Cardiff School of Sport  
**DISSERTATION ASSESSMENT PROFORMA:**  
Empirical

<table>
<thead>
<tr>
<th>Student name:</th>
<th>Student ID:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sam Pickles</td>
<td>St20065578</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Programme:</th>
</tr>
</thead>
<tbody>
<tr>
<td>iSES</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dissertation title:</th>
</tr>
</thead>
<tbody>
<tr>
<td>The Effect of Intensity on Post-Exercise Hypotension: Is Post-Exercise Hypotension different following high intensity interval exercise when compared to continuous exercise and do antihistamines blunt the hypotensive response?</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Supervisor:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dr Mike Hughes</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Comments</th>
<th>Section</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Title and Abstract (5%)</strong></td>
</tr>
<tr>
<td></td>
<td>Title to include: A concise indication of the research question/problem.</td>
</tr>
<tr>
<td></td>
<td>Abstract to include: A concise summary of the empirical study undertaken.</td>
</tr>
<tr>
<td></td>
<td><strong>Introduction and literature review (25%)</strong></td>
</tr>
<tr>
<td></td>
<td>To include: outline of context (theoretical/conceptual/applied) for the question; analysis of findings of previous related research including gaps in the literature and relevant contributions; logical flow to, and clear presentation of the research problem/ question; an indication of any research expectations, (i.e., hypotheses if applicable).</td>
</tr>
<tr>
<td></td>
<td><strong>Methods and Research Design (15%)</strong></td>
</tr>
</tbody>
</table>

---

1 This form should be used for both quantitative and qualitative dissertations. The descriptors associated with both quantitative and qualitative dissertations should be referred to by both students and markers.
<table>
<thead>
<tr>
<th>Section</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>To include:</td>
<td>details of the research design and justification for the methods applied; participant details; comprehensive replicable protocol.</td>
</tr>
<tr>
<td><strong>Results and Analysis (15%)</strong></td>
<td>To include: description and justification of data treatment/ data analysis procedures; appropriate presentation of analysed data within text and in tables or figures; description of critical findings.</td>
</tr>
<tr>
<td><strong>Discussion and Conclusions (30%)</strong></td>
<td>To include: collation of information and ideas and evaluation of those ideas relative to the extant literature/concept/theory and research question/problem; adoption of a personal position on the study by linking and combining different elements of the data reported; discussion of the real-life impact of your research findings for coaches and/or practitioners (i.e. practical implications); discussion of the limitations and a critical reflection of the approach/process adopted; and indication of potential improvements and future developments building on the study; and a conclusion which summarises the relationship between the research question and the major findings.</td>
</tr>
<tr>
<td><strong>Presentation (10%)</strong></td>
<td>To include: academic writing style; depth, scope and accuracy of referencing in the text and final reference list; clarity in organisation, formatting and visual presentation.</td>
</tr>
</tbody>
</table>

2 There is scope within qualitative dissertations for the RESULTS and DISCUSSION sections to be presented as a combined section followed by an appropriate CONCLUSION. The mark distribution and criteria across these two sections should be aggregated in those circumstances.
'The Effect of Intensity on Post-Exercise Hypotension: Is Post-Exercise Hypotension different following high intensity interval exercise when compared to continuous exercise and do antihistamines blunt the hypotensive response?'

(Dissertation submitted under the Physiology and Health area)

Sam Pickles- ST20065578
‘THE EFFECT OF INTENSITY ON POST-EXERCISE HYPOTENSION: IS POST-EXERCISE HYPOTENSION DIFFERENT FOLLOWING HIGH INTENSITY INTERVAL EXERCISE WHEN COMPARED TO CONTINUOUS EXERCISE AND DO ANTIHISTAMINES BLUNT THE HYPOTENSIVE RESPONSE?’
Certificate of student

By submitting this document, I certify that the whole of this work is the result of my individual effort, that all quotations from books and journals have been acknowledged, and that the word count given below is a true and accurate record of the words contained (omitting contents pages, acknowledgements, indices, tables, figures, plates, reference list and appendices). I further certify that the work was either deemed to not need ethical approval or was entirely within the ethical approval granted under the code entered below.

Ethical approval code:   ______ 15/1/02S__________________ (enter code or 'exempt')
Word count:   _______9238________________
Name:    _______Sam Pickles________________
Date:    _______14/04/2015________________

Certificate of Dissertation Supervisor responsible

I am satisfied that this work is the result of the student’s own effort and was either deemed to not need ethical approval (as indicated by 'exempt' above) or was entirely within the ethical approval granted under the code entered above.

I have received dissertation verification information from this student

Name:    __________________________
Date:    __________________________

Notes:
The University owns the right to reprint all or part of this document.
CONTENTS

List of Tables

List of Figures

List of Plates

List of Tables ......................................................................................................................... 8
List of Figures .......................................................................................................................... 9
List of Plates ........................................................................................................................... 10
ACKNOWLEDGEMENTS ........................................................................................................... i
ABSTRACT ............................................................................................................................... ii
CHAPTER 1: INTRODUCTION ................................................................................................. 1
  1.1 Hypertension and Cardiovascular Disease ................................................................. 1
  1.2 Treating Hypertension ............................................................................................... 1
  1.3 Cardiovascular Responses to Exercise ..................................................................... 2
  1.4 Optimal Exercise for Post-exercise Hypotension .................................................... 2
  1.5 Mechanisms Causing Post-exercise Hypotension .................................................... 3
CHAPTER 2: REVIEW OF THE LITERATURE ....................................................................... 4
  2.1 Mechanisms Causing Post-exercise Hypotension ....................................................... 4
    2.1.1 Central Regulation and Autonomic Function ...................................................... 4
    2.1.2 Histamine and Vascular Responsiveness ........................................................ 5
    2.2 Factors Affecting Post-exercise Hypotension ........................................................ 7
      2.2.1 Resting Blood Pressure .................................................................................... 8
      2.2.2 Fitness Level .................................................................................................... 8
      2.2.3 Type of Recovery ............................................................................................. 9
      2.2.4 Position of Patient Post-exercise ................................................................ 9
      2.2.5 Time of Day .................................................................................................... 10
      2.2.6 Age ................................................................................................................ 10
      2.2.7 Sex and Ethnicity ............................................................................................ 10
      2.2.8 Heat ............................................................................................................... 11
  2.3 What are the optimal characteristics of an exercise bout to induce post-exercise hypotension? ................................................................................................................. 11
List of Tables

Table 1. Study designs investigating the influence of HIIT and SIT on PEH 14

Table 2. Characteristics of participants 22

Table 3. Comparison of exercise bout characteristics 24

Table 4. Comparison of systolic BP pre and post-exercise 25

Table 5. Comparison of diastolic BP pre and post-exercise 25
List of Figures

**Figure 1.** Changes in autonomic control relating to post-exercise hypotension 5

**Figure 2.** The underlying mechanisms resulting in post-exercise hypotension 7

**Figure 3.** Schematic showing the timeline of the study and measurements taken for continuous and interval sessions 17

**Figure 4a.** Schematic showing the duration and intensities (% VO$_{2\text{max}}$) of the continuous exercise bout 19

**Figure 4b.** Schematic showing the duration and intensities (% VO$_{2\text{max}}$) of the interval exercise bout 19

**Figure 5.** Flow chart showing participant numbers 22

**Figure 6a.** Comparison of systolic and diastolic BP following interval and continuous exercise bouts 26

**Figure 6b.** Comparison of systolic and diastolic BP following continuous and continuous with antihistamine exercise bouts 26

**Figure 6c.** Comparisons of systolic and diastolic BP following interval and interval with antihistamine exercise bouts 27
List of Plates

**Plate 1.** Patient resting in the seated position pre-exercise. The right hand was supported by towels on the plinth and the participant rested the forearm in the mid-pronation position, minimising pressure put on the finger cuff.

