I understand that results of blood tests to measure HbA1c (measure of glucose control) will be passed from the healthcare team to the Researcher for the purposes of this study
- I give permission for the Researcher to inform my GP that I am taking part in this study

If you are satisfied that you understand the information and are happy to take part in this study please put a tick in the box aligned to each sentence and print and sign below.

Signature of Participant:	Signature of Researcher:
Print:	Print:
Date:	Date:

(One copy to be retained by Participant & Researcher) Version 1.0, 24.Apr.2015

Appendix 15. **Publication in *Diabesity in Practice***

Available at: http://eprints.hud.ac.uk/id/eprint/16807/

Haines, Matthew, Gillibrand, Warren P. and Garbutt, Gerard

High-intensity interval training (HIT): A time-efficient exercise prescription for pre-diabetes?

Original Citation

Haines, Matthew, Gillibrand, Warren P. and Garbutt, Gerard (2012) High-intensity interval training (HIT): A time-efficient exercise prescription for pre-diabetes? Diabesity in Practice, 1 (4). pp. 133-140.

High-intensity interval training (HIT): A time-efficient exercise prescription for pre-diabetes?

Matthew Haines, Warren Gillibrand, Gerard Garbutt

Pre-diabetes invariably precedes type 2 diabetes, for which the personal and economic burdens are well known. Exercise is usually recommended as part of lifestyle interventions that aim to prevent progression from pre-diabetes to diabetes. However, adherence to such interventions is often poor, with lack of time usually cited as the main barrier to exercise. High-intensity interval training, or HIT, has been put forward as a more time-efficient approach to exercise compared to traditional exercise guidelines. This article considers the nature of HIT in comparison to traditional exercise guidelines and the basis of how insulin sensitivity and glucose transport might be improved. Finally, implications for practice with individuals with pre-diabetes are considered.

Pre-diabetes (impaired glucose tolerance and impaired fasting glucose, as defined in *Table 1*) represents a transitory state between normoglycaemia and type 2 diabetes. Without intervention it is estimated that the majority of those people with pre-diabetes will progress to type 2 diabetes within 5–10 years (Nathan et al, 2002). Therefore, interventions for people who are diagnostically considered to have pre-diabetes should be a priority.

Lifestyle intervention, including exercise, is considered a cornerstone of diabetes prevention and management. Nevertheless, despite strong evidence that exercise can delay or prevent type 2 diabetes (Knowler et al, 2002) the challenge of encouraging individuals and populations to lead a more active lifestyle remains. Here we contrast traditional exercise guidelines with the development of high-intensity interval training (HIT), which has been put forward as a more time-efficient approach to exercise.

Early Japanese research dates back more than 15 years (Tabata et al, 1996), but more recently HIT has been pioneered by Gibala and colleagues in Canada from 2004 to the present day (e.g. Burgomaster et al, 2004; Gibala et al, 2012). Research interest is developing significantly, although participants involved in HIT research are typically young, healthy individuals familiar with exercise rather than individuals with long-term health conditions. The aim of this article is to consider the evidence for using HIT, in addition to looking at issues of implementation in practice.

Traditional exercise guidelines for health

Early studies focused on patterns of exercise and time spent sitting in the occupational setting, although since then exercise guidelines have evolved (Haskell et al, 2007; Brown et al, 2009). A focus on vigorous aerobic exercise during the mid-1970s was replaced by 30 minutes of moderate-intensity activity on most days of the week by the 1990s. The American College of Sports Medicine later clarified this as 30 minutes "on at least five days per week" establishing the 150 minutes per week that persists to the current day (Haskell et al, 2007). Recent perspective has shifted focus onto drivers of inactivity in what has been termed an obesogenic environment; that is, profiles of activity and inactivity in transport, occupation, domestic and leisure pursuits of everyday life (Brown et al, 2009).

Citation: Haines M, Gillibrand W, Garbutt G (2012) High-intensity interval training (HIT): A time-efficient exercise prescription for pre-diabetes? *Diabesity in Practice* 1: 133–40

Article points

1. Exercise is usually recommended as part of lifestyle interventions to prevent progression from pre-diabetes to diabetes, but lack of time is a frequently cited reason for poor adherence.
2. High-intensity interval training (HIT) has been proposed as a time-efficient alternative.
3. HIT may be considered as part of lifestyle interventions for treating diabesity in suitable individuals.
4. Appropriate health screening must be carried out by healthcare professionals before prescribing HIT.