**Plate 2.** Participant cycling on the leg ergometer, attached to the breath by breath VO$_2$ and the Finometer. The right hand was rested on a pillow on the ergometer, with the forearm in the mid-pronation position, minimising pressure put on the finger cuff.
ACKNOWLEDGEMENTS

I would like to thank Dr Mike Hughes and the team at the Cardiff Metropolitan Physiology laboratory for their kindness and invaluable guidance throughout the undertaking of this project.
ABSTRACT

Introduction: An acute drop in blood pressure is seen following exercise, this is called post-exercise hypotension (PEH). High intensity interval training is superior to continuous training in terms of improving aerobic and metabolic fitness, however little is known about the effect of interval exercise on PEH, in this study we matched the total work done when comparing high intensity interval exercise (4x4 minutes at 85% VO$_{2\text{max}}$) with continuous exercise (30 minutes at 70% VO$_{2\text{max}}$). Histamine release is implicated in the mechanisms causing PEH, we investigated the effect of antihistamines on both types of exercise.

Methods: Participants attended 5 sessions: a VO$_{2\text{max}}$ test, two continuous exercise sessions and two interval exercise sessions. Of these, one continuous and one interval session were completed following antihistamine ingestion. The primary outcome measure was blood pressure measured before, during and for 1 hour post-exercise.

Results: A total of 5 participants completed the study, a similar magnitude of post-exercise hypotension was observed following interval and continuous exercise bouts (-8.6/-2.9 mmHg and -12.3/-3.5 mmHg respectively (systolic/diastolic)). Antihistamine ingestion reduced the scale of PEH (125.7/75.0 mmHg compared to 122.0/71.8 mmHg) by a clinically significant amount following both exercise types, however these results (mean reduction in PEH of 3.7/3.2 mmHg) were not statistically significant. (p=0.177 and 0.183 respectively).

Conclusion: These results confirm the involvement of histamine in the PEH response, antihistamines taken at the recommended daily dosage reduced the size of PEH in both continuous and interval exercise bouts by a clinically significant amount. Individuals performing exercise as an antihypertensive treatment may be reducing the effectiveness of the exercise as an intervention, further research is required to determine the clinical implications of the interaction between antihistamines and the scale of PEH when prescribing antihistamines for patients using exercise as an intervention for hypertension.
CHAPTER 1: INTRODUCTION

1.1 Hypertension and Cardiovascular Disease
Cardiovascular disease (CVD) defines a group of disorders affecting the heart and/or blood vessels (WHO, 2015). CVD includes stroke, myocardial infarction, heart failure and renal disease and is the leading cause of morbidity and mortality in the industrialised world (Ong et al., 2007; Turnbull et al., 2008): The Caerphilly Framingham Study found that by the age of 65 the risk of developing a CVD is 37% for men and 18% for women (Kannel et al., 1976). High blood pressure (hypertension) is a modifiable risk factor for CVD (Staessen et al., 2001). In England, 32% of men and 30% of women aged over 16 have hypertension (Maryon-Davis, 2005). Hypertension can be primary (essential) or secondary - 95% of cases of hypertension are essential. The pathogenesis of essential hypertension is multifactorial and several environmental factors interact with genetic predispositions. Secondary hypertension is a consequence of an underlying disease and is treated differently to essential hypertension. Clinically normal blood pressure (BP) is defined as 120/80mmHg and hypertension constitutes a BP of >140/90mmHg (Ciocac et al., 2009; Krause et al., 2011). Despite these clinical values, BP is normally distributed within the population and small increases in BP are associated with increased risks of CVD: a 2mmHg rise in systolic BP increases the risk of mortality from ischaemic heart disease and stroke by 7% and 10% respectively (Krause et al., 2011).

1.2 Treating Hypertension
A decrease in BP by 12-13mmHg has been shown to reduce mortality by 13% (He and Whelton, 1999). National Institute of Clinical Excellence (NICE) guidelines advocate both pharmacological and lifestyle interventions (including exercise) for the treatment of essential hypertension (Krause et al., 2011). Physical activity has been validated to reduce BP in hypertensive populations by approximately 11/8 mmHg (systolic/diastolic BP) (Hagberg et al., 2000; Whelton et al., 2002) and has a beneficial effect on other established risk factors for CVD (increased exercise tolerance, HDL cholesterol and insulin sensitivity and a reduction in body weight and LDL cholesterol) (Myers, 2003; Eicher et al., 2010). Hypertension can be effectively treated using pharmacological interventions, however antihypertensive drugs are renowned for their adverse side effects that may impact quality of life (QoL) (Pescatello et al., 2004). Management can also be difficult, with
only 25% to 62% of patients achieving clinically normal values (Ciolac et al., 2009; BNF, 2013; Halliwill et al., 2013).

1.3 Cardiovascular Responses to Exercise
During aerobic exercise, BP rises and control is tightly linked to exercise intensity (MacDougall, 1994). Systolic BP can reach values of over 200mmHg (Pocock et al., 2013). Following a single bout of exercise, an acute reduction in BP can be observed (McCord and Halliwill, 2006; Lacombe et al., 2011; Keese et al., 2012). This transient decrease in BP, below that of resting (pre-exercise), was coined ‘postexercise hypotension’ (PEH). This period can last from minutes to hours, depending on the type of exercise performed (MacDonald, 2002). PEH occurs as the cardiovascular system adapts from the demands of exercise to a resting state (Halliwill, 2001). Regular exercise will result in repeated episodes of PEH which may directly contribute to the chronic reductions in blood pressure seen with exercise training. Hecksteden et al. (2013) concluded that the magnitude of PEH is associated with decreases in BP related to long term training. PEH is therefore clinically relevant in the management of blood pressure.

1.4 Optimal Exercise for Post-exercise Hypotension
PEH has been observed following aerobic and resistance exercise (Fitzgerald, 1981; Headley, 1996; MacDonald et al., 1999; MacDonald et al., 2000a, b). Traditionally essential hypertension has been treated with moderate intensity continuous aerobic exercise, lasting between 30 minutes to 1 hour (Pescatello et al., 2004). The frequency, duration and intensity determine the scale of the adaption to the exercise stimulus (Wisløff et al., 2009; Seiler, 2010), however it is unclear to what extent these components influence PEH (MacDonald, 2002; Pescatello et al., 2004; Ciolac et al., 2009).

Peak oxygen uptake (VO\(_{2}\)max) refers to the upper limit of aerobic metabolism and has been identified as a key marker of athletic performance (Wisløff et al., 2007; Joyner and Coyle, 2008). \(\text{VO}_{2\text{max}}\) is also the single best predictor of mortality in patients with CVD (Wisløff et al., 2007). The advent of effective exercise programmes will therefore increase aerobic capacity and improve survival in patients with CVD. Several studies have demonstrated that interval training (repeated bouts of high intensity exercise interspersed with recovery periods (Billat, 2001)) is superior in terms of improving aerobic and metabolic fitness, when compared to lower intensity continuous exercise (Kemi et al., 2005; Burgomaster et al., 2008; Wisløff et al., 2009). Whilst interval training is established as an exercise modality,
research examining the effect of interval training on PEH is insufficient (Ciolac et al., 2009; Lacombe et al., 2011).

1.5 Mechanisms Causing Post-exercise Hypotension
In order to fully elucidate the underlying mechanisms responsible for PEH, it is first necessary to consider the physiological mechanisms controlling blood pressure. Mean arterial pressure (MAP) is determined by cardiac output (CO) and systemic vascular resistance (SVR), thus PEH is caused by changes in one, or both of CO and TPR (Chen and Bonham, 2010; Pocock et al., 2013). Following exercise, CO is raised due to increases in heart rate and stroke volume (Halliwill, 2001). Vasodilation causes a drop in SVR, however this is not compensated for by an increase in CO. It is this fundamental imbalance that underpins the development of PEH (Halliwill, 2001; MacDonald, 2002; Pescatello et al., 2004). Sustained vasodilation post-exercise is dependent on the activation of histamine receptors (McCord and Halliwill, 2006). Antihistamines have been shown to blunt the PEH response in moderate intensity exercise, however the effect of antihistamines on PEH following interval training has not been explored (Lockwood et al., 2005). Existing studies exploring the role of antihistamines have used high dosages, this study will examine the effect of over-the-counter dosages (McCord and Halliwill, 2006).

The primary aim of this study was to validate the role of histamine release in post-exercise hypotension. We also investigated two forms of exercise training; continuous and interval, in order to determine which produced the largest magnitude of post-exercise hypotension. This study should provide insight into the optimal exercise type for patients with hypertension, thus identifying which modality should be advocated to prevent CVD.
CHAPTER 2: REVIEW OF THE LITERATURE

Whilst the literature on PEH largely focuses on deciphering the mechanisms underlying the drop in BP post-exercise, examination of variables that may affect the scale and duration of the hypotension are also investigated (Halliwill, 2001; MacDonald, 2002). This variability may reflect differences in the demographics of the population or characteristics of the exercise performed.

2.1 Mechanisms Causing Post-exercise Hypotension

The changes seen in CO and TPR post-exercise are a result of altered autonomic function, central regulation and vascular responsiveness (Halliwill, 2001; Chen and Bonham, 2010; Lacombe et al., 2011).

2.1.1 Central Regulation and Autonomic Function

Evidence suggests that changes in autonomic outflow, together with the central baroreflex, play a key role in PEH (Halliwill, 2001; Lacombe et al., 2011). The baroreceptor reflex is a negative feedback loop maintaining BP, during exercise the reflex is withdrawn and reset to a higher point. Post-exercise it is reset to lower levels causing reduced sympathetic outflow from the CNS (Floras et al., 1989; Halliwill, 2001; MacDonald, 2002; Halliwill et al., 2013)

Chen et al., (2009) stated that activation of afferent neurons, originating from baroreceptors, implied BP control was of neural origin. Afferent fibres (from baroreceptors in the arch of the aorta and carotid sinuses) synapse in the nucleus tractus solitarii (NTS), a spinal tract key to the integration of sensory information in the cardiovascular response to exercise (Mifflin, 2001; Chen and Bonham, 2010; Halliwill et al., 2013; Pocock et al., 2013). The main excitatory and inhibitory neurotransmitters within the NTS are glutamate and GABA respectively, thus it is the balance of these two substances which determines the output of baroreceptor signals from the NTS to the cardiovascular control centre in the medulla (Chen and Bonham, 2010). In normal baroreceptor function, raised BP triggers afferent neurons to fire more frequently, causing increased NTS activity. Sympathetic output from the medulla consequently drops, returning BP to previous levels (Chen and Bonham, 2010).
2.1.2 Histamine and Vascular Responsiveness

Previously it was thought that local vasodilatory substances played a role in post-exercise vasodilation, however nitric oxide and prostaglandin release have both been shown to influence little control over post-exercise vasodilation (Halliwill et al., 2000; Lockwood et al., 2005; McCord et al., 2006; McCord and Halliwill, 2006). McCord et al. (2006) have since shown that histamine 1-receptor (H1R) antagonists blunt post-exercise vasodilation, increasing TPR and minimising PEH (McCord et al., 2006). Mast cells are localized to the skin, gastrointestinal and respiratory tracts where, by an unknown mechanism, exercise has been identified as a trigger of their degranulation and subsequent release of inflammatory mediators (Sheffer et al., 1985). Increases in temperature, vibration, reactive oxygen species and the presence of cytokines during exercise are supposed antigen-independent mechanisms which promote degranulation (Grabbe, 2001; McCord et al., 2006). Histamine, a low-molecular-weight amine, is the main granule constituent in mast cells along with tryptase and other preformed mediators, including leukotrienes and prostaglandins (Simons, 2004). Histamine plays a key role in allergic inflammation and is a potent vasodilator, which has been found at higher concentrations during and after exercise (Campos et al., 1999; Simons, 2004). Rarely, moderately intense exercise can induce anaphylaxis, although the cause of this dysregulation of the degranulation of mast cells remains incompletely understood (Barg et al., 2011).
Whilst there are 4 major types of histamine receptors, the 2 most widely expressed are histamine 1 and 2 receptors (H1R and H2R), which are located on vascular endothelial walls and on vascular smooth muscle cells respectively (Simons, 2004; McCord et al., 2006). Histamine receptors are hepta-helical transmembrane molecules, which transduce signals via G proteins to intracellular second-messengers (Simons, 2004). The receptors exist in an equilibrium between active and inactive states, the balance of this equilibrium is stabilised by both agonists (histamine) and antagonists (antihistamines) which shift the equilibrium towards the active and inactive states respectively (Simons, 2004). H1R are activated immediately following exercise and mediate vasodilation of the first 30 minutes post-exercise, whilst H2R seem to play a role in sustained vasodilation from 30 to 90 minutes (McCord et al., 2006). Both receptors act via separate mechanisms to diminish vasodilation: blockage of H1R stops release of histamine locally decreasing the formation of local vasodilators including nitric oxide and prostacyclin and H2R antagonist's blocks a decrease in intracellular smooth muscle calcium following histamine binding, preventing smooth muscle relaxation (McCord and Halliwill, 2006).

At this point in time, there is no adequate method for collecting and analysing concentrations of histamine as it is difficult to measure when it is released locally, as it is metabolised quickly: since direct measurement is impractical, ingestion of antihistamines provides a simple and effective way to analyse the role of histamine release in post-exercise vasodilation (Halliwill et al., 2013). Whether histamine acts via a paracrine or endocrine mechanism following exercise remains a source of debate, with different hypotheses regarding the local and systemic effects: Histamine can only cause vasodilation in active muscles with no spill over into systemic circulation, and no change in vascular resistance in inactive muscles or exercise could simply increase the sensitivity of H1R to histamine (Lockwood et al., 2005).

Histamine can also be synthesised by histidine decarboxylase in non-mast cell tissues, including cells of the epidermis, gastric mucosa and neurones within the CNS, however it cannot be stored in this form (Lockwood et al., 2005; Halliwill et al., 2013). Research has found that increased sheer stress in large arteries promotes such de novo production of histamine, physical activity is a cause of increased sheer stress due to raised BP (Ciolac et al., 2009; Halliwill et al., 2013). High intensity interval training causes a greater increase in BP and a larger gradient of sheer stress exerted on blood vessels, which may promote superior improvements in endothelial function and increase histamine production, leading to a larger magnitude of PEH (Ciolac et al., 2009).
Figure 2. The underlying mechanisms resulting in post-exercise hypotension (Halliwill, 2001)

2.2 Factors Affecting Post-exercise Hypotension
BP is tightly regulated in order to maintain homeostasis, however variation exists due to individual’s genes and the environment in which they live. As such, these situational variations need to be examined in order to identify trends between specific sub groups of the population.
2.2.1 Resting Blood Pressure
Previously studies had shown that PEH did not occur in normotensive subjects, and was a phenomenon only associated with hypertensives (Pescatello et al., 1991). PEH has since been shown to occur in normotensive and hypertensive populations (MacDonald et al., 2000a; Raine et al., 2001; Jones et al., 2008; Ciolac et al., 2009; Eicher et al., 2010; Lacombe et al., 2011): A meta-analysis of 47 clinical trials by Kelley et al., (2001) showed that after an exercise training programme systolic BP decreases more in hypertensives than in a normotensive population (-6mmHg vs -2mmHg). These findings are also applicable to PEH: a greater magnitude is seen in hypertensive populations when compared to normotensive individuals post-exercise (MacDonald et al., 2000a). Initial inconsistencies in findings for normotensive subjects may have been due to an inability to detect these smaller changes.