Key words

- Exercise
- Pre-diabetes
- Prevention

Authors

Authors' details can be found at the end of the article.

Page points

1. A commonly cited barrier for engaging in exercise is lack of time.
2. There is a growing interest in shorter-duration but higher-intensity exercise, such as HIT.
3. HIT is typically performed on a cycle ergometer for a period of approximately 15–30 minutes inclusive of a warm-up and cool-down period.

Table 1. Diagnostic criteria for pre-diabetes.

	World Health Organization (2006)	American Diabetes Association (2010)
IGT	*2-h glucose: ≥7.8 and <11.1 mmol/L *and* Fasting glucose: <7.0 mmol/L	*2-h glucose: ≥7.8 and <11.1 mmol/L
IFG	Fasting glucose: 6.1–6.9 mmol/L *and* *2-h glucose: <7.8 mmol/L (if measured)	Fasting glucose: 5.6–6.9 mmol/L

IFT=impaired fasting glucose; IGT=impaired glucose tolerance.
*Venous plasma glucose 2 hours after ingesting 75 g glucose load. It should be noted that IGT and IFG can occur as mutually exclusive conditions or they can occur in combination.

Current guidelines for exercise in the UK (e.g O'Donovan et al, 2010; Department of Health, 2011) focus on high-volume, time-consuming exercise. In particular, adults at high risk of type 2 diabetes are recommended to engage in 300 minutes or more of moderate-intensity aerobic activity each week, or 150 minutes or more of vigorous-intensity aerobic activity each week. This can be problematic, since the most commonly cited barrier for engaging in exercise is lack of time (Korkiakangas et al, 2009). As a result there is a growing interest in shorter-duration but higher-intensity exercise, such as HIT, which might be time-efficient and appealing to individuals who otherwise would not adhere to the volumes of exercise outlined in traditional guidelines. This is important because the efficacy of any exercise intervention should be considered not only in terms of the physiological effectiveness of the activity but also the likelihood that individuals will engage with it. The acceptability and accessibility of the activity to those for whom the intervention is intended, and the practicalities of building the activity into everyday life, also need to be considered.

Although the independent relationship between physical inactivity and a range of diseases, including diabetes, has been established (Booth et al, 2002), the optimal dose of exercise remains unclear. Church and Blair (2009) highlight that the commonly prescribed dose of 150 minutes per week of moderate-intensity physical activity is the result of a self-fulfilling prophecy whereby, based primarily on epidemiological data, 150 minutes per week was identified as a good recommendation. Subsequent research has used this threshold to define intervention goals resulting in research examining 150 minutes per week rather than research examining different doses, intensities, types or frequencies of exercise.

What is high-intensity interval training (HIT)?

HIT is typically performed on a cycle ergometer (specialised stationary bicycle; *Figure 1*) for a period of approximately 15–30 minutes inclusive of a warm-up and cool-down period. Most of this time is spent at low intensity, with the caveat that a series (4–12) of maximal or "all out" cycling sprints are included throughout this time period, with each sprint lasting 30–60 seconds. This approach to exercise is performed three times per week resulting in a total weekly time commitment of 45–90 minutes.

Most studies on HIT have used 30-second cycling sprints against a braking force equal to 7.5% of body weight, commonly known as the Wingate Test (Bar-Or, 1987). This is a very intense protocol resulting in considerable fatigue. Nevertheless, this short but intense protocol has demonstrated a remarkable ability to induce beneficial changes in a range of physiological parameters important for metabolic health. For example, Gibala et al (2006) used this protocol to compare active men assigned to HIT or traditional cardiovascular training (90–120 minutes of moderate-intensity continuous cycling) over 2 weeks. The training volume for the HIT group was approximately 90% lower than the traditional exercise group (approximately 150 kcal versus 1550 kcal energy expenditure per week). Despite this, muscle biopsy samples obtained before and after training revealed similar increases in muscle oxidative capacity and glycogen content.