2.2.2 Fitness Level
CO and TPR are influenced by an individual’s level of fitness, which led to the suggestion that PEH was a result of a sedentary lifestyle rather than a physiological response to exercise (Senitko et al., 2002). This theory was tested by comparing endurance trained men and women to a sedentary population, with the hypothesis that PEH would be blunted in endurance trained individuals. The magnitude of change in PEH was found to be similar between endurance trained and sedentary groups (approximately 4 to 5 mmHg, p<0.05), disproving this hypothesis. Rodriguez et al., (2011) confirmed that no difference in PEH occurred between trained and sedentary individuals participating in land and water based walking, however it was suggested that the male endurance athletes used different mechanisms to achieve the same decreases in BP (Senitko et al., 2002). This is supported by recent evidence from Cote et al., (2015), who found that endurance trained individuals experienced a greater drop in systolic BP following high intensity interval training, however MAP remained similar regardless of training status suggesting altered autonomic function in endurance trained individuals.
2.2.3 Type of Recovery
Carter et al., (1999) suggested that active recovery would decrease the magnitude of PEH, as a result of the muscle pump minimising venous pooling and maintaining BP (Carter et al., 1999; Halliwill, 2001). Results from this study showed BP, taken 15 seconds post-exercise, decreased less during active and passive recovery when compared to inactive recovery (-3±1 mmHg and -6±1 mmHg respectively compared to -18±2 mmHg). These differences persisted for the first 4 minutes following exercise, however recovery was only examined for 5 minutes, and thus the implications over a longer time period remain undetermined (Carter et al., 1999).

2.2.4 Position of Patient Post-exercise
The position of the patient during the recovery period may impact PEH: TPR and the effect of gravity change with recovery positions, it has been suggested that this may be a confounder for conflicting results in the literature. Supine and seated recovery were compared by Raine et al. (2001), who found no significant difference in MAP between the two positions. This somewhat surprising result contradicts popular belief, as the seated position places the major vasodilatory vascular beds below the heart, theoretically leading to greater venous pooling due to the effect of gravity (Halliwill, 2001). Raine et al., (2001) confirmed that greater demand was exerted on the cardiovascular system in normotensive individuals in the seated position, suggesting that hypotension was more likely to occur. Further research is needed in a hypertensive population to investigate if this leads to significant differences in BP.
2.2.5 Time of Day
BP displays circadian variation with a nocturnal fall and a morning peak. Jones et al., (2008) found the magnitude of PEH was less pronounced in the morning following 30 minutes of continuous exercise (70% VO$_{2max}$). Scheduling exercise bouts to take place in the afternoon is more effective and offers the largest drop in BP. To negate the potential confounder of circadian BP variation, studies should ensure exercise bouts take place at the same time of day (Jones et al., 2008).

2.2.6 Age
PEH occurs independently of age and has been shown to occur in similar magnitudes in young (20 to 30 years old (YO)) (Raine et al., 2001; Jones et al., 2008), middle aged (40 to 50 YO) (Rueckert et al., 1996; Wallace et al., 1997; Ciolac et al., 2009) and older adults (50-70 YO) (Hagberg et al., 1987; Lacombe et al., 2011). Hypertension increases in prevalence with age, making it hard to determine if age is a causative or correlative factor for PEH (Kannel et al., 1976).

2.2.7 Sex and Ethnicity
Hypertension has an earlier onset and is more prevalent in Black Americans than White Americans, presenting a confounding factor when analysing differences in PEH with ethnicity (Pescatello et al., 2003). Chatuverdi et al., (2012) found that PEH is smaller in South Asians when compared to Europeans despite similar resting and exercise BP. However, an increased prevalence of strokes in this ethnic group suggests that these differences in PEH may be due to differences in cardiovascular risk factors, another potential confounder (Chaturvedi et al., 2012).

Pescatello et al., (2003) hypothesised that differences in TPR responses to pharmacological and environmental stimuli in Black people would cause a smaller magnitude and duration of PEH. No PEH was observed in Black premenopausal women with borderline hypertension (Pescatello et al., 2003), however the results of this study can only be applied to this group and shouldn’t be extrapolated to the general Black American population. The two groups were not matched for initial BP and VO$_{2max}$ and the small sample size could contribute to a type 1 error. There is little other data present on the effect of ethnicity on PEH meaning that clear-cut conclusions cannot be drawn (Pescatello et al., 2004). Senitko et al., (2002) found similar magnitudes of PEH in endurance trained
men and women and there is no evidence to suggest that gender differences exist in PEH (Pescatello et al., 2004).

2.2.8 Heat
Exercise in the heat will exacerbate PEH: Plasma volume will decrease due to higher levels of sweating and vasodilation of cutaneous blood vessels will further decrease TPR (Casa, 1999; Halliwill, 2001). This will heighten venous pooling following exercise, decreasing venous return to the heart and lowering CO (Armstrong, 1998). This theory was confirmed by Franklin et al., (1993) who found that recovery in warm conditions (31.1±0.4°C) caused a significant reduction in BP when compared to neutral (21.4±0.5°C) and cool (17±0.8°C) temperatures over 60 minutes post-exercise, however exercise in the heat increases the risk of syncope, fluid replacement would decrease the scale of PEH and minimise the risk of syncope in the heat by expanding plasma volume (Maughan et al., 1997; Cheung et al., 2000).

2.3 What are the optimal characteristics of an exercise bout to induce post-exercise hypotension?
The characteristics of an exercise bout influence the body's adaptation to the exercise stimulus. The extent to which these characteristics influence PEH has been researched extensively and whilst advances have been made, the role of many of these variables remains undetermined.

2.3.1 Type of Exercise
PEH has been observed following a variety of activities including walking, running, arm ergometry, cycling on a leg ergometer and following resistance exercise (Somers et al., 1991; Hara and Floras, 1992; Brownley et al., 1996; Forjaz et al., 1998b; Wallace et al., 1999; MacDonald et al., 2000b; Forjaz et al., 2004; Eicher et al., 2010; Lacombe et al., 2011). Macdonald et al., (2000b) compared arm and leg ergometry with the hypothesis that differences in active muscle masses would impact on the magnitude of PEH, however it was concluded that PEH is not influenced by the size of the exercising muscle mass.
2.3.2 Duration
PEH has been observed after exercising for as little as 10 minutes (MacDonald et al., 1999), however most studies have used an exercise duration of 20 to 60 minutes (MacDonald, 2002). MacDonald et al., (2000a) used two studies within one paper when determining the effects of duration on PEH, both studies kept intensity constant at 70% VO\textsubscript{2max}. Study 1 showed the effects of varying lengths of exercise resulted in no difference in the magnitude of PEH in a normotensive population. This led to the authors concluding that PEH occurs independently of exercise duration (MacDonald et al., 2000a). In the second study a hypertensive population was recruited, 10 and 30 minutes of exercise were compared, again showing no statistically significant difference between the two durations. Brief durations of exercise appear to be as effective as longer bouts in eliciting PEH (MacDonald et al., 2000a).

2.3.3 Exercise Intensity and High-Intensity Interval Training (HIIT)
The effect of intensity in aerobic exercise on PEH remains unclear, some authors have concluded that exercise intensity shows no effect on the magnitude or duration of PEH (Pescatello et al., 1991; Forjaz et al., 1998a), whilst others have reported a dose-response effect with higher intensities causing greater magnitudes of PEH (Eicher et al., 2010). Pescatello et al., (1991) and Forjaz et al., (1998a) both found PEH was not influenced by intensity when comparing exercise ranging from 30% VO\textsubscript{2max} to 80% VO\textsubscript{2max} over 30 to 45 minutes. Eicher et al., (2010) found a dose response when studying a graded maximal intensity bout (100% VO\textsubscript{2max}), with 40 and 60% VO\textsubscript{2max} bouts for 30 minutes. It is likely that the variation in these findings is due to the differences in study design. Participants and data collection varied between studies: BP status, age, fitness levels, data collection periods (acute vs ambulatory) and frequency of BP measurements made inter-study comparison problematic (MacDonald et al., 2000a; Lacombe et al., 2011).

Jones et al., (2007) investigated the magnitude of PEH when the total amount of work done was controlled, taking into consideration that differences in PEH may be due to the variation in work done, rather than the differences in exercise intensity and duration. They found that the magnitude of PEH is similar when the work done (intensity x duration) was the same, implying that the total amount of work done is an important factor when planning a bout of exercise (Jones et al., 2007). More research is required to determine the effect of intensity on the magnitude of PEH.
High intensity interval training (HIIT) has been shown to rapidly improve exercise capacity in sedentary and recreationally active individuals via increases in VO$_{2\text{max}}$, SV and increased contributions from aerobic and anaerobic metabolism in skeletal muscles, enhancing ATP availability and improving muscular oxidative capacity (Helgerud et al., 2007; Kessler et al., 2012). HIIT programmes have also been shown to have beneficial effects on cardiovascular risk factors, including insulin sensitivity, fasting glucose, HDL cholesterol and anthropometric changes (Kessler et al., 2012). Helgerud et al., (2007) found that HIIT was a more effective method of training than continuous (low and moderate intensity) training, this may be due to the increased time spent at or near VO$_{2\text{max}}$. This concept was described by Billat et al., (2001), who suggested ‘time at VO$_{2\text{max}}$’ was a predictor for enhancing VO$_{2\text{max}}$ in training. HIIT increases the time spent at or near VO$_{2\text{max}}$ through repeated bouts of exercise at an intensity equal to approximately 85 to 100% of VO$_{2\text{max}}$ (greater than the anaerobic threshold) (Laursen and Jenkins, 2002; Seiler and Tønnessen, 2009). The duration of each bout is dependent on the intensity and can last from 1 to 8 minutes, bouts are separated by rest periods (low intensity exercise or inactivity) of 1 to 5 minutes which allow partial recovery (Laursen and Jenkins, 2002; Seiler and Tønnessen, 2009).

HIIT can utilise either short or long durations of high intensity exercise bouts. Continuous exercise was compared to short and long bouts of HIIT by Franch et al., (1998), who found that long HIIT and continuous exercise improved VO$_{2\text{max}}$ significantly more than short HIIT (6 vs 3%, p<0.05). More recently short HIIT (or sprint-like interval training (SIT)) has been researched in detail, however similar adaptations to endurance training were seen (Burgomaster et al., 2008). SIT involves maximal ‘all out’ high intensity bouts, lasting from 10 to 30 seconds and is a more time efficient mode of training than traditional continuous training, however it requires a high level of motivation and participants can experience nausea and discomfort due to the raised levels of exertion (Little et al., 2010). Whilst safety concerns exist over the use of HIIT in patients with CVD, a review by Kessler et al., (2012) found that supervised HIIT was safe, with no training-related adverse events reported in 5 trials.

Three studies have examined the effect of HIIT and SIT on PEH: both hypertensive and normotensive samples were used and age, sample size, baseline fitness and gender also varied between the studies (Ciolac et al., 2009; Rossow et al., 2010; Lacombe et al., 2011).
Table 1. Study designs investigating the influence of HIIT and SIT on PEH

<table>
<thead>
<tr>
<th>Study</th>
<th>Continuous exercise</th>
<th>Interval exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lacombe et al., (2011)</td>
<td>60% VO$_{2\text{max}}$ for 21 minutes</td>
<td>5 sets of 2 minutes at 85% VO$<em>{2\text{max}}$ with 2 minutes active recovery at 40% VO$</em>{2\text{max}}$</td>
</tr>
<tr>
<td>Ciolac et al., (2009)</td>
<td>60% HR$_{\text{reserve}}$ for 40 minutes</td>
<td>40 minutes of 2 minutes active recovery at 50% HR$<em>{\text{reserve}}$ and 1 minute at 80% HR$</em>{\text{reserve}}$</td>
</tr>
<tr>
<td>Rossow et al., (2010)</td>
<td>60% HR$_{\text{reserve}}$ for 60 minutes</td>
<td>4 sets of 30 second all out exercise with 4 and a half minutes active recovery between sets</td>
</tr>
</tbody>
</table>

Despite differences in study designs and sample groups, all three studies reached the conclusion that interval training and endurance exercise both caused similar reductions in BP post-exercise. However, none of these exercise protocols (see Table 1) are truly based on a long HIIT interval such as that designed and utilised by Slordahl et al., (2004), Helgerud et al., (2007) and Franch et al., (1998) (4 x 4 minute exercise bouts at 85%-90% VO$_{2\text{max}}$ with 2 to 3 minutes active recovery at 50% to 60% VO$_{2\text{max}}$). HIIT has been shown to be an effective method of improving health and fitness, yet the effect of this mode of HIIT on PEH is yet to be fully understood.

2.4 Study Design
Demographic differences are not the only cause of variations in PEH: Each study has its own experiment procedures and differ in methods of data collection and analysis, which could lead to disparate conclusions being drawn.

2.4.1 Data Collection
Studies fall into two categories when collecting data for PEH: acute or ambulatory. Acute BP data collection involves keeping the patient in the laboratory for up to 2 hours, regularly measuring BP in a resting position (Eicher et al., 2010; Lacombe et al., 2011). This rest
period post-exercise enables comparisons to be made between exercise modalities (Eicher et al., 2010; Lacombe et al., 2011). Ambulatory BP monitoring extends the measurement period by giving patients ambulatory BP devices to take home with them, these record data for up to 24 hours post-exercise enabling the effects of PEH on the circadian variation of BP to be analysed (Brownley et al., 1996; Wallace et al., 1999; Jones et al., 2008).

2.4.2 Use of Antihistamines
McCord et al., (2006) and Lockwood et al., (2005) both used 540mg Fexofenadine orally to block H1R. Fexofenadine does not cross the blood brain barrier and as such is non-sedative, it also has no cardiovascular side effects (McCord and Halliwill, 2006; BNF, 2013). The justification for using a high dosage (540mg is 4.5x higher than the normal daily dose of 120mg once daily) was that it adequately blocked H1R (time to peak concentration =1.5 hours and half-life = 12 hours). Whilst 540mg was an acceptable dosage when initially considering the role of histamine in PEH, it is highly unlikely that an individual will consume this concentration of H1R-antagonists. The use of over-the-counter dosages of antihistamines should be utilised to examine whether PEH is affected in an everyday situation.

2.5 Summary and Implications for Study Design:
H1R and H2R are implicated in the control of PEH, despite extensive research into the role of histamine there is a paucity of evidence examining the effect of antihistamines on the response to interval training.

When planning participant inclusion and exclusion criteria and study design, it is important to consider the wide range of factors influencing PEH and the effect these may have on data collected. Extensive revision of the literature has enabled the strengths and weaknesses of previous studies to be drawn on and has facilitated the development of the current study design.

The effect of exercise intensity on PEH remains undecided, with evidence being inconclusive. HIIT has been shown to elucidate the same post-exercise hypotension as CE, however of the few studies investigating HIIT none have utilised a longer interval of high intensity.
CHAPTER 3: METHODS

3.1 Ethical Approval
This study was approved by the research ethics committee for the School of Sport at Cardiff Metropolitan University (Wales) and conforms to the Declaration of Helsinki.