Similar studies have demonstrated improvements in insulin sensitivity. Babraj et al (2009) showed that after just 2 weeks of HIT (equal to approximately 250 kcal of work each week) the area under the plasma glucose, insulin and non-esterified fatty acid concentration–time curves were all reduced (12%, 37% and 26%, respectively) demonstrating an improvement in risk factors for metabolic disease. In addition, peripheral insulin sensitivity and muscular glucose uptake was improved by 23%. Similarly, Little et al (2010) used a HIT protocol, equal to approximately 150 kcal per week, to demonstrate increases in resting muscle glycogen and total glucose transporter (GLUT)-4 protein content after 2 weeks. Considering the potency of HIT to induce physiologically meaningful changes for a range of factors important to health and diabetes risk, it is clear to see why exercise physiologists are interested in this alternative form of exercise. Nevertheless, it is apparent that such time-efficient approaches to exercise might suffer from similarly poor adherence because the high-intensity nature of the activity is likely to present another barrier for most people. Additionally, it is unknown if the general population could safely or practically adopt this type of exercise.

Gibala (2007) has suggested that the focus needs to shift to identify modified (less intense) approaches to HIT to establish the optimal combination of intensity and volume of exercise necessary to induce adaptations in a practical, time-efficient manner across various populations, including those with pre-diabetes. Recent research has postulated that the traditional approach to HIT (as outlined above) might be unnecessarily strenuous. Metcalfe et al (2012) used a reduced-exertion HIT exercise intervention three times per week over 6 weeks. The reduced-exertion HIT consisted 10 minutes of low-intensity cycling interspersed with 1–2 "all out sprints" of 10–20 seconds against a braking force of 7.5% body weight. The 10 minutes of cycling included a 3-minute warm-up and 3-minute cool-down period, meaning the total exercise time per week was just 30 minutes. Despite this, aerobic capacity improved by 12–15% and insulin sensitivity, assessed in response to ingesting a 75 g glucose load, increased by 28%. These early findings are encouraging because they show that a more practical approach to HIT might be beneficial for metabolic health.

Figure 1. A demonstration of HIT using a cycle ergometer. (Image author's own.)

"Recent research has postulated that the traditional approach to HIT might be unnecessarily strenuous."

Why might HIT work for pre-diabetes? The physiological rationale

The exact mechanistic basis underlying how exercise increases insulin sensitivity and stimulates muscle glucose transport is

Page points

1. Intracellular changes are mediated in response to the metabolic status of the muscle caused specifically by muscle contraction.
2. As the insulin-independent increase in glucose transport diminishes, depletion of muscle glycogen in response to exercise increases muscle insulin sensitivity.
3. More intense exercise might be of greater benefit to people with pre-diabetes because higher-intensity exercise will place greater reliance on intramuscular glycogen as fuel, thus mediating enhanced insulin-stimulated glucose transport.

not completely understood. Holloszy (2005) suggested that these are extremely complex processes and it will be some time before mechanisms responsible for mediating this phenomenon are understood. However, how exercise can improve glucose homeostasis has been described (for reviews see Wojtaszewski et al, 2003; Hawley and Lessard, 2008). It is useful for the reader to consider exercise-induced improved regulation of muscle glucose transport operating via two separate pathways.

Firstly, molecular signalling mechanisms increase glucose uptake. These intracellular changes are mediated in response to the metabolic status of the muscle caused specifically by muscle contraction. For example, release of calcium from the sarcoplasmic reticulum changes ion balance activating the Ca^{2+}/calmodulin-dependent protein kinase pathway, which stimulates glucose transport (Wright et al, 2005). Similarly, another feedback pathway involves changes to substrate levels. During muscle contractions, decreases in cellular chemical energy (ATP and creatine phosphate) increase adenosine monophosphate (AMP) levels, evoking the AMP-activated protein kinase (AMPK) mechanism which also improves insulin sensitivity (Jessen and Goodyear, 2005). Furthermore, feed-forward control mechanisms such as the stimulation frequency of motor nerves might further regulate glucose transport (Richter et al, 2003). It is important to note that these mechanisms are "insulin independent" and therefore bypass the typical insulin signalling defects associated with insulin resistance conditions (Hawley and Lessard, 2008). It is possible that these mechanisms are responsible for the acute increase in glucose transport 2–4 hours after exercise (Holloszy, 2005) and that high-intensity exercise could activate them to a greater extent than moderate-intensity exercise.

Secondly, as the insulin-independent increase in glucose transport diminishes, depletion of muscle glycogen in response to exercise increases muscle insulin sensitivity. This is caused by up-regulation of the enzyme glycogen synthase and GLUT-4 protein. GLUT-4 allows facilitated diffusion of glucose into the muscle cells where it can be polymerised and stored as glycogen. Since exercise depletes this stored glycogen, muscle cells must recover during the post-exercise period and often overcompensate in a process known as muscle glycogen super-compensation (Wojtaszewski et al, 2003). This is achieved by an increase in glucose transport mediated by translocation of more GLUT-4 to the muscle sarcolemma (cell surface) from intracellular storage sites followed by an increase in the intrinsic activity of the transporters (Furtado et al, 2003). In this way, exercise is able to enhance insulin-stimulated glucose transport post-exercise because of an enhanced recruitment and activity of GLUT-4 in response to glycogen depletion. This may last for 16–48 hours (Perseghin et al, 1996).

Wright and Swan (2001) suggested that more intense exercise such as HIT might be of greater benefit to people with pre-diabetes because the higher-intensity exercise will place greater reliance on intramuscular glycogen as fuel, thus mediating enhanced insulin-stimulated glucose transport. It has been demonstrated experimentally using exercise protocols similar to those of HIT that significant glycogenolysis–the use of glycogen as fuel–does indeed occur in cycle sprints of less than 30 seconds (Parolin et al, 1999). It should be acknowledged that much of the physiological research surrounding the improvements in insulin sensitivity and muscle glucose transport have been carried out using animal studies. Also, little evidence specifically supports HIT because research has generally considered more traditional higher volume approaches to exercise.

Implications for practice

It is unlikely that HIT would result in sufficient calorific expenditure to create the negative energy balance required for significant weight loss. However, Yates (2012) stated that the historic preoccupation of judging lifestyle interventions solely by their effects on body weight might be damaging and that emphasising healthy lifestyles for their own sake will allow exercise to be used to its full potential. In fact, the question of whether exercise without weight loss can improve insulin sensitivity has been considered and, although the evidence is equivocal, there is little doubt that the acute effects of each exercise session are beneficial (Ross, 2003; Yates et al, 2007). When exercise is performed regularly these benefits are "topped up", irrespective of weight loss. Nevertheless, there is little doubt that excessive body fat is harmful to health and it is very likely that the beneficial impact of exercise on insulin resistance would be magnified if associated with diminished body fat. Therefore the suggestion is not that HIT should replace other exercise advice but that it should complement it, and in particular be considered as a time-efficient approach to health improvement. This approach would allow for use of HIT to elicit clinically meaningful benefits in people with pre-diabetes.

A common criticism of exercise as a treatment is poor adherence. As previously stated "lack of time" is cited as the most prevalent barrier to exercise. The potential for HIT to reduce the time burden and appeal to individuals who otherwise would not engage with exercise should not be overlooked. In addition, high-intensity interval exercise has been perceived to be more enjoyable than moderate-intensity continuous exercise (Bartlett et al, 2011) and reduced-exertion HIT has been shown to result in only modest ratings of perceived exertion (Metcalfe et al, 2012). Taken together, this information is encouraging in that HIT might be relevant for improving exercise adherence. Furthermore, it is possible that HIT could be administered by the patient at home, by fitness industry personnel and by a range of healthcare professionals, such as specialist diabesity nurses, who are likely to be in contact with people with pre-diabetes. The protocol is straightforward to communicate, requires minimal equipment and could clearly be incorporated into a multidisciplinary diabesity clinic. Nurses could have an important role to play in treating diabesity through exercise interventions but would need appropriate training and organisational support to do so.

Potential limitations to the approach

Although the relative risk of an acute cardiac event increases during exercise, the absolute risk is low and has been reported in prospective research as one death per 1.51 million episodes of exercise in healthy people (Albert et al, 2000), although data were collected using subjective interpretation of vigorous exercise defined as "How often do you exercise vigorously enough to work up a sweat?" Whilst higher-intensity exercise increases risk, people who experience an exercise-related cardiac event generally have underlying structural cardiac disease (Thompson et al. 2007). Therefore, appropriate screening for high-risk individuals should be carried out before commencing HIT because risk could be substantial in this population.