3.2 Participants
All subjects were current students at Cardiff Metropolitan University, who volunteered to participate and were recruited via email and personal communication.

Participants were screened using a Physical Activity Readiness Questionnaire (PAR-Q) (See Appendix A) and a resting 12 lead ECG (SECA-CT80000P) was taken along with manual BP measurement (Yamasu-535), prior to beginning their involvement in the study. Exclusion criteria included hypertension (classified as a resting BP greater than 140/90mmHg, in line with the American College of Sports Medicine (ACSM) classification of hypertension (Pescatello et al., 2004)), ECG abnormalities and issues identified by the PAR-Q as unsuitable: contraindications to antihistamines such as asthma, eczema, hay fever and pregnancy excluded further participation in the study. At the start of each visit, participants completed a brief form, which aimed to identify any changes in their health since the PAR-Q was completed (See appendix B). Subjects were not taking any medication other than the contraceptive pill.

3.3 Consent
An information sheet was provided detailing the background of the study, the methods, potential risks and benefits, rights and exclusion criteria (See Appendix A). Each participant provided written informed consent prior to participation in the study.
3.4 Experimental Design
Testing took place in the Cardiff Metropolitan Exercise Physiology Laboratory. Each participant attended 5 sessions, these sessions consisted of: a \( \text{VO}_{2\text{max}} \) test, two continuous exercise sessions and two interval exercise sessions. The order of the continuous and interval sessions was randomised. One continuous and one interval session was completed following antihistamine ingestion, participants were given 3x10mg tablets of Loratadine for oral consumption: one tablet was taken on each of the two days prior to exercise and on the day of exercise, at a time corresponding to one hour before their session. Loratadine is a non-sedating antihistamine which has no effect on the cardiovascular system, 10mg once daily is the prescribed dosage as recommended in the British National Formulary (BNF, 2013). Each session was separated by at least 72 hours and all exercise was performed on a cycle ergometer (Monark cycle Ergometer-824E). Each session commenced between the hours of 12pm and 5pm, negating the morning peak in BP (Jones et al., 2008), both interval and continuous sessions were matched for duration and total amount of work done, enabling analysis of the effect of HIIT on PEH (Jones et al., 2007).

**Figure 3.** Schematic showing the timeline of the study and measurements taken for continuous and interval sessions
3.4.1 Graded Exercise Testing
Following pre-test screening, participants completed a standardised step incremental exercise test. This involved cycling at 75 revolutions per minute (rpm) against a progressively increasing resistance (resistance was increased by 25 watts every 3 minutes) until exhaustion, the test was finished when the participant could no longer maintain 75 rpm. HR, power output (PO) and \( \text{VO}_2 \) were recorded at rest and throughout the exercise, with tests lasting approximately 20 minutes. The \( \text{VO}_{2\text{max}} \) achieved in this test was used to determine the workload of the subsequent two exercise bouts (see appendix C), and provided participants the opportunity to become familiarised with the laboratory environment and the experimental procedures. Ergonomic measurements of the participants’ position on the leg ergometer were taken and used for the remaining 4 exercise bouts.

3.4.2 Continuous Exercise Bout
For the 4 continuous and interval exercise bouts, the Finometer was attached to the right arm. Finger arterial pressure was taken from the second phalange via a finger cuff and calibrated to brachial BP. Throughout rest and exercise the right arm was supported by pillows and towels, and subjects were instructed not to put any weight on the arm or the finger. The thermostat was set to 21°C, enabling PEH to be observed whilst minimising the risk of heat syncope (Maughan et al., 1997).

After filling in the questionnaire, subjects rested for 10 minutes in the seated position (seated on a medical plinth with legs straight and the back rest at 45°) (Raine et al., 2001). The exercise bout consisted of 35 minutes cycling at 75 rpm. The first 3 minutes and last 2 minutes served as a warm up and cool down at a PO equivalent to 50% of \( \text{VO}_{2\text{max}} \) (as calculated from the graded exercise test), the remaining 30 minutes were performed at a PO corresponding to 70% of \( \text{VO}_{2\text{max}} \). The duration and intensity of the continuous exercise bout can be seen in Figure 4a, on completion of the 35 minutes of exercise participants rested in the seated position for 1 hour.
3.4.3 Interval Exercise Bout
As with the continuous bout, participants filled in the questionnaire and rested in the seated position for 10 minutes before pedalling for 35 minutes on the leg ergometer at 75 rpm. The warm up and cool down for this bout were 6 and 2 minutes respectively at 50% VO\(_{2\text{max}}\). The central portion of exercise involved 4 sets of 4 minutes high intensity at 85% VO\(_{2\text{max}}\) and 3 minutes active recovery at 50% VO\(_{2\text{max}}\). The final high intensity interval was followed by a final 2 minutes at 70% VO\(_{2\text{max}}\) before the cool down, ensuring the total work done was the same in both bouts (Jones et al., 2007). The duration and intensity of the interval exercise bout can be seen in Figure 4b. Following completion of the 35 minutes exercise, participants followed the same protocol as continuous exercise for the post-exercise 1 hour recovery period and rested in the seated position.
Plate 1. Patient resting in the seated position pre-exercise. The right hand was supported by towels on the plinth and the participant rested the forearm in the mid-pronation position, minimising pressure put on the finger cuff.

Plate 2. Participant cycling on the leg ergometer, attached to the breath by breath VO₂ and the Finometer. The right hand was rested on a pillow on the ergometer, with the forearm in the mid-pronation position, minimising pressure put on the finger cuff.
3.5 Outcome Measures
Outcome measures were assessed during the continuous and interval sessions. The primary outcome measure was BP, which was measured using automated sphygmomanometry (via Finometer-Pro) before, during and after exercise. Manual BP was taken 3 times pre-exercise, and 2 repeats were taken at 10 minute intervals throughout the rest period.

Each exercise session was characterised using HR, blood lactate concentration, core temperature and VO\textsubscript{2}. HR was measured using Polar Electro-FT1 and averaged over 30 second intervals throughout the exercise period and the post-exercise recovery period. HR was averaged over 5 minute periods for the 60 minutes rest. Blood samples were taken at 17 and at 31 minutes from the ear of the participant, from which the blood lactate concentration was determined. Core body temperature was measured using a rectal temperature probe in the interval and continuous sessions.

Before participation, subjects were weighed (to the nearest 0.1kg) (SECA-770) and had their height measured (to the nearest 0.1cm) (Holtain-fixed stadiometer). Prior to each subsequent exercise bout participants were weighed again.

3.6 Statistical Analysis
The one hour post-exercise data collection period was divided into 5 minute segments and the mean for each of these sections taken. Differences in the mean post-exercise BP were compared between the antihistamine and non-antihistamine exercise bouts, and between continuous and interval sessions, using a three way repeated measures ANOVA on SPSS statistics. The characteristics (mean VO\textsubscript{2}, mean % of VO\textsubscript{2max}, mean HR, maximum and minimum values for HR and VO\textsubscript{2}, mean core temperature and mean blood lactate) of each type of exercise were analysed using paired, two-tailed students T-tests, these means were obtained from all of the readings within the exercise period. For all statistical analysis, we selected p<0.05 as the required p value for statistical significance.
CHAPTER 4: RESULTS

A total of 9 participants started the study (5 Males and 4 Females), reflecting sample sizes used in previous studies of a similar nature (Lockwood et al., 2005; Jones et al., 2008; Lacombe et al., 2011). The mean characteristics of subjects finishing the study are shown in Table 1, 4 participants dropped out (1 male and 3 females) due to reasons shown in Figure 5. Participants were normotensive, active individuals who did not smoke and were otherwise healthy.