This has resource implications. An appropriate Physical Activity Readiness Questionnaire (PAR-Q) must be administered by healthcare professionals and fitness industry personnel including those involved in exercise referral schemes who prescribe exercise. Medical conditions that complicate the exercise prescription include knowledge of risk factors or conditions associated with cardiovascular and chronic obstructive pulmonary disease, diabetes, arthritis and osteoporosis. Individual risk stratification should be completed using an established pre-participation algorithm to classify individuals as low, moderate or high risk (e.g. ACSM, 2006). At this stage individuals considered to be at moderate risk might need to undergo health-related physical testing or clinical exercise testing with the breadth and depth of testing dependent on risk. High-risk individuals should be excluded from HIT because the benefit-to-risk ratio for this

Page points

1. Nurses could have an important role to play in treating diabesity through exercise interventions but would need appropriate training and organisational support to do so.
2. Appropriate screening for high-risk individuals should be carried out before commencing HIT because risk could be substantial in this population.
3. Individual risk stratification should be completed using an established pre-participation algorithm to classify individuals as low, moderate or high risk.

"Caution should be exercised in people with diabetes using insulin because of the risk of hypoglycaemia caused by exercise-induced increase in the rate of glucose clearance into skeletal muscles."

population might be more favourable with moderate-intensity exercise.

Furthermore, caution should be exercised in people with diabetes using insulin because of the risk of hypoglycaemia caused by exercise-induced increase in the rate of glucose clearance into skeletal muscles. However, no adverse events were reported in recent research using HIT with individuals with type 2 diabetes (Little et al, 2011). People with pre-diabetes may not have many of the disease complications associated with type 2 diabetes because of the relatively early state of disease progression (Wright and Swan, 2001). Consequently the prescription of HIT to this population group should be acceptable as long as other co-morbidities have been appropriately screened for.

Cost

Regarding cost considerations, the cycle ergometer pictured in *Figure 1* costs in the region of £1200. However, cheaper ergometers and potentially cheaper standard exercise bikes could feasibly be used as an alternative to perform HIT exercise.

Conclusion

HIT represents an intriguing alternative to traditional exercise guidelines and might improve exercise adherence whilst benefitting a range of parameters that are clinically meaningful for health. HIT could be considered part of lifestyle interventions for treating diabesity and might be ideally suited to people with pre-diabetes as long as their overall risk profile is minimal. However to ensure an optimal benefit-to-risk ratio, healthcare professionals must use appropriate health screening measures before prescribing HIT and this has inevitable resource implications. Currently, there is insufficient evidence to suggest that HIT be adopted by everyone with diabesity and the approach is likely to be hazardous for high-risk and sedentary individuals. However, further research on HIT as a means of preventing future burden of type 2 diabetes is warranted. ■

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Online CPD activity

Visit www.diabetesonthenet.com/cpd to record your answers and gain a certificate of participation

Participants should read the preceding article before answering the multiple choice questions below. There is ONE correct answer to each question. After submitting your answers online, you will be immediately notified of your score. A pass mark of 70% is required to obtain a certificate of successful participation; however, it is possible to take the test a maximum of three times. A short explanation of the correct answer is provided. Before accessing your certificate, you will be given the opportunity to evaluate the activity and reflect on the module, stating how you will use what you have learnt in practice. The CPD centre keeps a record of your CPD activities and provides the option to add items to an action plan, which will help you to collate evidence for your annual appraisal.

1. Which ONE of the following is the MAIN barrier for patients wanting to exercise as part of lifestyle intervention to prevent progression of pre-diabetes?

A. Cardiac co-morbidity
B. Embarrassment
C. Fatigue
D. Knee-joint pain in obese people
E. Lack of time

2. Which ONE of the following molecular mechanisms BEST explains how high-intensity interval training (HIT) could increase insulin sensitivity?

A. Decreased muscle adenosine monophosphate levels
B. Decreased glucogenolysis
C. Decreased glucose uptake
D. Increased glucose transporter (GLUT)-4 activity
E. Increased muscle glycogen storage

3. Pre-diabetes without intervention is estimated to progress to type 2 diabetes in the majority of individuals within HOW MANY years? Select ONE option only.