Table 2. Characteristics of participants

<table>
<thead>
<tr>
<th>Participant characteristics</th>
<th>Number (n=5) (mean± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>20.0± 1.1</td>
</tr>
<tr>
<td>Weight (kgs)</td>
<td>81.6± 7.8</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>179.2± 5.2</td>
</tr>
<tr>
<td>VO_2max (ml/kg/min)</td>
<td>44.8± 7.5</td>
</tr>
<tr>
<td>Max Power output (W)</td>
<td>250.0± 46.3</td>
</tr>
<tr>
<td>Resting systolic BP (mmHg)</td>
<td>112.9± 5.9</td>
</tr>
<tr>
<td>Resting diastolic BP (mmHg)</td>
<td>75.1± 8.0</td>
</tr>
</tbody>
</table>

Figure 5. Flow chart showing participant numbers
Characterisation of the exercise bouts can be seen in Table 2, mean VO$_2$, mean % VO$_{2\text{max}}$, core temperature and mean HR were not significantly different (p>0.05). Whilst these measures did not measure the total work, they are indicative that, as planned the total work done was the same for continuous and interval exercise bouts. Lactate levels were significantly higher in interval bouts and greater maximum values for VO$_2$ and HR were seen in the interval bouts highlighting the amplitude of exercise intensity change (see Appendix D).

 Decreases in mean BP from pre-exercise to the hour post-exercise are shown in Table 3. Results from the 3 way ANOVA were non-significant for both systolic and diastolic BP, with no statistically significant findings when comparing the presence of antihistamines with exercise type (p=0.443), antihistamines with time (p=0.989), the exercise type with time (p=0.373) and antihistamines with exercise type and with time (p=0.739).
<table>
<thead>
<tr>
<th></th>
<th>Continuous</th>
<th>Continuous + Antihistamines</th>
<th>Interval</th>
<th>Interval + Antihistamines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average VO$_2$ (ml/kg/min)</td>
<td>30.6</td>
<td>30.9</td>
<td>31.3</td>
<td>31.5</td>
</tr>
<tr>
<td>Minimum and Maximum VO$_2$ (ml/kg/min)</td>
<td>22.8</td>
<td>30.7</td>
<td>24.6</td>
<td>24.4</td>
</tr>
<tr>
<td></td>
<td>33.5</td>
<td>34.1</td>
<td>39.0</td>
<td>39.7</td>
</tr>
<tr>
<td>Average % VO$_2$max</td>
<td>68.2</td>
<td>69.0</td>
<td>69.1</td>
<td>69.3</td>
</tr>
<tr>
<td>Average % HR peak</td>
<td>76.5</td>
<td>79.6</td>
<td>80.9</td>
<td>79.9</td>
</tr>
<tr>
<td>Minimum and Maximum HR (beats per minute)</td>
<td>119.9</td>
<td>124.6</td>
<td>129.3</td>
<td>132.3</td>
</tr>
<tr>
<td></td>
<td>166.0</td>
<td>168.1</td>
<td>169.9</td>
<td>172.6</td>
</tr>
<tr>
<td>Lactate 1 (mmol/L)</td>
<td>3.9</td>
<td>3.8</td>
<td>5.0*</td>
<td>5.9*</td>
</tr>
<tr>
<td>Lactate 2 (mmol/L)</td>
<td>4.3</td>
<td>4.2</td>
<td>5.5*</td>
<td>6.9*</td>
</tr>
<tr>
<td>Core temperature (°C)</td>
<td>37.3</td>
<td>37.1</td>
<td>37.3</td>
<td>36.8</td>
</tr>
</tbody>
</table>

*=statistically significant difference in lactate with exercise type (p=0.027)
Table 4. Comparison of systolic BP pre and post-exercise (mean)

<table>
<thead>
<tr>
<th></th>
<th>Continuous</th>
<th>Continuous + Antihistamines</th>
<th>Interval</th>
<th>Interval + Antihistamines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-exercise Resting BP (mmHg)</td>
<td>132.6</td>
<td>127.7</td>
<td>132.2</td>
<td>127.8</td>
</tr>
<tr>
<td>1 hr post-exercise BP average (mmHg)</td>
<td>120.3</td>
<td>123.8</td>
<td>123.6</td>
<td>127.6</td>
</tr>
<tr>
<td>Change from resting to post-exercise (mmHg)</td>
<td>-12.3</td>
<td>-3.9</td>
<td>-8.6</td>
<td>-0.2</td>
</tr>
<tr>
<td>% Change from resting to post-exercise</td>
<td>-9.2%</td>
<td>-3.1%</td>
<td>-6.5%</td>
<td>-0.2%</td>
</tr>
</tbody>
</table>

Table 5. Comparison of diastolic BP pre and post-exercise (mean)

<table>
<thead>
<tr>
<th></th>
<th>Continuous</th>
<th>Continuous + Antihistamines</th>
<th>Interval</th>
<th>Interval + Antihistamines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-exercise Resting BP (mmHg)</td>
<td>72.5</td>
<td>73.8</td>
<td>77.4</td>
<td>74.2</td>
</tr>
<tr>
<td>1 hr post-exercise BP average (mmHg)</td>
<td>69.1</td>
<td>74.8</td>
<td>74.5</td>
<td>75.3</td>
</tr>
<tr>
<td>Change from resting to post-exercise (mmHg)</td>
<td>-3.5</td>
<td>0.9</td>
<td>-2.9</td>
<td>1.1</td>
</tr>
<tr>
<td>% Change from resting to post-exercise</td>
<td>-4.8%</td>
<td>1.3%</td>
<td>-3.8%</td>
<td>1.4%</td>
</tr>
</tbody>
</table>

Both continuous and interval training showed beneficial effects on BP, with PEH displayed in systolic and diastolic BP following both exercise bouts, however no statistically significant differences in the magnitude of PEH existed between the exercise types (p=0.521 for systolic and 0.518 for diastolic). Taking antihistamines resulted in a smaller magnitude of PEH in both continuous and interval bouts, with a mean BP of 125.7/75.0 mmHg compared to 122.0/71.8 mmHg for non-antihistamine exercise bouts. These differences of 3.7 and 3.2 mmHg (systolic and diastolic) were not statistically significant (p=0.177 and 0.183 respectively). When analysing change in BP during the data collection
period post-exercise, change in systolic BP was non-significant \( (p>0.05) \), however statistically significant changes in diastolic BP were seen \( (p<0.05) \). For all exercise bouts, blood pressure was at its lowest immediately following exercise, with a general trend of a slow increase back towards baseline values, these trends can be seen in Fig 6a, b and c. This trend was the same for bouts completed whilst taking antihistamines however initial values were not as low and recovery to baseline values occurred much quicker.

**Figure 6a.** Comparison of systolic and diastolic BP following interval and continuous exercise bouts

**Figure 6b.** Comparison of systolic and diastolic BP following continuous and continuous with antihistamine exercise bouts
Figure 6c. Comparisons of systolic and diastolic BP following interval and interval with antihistamine exercise bouts
CHAPTER 5: DISCUSSION

5.1 What is the optimal type of exercise for patients with hypertension?
Past literature is inconclusive on the effect of exercise intensity on PEH, with evidence both for and against a dose response effect (Pescatello et al., 1991; Eicher et al., 2010). Few studies have investigated the effect of HIIT on PEH, and these have not utilised a longer duration of high intensity intervals (Ciolac et al., 2009; Rossow et al., 2010; Lacombe et al., 2011). A lack of clarity exists over the optimal interval exercise protocol, interval training stimuli vary and the effect of these different protocols on PEH is unknown (Lacombe et al., 2011). We utilised 4 sets of 4 minute intervals at 85% VO\(_{2\text{max}}\) based on the theory that maximising ‘time at VO\(_{2\text{max}}\)’ was a predictor for enhancing VO\(_{2\text{max}}\). Similar training procedures have been previously used, showing a large range of beneficial adaptations to aerobic performance measures when compared to continuous exercise and SIT, we hypothesised that these longer intervals may cause a greater magnitude of PEH when compared to continuous exercise (Franch et al., 1998; Billat, 2001; Helgerud et al., 2007). This is the first study to investigate the effects of antihistamines on PEH following HIIT and the utilisation of over the counter dosage of antihistamines is unique in terms of study design.