A. 0–1
B. 2–4
C. 5–10
D. 11–15
E. 16–25

4. According to current evidence, what is the OPTIMAL amount of physical activity per week (in minutes) that should be recommended as part of a healthy lifestyle? Select ONE option only.

A. 100
B. 150
C. 200
D. 300
E. None of the above

5. HIT typically consists of which type of exercise? Select ONE option only.

A. Aerobics classes
B. Cycling (stationary)
C. Jogging
D. Sprinting
E. Swimming

6. For WHAT LENGTH of TIME have studies that demonstrated improved insulin sensitivity been carried out for? Select ONE option only.

A. 1 day
B. 2 weeks
C. 3 months
D. 6 months
E. 1 year

7. Which of the following is the MOST appropriate statement about HIT? Select ONE option only.

A. A less intense approach to HIT shows significant benefit compared to standard HIT
B. HIT has been shown to improve concordance with exercise advice
C. HIT is recommended for people with pre-diabetes
D. HIT is safer for people with type 2 diabetes than for people with type 1 diabetes
E. Screening for high-risk individuals should be carried out before commencing HIT

8. HIT has been shown to REDUCE which ONE, if any, of the following?

A. BMI
B. Cholesterol
C. HbA_{1c}
D. Weight
E. None of the above

9. HIT has been shown to IMPROVE outcomes in which ONE, if any, of the following?

A. Gestational diabetes
B. Pre-diabetes
C. Type 1 diabetes
D. Type 2 diabetes
E. None of the above

10. If 3 million healthy people undertake an episode of exercise, how many acute cardiac events resulting in death are likely to occur? Select ONE option only.

A. <1
B. 2
C. 3
D. 5
E. 10

***Appendix 16*. Publication in *Journal of Sports Sciences*.**

Available at: http://eprints.hud.ac.uk/id/eprint/26612/

Assessing the feasibility of a reduced exertion, low-volume, high-intensity interval training (HIT) protocol: a pilot study

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Divergence between the evolutionary design of our genome and lifestyle triggers cardiometabolic disease, including diabetes mellitus. Various iterations of low-volume, high-intensity interval training (HIT) can improve risk factors in a manner considered more time-efficient than traditional exercise guidelines. However, the intensity of HIT may present another barrier to participation. Reduced-exertion HIT has shown beneficial effects with relatively low ratings of perceived exertion (RPE) in healthy young participants (Metcalfe *et al.*, 2011, *European Journal of Applied Physiology*, 112, 2767–2775). The aim of this study was to replicate this finding to assess feasibility for a larger trial using diabetic patients. With institutional ethics approval, 11 recreationally active participants (3 females, 8 males; age, 22.3 ± 7.3 years; stature, 1.73 ± 0.1 m; mass, 71.9 ± 13.6 kg, BMI, 23.8 ± 2.2 $kg \cdot m^2$) (mean ± SD) took part in a HIT intervention consisting 10 minutes of cycling at 60 W interspersed with 2 × 10–20 s cycling sprints against a braking force equal to 7.5% of body weight. The number of sprints increased over the course of the intervention (2 × 10 s in week 1; 2 × 15 s in weeks 2–3; and 2 × 20 s in week 4). A warm-up (3 min at 30–60 W) and cool down (3 min at 30 W) were also included. Participants performed this activity 2–3 times per week resulting in a total duration of exercise per week of 20–30 minutes. RPE was reported immediately after completion of each HIT session. Whole blood fasting glucose, peak oxygen uptake and body composition were also measured before and after the 4 week intervention. HIT resulted in higher average RPE values (17 ± 1) than those reported by Metcalfe *et al.* (~13 ± 1). VO_{2peak} was increased post-intervention (49.27 ± 9.17 $ml \cdot kg \cdot min^{-1}$ [95% CI 43.11–55.43]) compared to baseline (48.27 ± 9.23 $ml \cdot kg \cdot min^{-1}$ [95% CI 42.07–54.47]) ($p = 0.02$). However, fasting glucose and body composition were not different. The results suggest that short duration (4 weeks) reduced-exertion HIT can improve aerobic capacity. However, the intensity of the protocol might be intolerable for most people, presenting a significant barrier to exercise for less fit patients with conditions such as diabetes. The volume-intensity relationship of HIT could be considered *ad infinitum*; however, the acceptability of the activity to those for whom the intervention is intended needs consideration.