The magnitude of PEH we observed following continuous (a decrease of 12.3/3.5 mmHg, systolic/ diastolic) and interval (8.6/2.9 mmHg, systolic/diastolic) exercise bouts was similar to values previously observed (5-10mmHg) in young healthy normotensive populations (Halliwill, 2001). The extent of the influence of HIIT on PEH remains undetermined, as in previous studies no difference in the magnitude of PEH was detected between continuous and interval exercise bouts, with non-significant differences between systolic (12.3mmHg and 8.6mmHg, continuous and interval exercise respectively) and diastolic BP (3.5 mmHg and 2.9 mmHg) (Ciolac et al., 2009; Rossow et al., 2010; Lacombe et al., 2011). HIIT has been extensively researched and has been shown to be a safe and effective method of training, which can lead to greater improvements in aerobic and muscular oxidative capacities when compared to continuous exercise, however research thus far has not proven that HIIT results in a greater decrease in PEH (Franch et al., 1998; Helgerud et al., 2007; Ciolac et al., 2009; Lacombe et al., 2011). Despite our results finding no differences in PEH between training types, interval training should be considered as an intervention for hypertensive patients for the following reasons: Firstly, interval training is superior to continuous training in terms of improving VO\(_{2\text{max}}\), the strongest predictor of mortality in
patients with CVD (Wisløff et al., 2007). Secondly, Ciolac et al., (2009) hypothesised that greater improvements in endothelial function should be seen with HIIT due to the different gradients of sheer stress exerted on arteries. Better cardiovascular function and capacity should lead to better quality of life of patients, as activities of daily living will elicit a smaller cardiovascular response.

Few studies have matched the total work done when investigating HIIT and PEH, we matched the total amount of work done in both exercise bouts, negating this as a confounding factor for differences in PEH with exercise type. Our findings add support to the theory that when the work done is the same between exercise bouts, the magnitude of PEH will be similar (Jones et al., 2007). Differences in blood lactate were expected, as higher intensities result in greater anaerobic contribution to ATP production (Laursen and Jenkins, 2002). Minimum and maximum values for HR and VO₂ illustrate the changes in intensity that occur with HIIT (see appendix D for graph illustrating the changes in HR and VO₂ for both exercise bouts). Despite these differences in the characteristics of each exercise bout, non-significant differences in variables measuring the product of the total work done (mean VO₂, HR and core temperature) indirectly indicated that the total work done was the same (Jones et al., 2007; Ciolac et al., 2009; Lacombe et al., 2011).

5.2 The Role of Histamine Release in PEH
The primary finding of this research was a clinically, but not statistically significant reduction in the magnitude of hypotension when taking antihistamines. Following both continuous and interval training, a mean difference of 3.7/3.2 mmHg (systolic/diastolic) was observed when compared to non-antihistamine exercise bouts. A rise of 2mmHg in systolic BP increases the risk of mortality from ischaemic heart disease and stroke by 7% and 10% respectively. If the magnitude of PEH is repeatedly minimised, this raise in BP will increase an individual's risk of developing hypertension and CVD (Krause et al., 2011). Despite this difference being of clinical importance it was not statistically significant, perhaps due to the small sample size. This resulted in a lack of power to accurately detect a significant change in BP. Following ingesting of antihistamines the magnitude of PEH was smaller and values returned to baseline quicker than following exercise with no antihistamine, this trend can be seen following both continuous and interval exercise bouts. The mechanisms causing PEH, as discussed in seminal reviews by Halliwill et al., (2001) and MacDonald et al., (2002), implicated the role of histamine in PEH as part of an
integrated response to exercise. Histamine release during exercise causes peripheral vasodilation, decreasing TPR and increasing the scale of PEH (McCord and Halliwill, 2006). In previous studies showing an antihistamine-induced reduction in PEH, the dosage of antihistamines investigated was x 4.5 the recommended daily dosage. We showed that administration of the recommended daily dosage (10mg once daily) of loratadine (a H1 antagonist) also minimises PEH (McCord and Halliwill, 2006). Following a single bout of exercise, PEH is of clinical importance as BP can be lowered for an extended period of the day (MacDonald, 2002). If a patient were taking antihistamines, the size of this drop would be reduced, minimising the benefits of exercise on BP. H1R antihistamines can be indicated for nasal allergies, vasomotor rhinitis, urticaria, pruritus, insect bites and stings, drug allergies and as anti-emetics whilst H2R antihistamines are indicated for gastric and duodenal ulcers, gastro-oesophageal reflux disease and functional dyspepsia (BNF, 2013). Patients with these conditions should consider alternative medication, if using exercise to control BP. The normal BP response to exercise is altered when taking antihistamines, reducing the antihypertensive benefits of exercise (Lockwood et al., 2005).

Over-the-counter and prescription treatments are both affected by this finding, hypertension is increasingly prevalent and in combination with an independent increase in the prevalence of allergies, a clinical awareness of this interaction is required (Romagnani, 2004; Maryon-Davis, 2005).

5.3 Limitations
The main limitation of this study was the small sample size. Participant drop out was larger than expected, potentially leading to an inability to detect significant changes in BP. More males (n=4) than females (n=1) completed the study, however there is no evidence to suggest that Gender influences PEH, as such this imbalance would not affect our results (Pescatello et al., 2004).

We hypothesised that antihistamines would minimise the magnitude of PEH, however we did not measure any of the variables associated with the mechanisms such as SV, CO and TPR. Assessment of these variables would have further contributed to the understanding of the complex mechanisms underlying PEH, however we still observed a clinically significant drop in BP with antihistamines, further implicating the role of histamine in PEH. Measuring changes in BP with and without antihistamines enabled indirect analysis of the role of histamine in PEH. Ideally blood histamine concentration would be directly
measured, however currently there is no accurate or simple method to collect and analyse histamine concentrations as it is released locally and quickly metabolised (Halliwill et al., 2013).

Ideally each participant would complete a control ‘bout’ of exercise, in which they rested for 35 minutes on the ergometer and for the hour ‘post-exercise’. The one hour rest period post-exercise was compared to a 10 minute rest period pre-exercise, whilst this pre-exercise period gives an indication of resting BP, it was not a control. A control session would enable a longer data collection period giving a better representation of baseline BP, however this mode of study design is mostly utilised by studies analysing the effect of exercise on BP via ambulatory monitoring, validating our use of a pre-exercise period for baseline values (Rueckert et al., 1996; Wallace et al., 1999; Jones et al., 2007).

We solely investigated the acute effect of exercise on BP, whilst 4 exercise bouts were used, this was not an intervention study and the longer term impact of different types of exercise on BP were not considered. Despite this limitation, better understanding of the acute response to HIIT is needed before longer term implications are assessed, justifying our study design (Ciolac et al., 2009).

In order for PEH to be clinically significant, decreases in BP need to be maintained during activities of daily living (MacDonald et al., 2001). This can be examined by simulating ADL in the laboratory or through the use of ambulatory BP over a longer time period (Brownley et al., 1996; MacDonald et al., 2001). Whilst ambulatory BP may provide a realistic picture of a patient’s daily BP, researchers lose the ability to quantify the amount of activity individuals complete once they leave the laboratorial setting (MacDonald et al., 2001). As in previous studies, we chose a 1 hour data collection period post-exercise (Rossow et al., 2010; Lacombe et al., 2011). Whilst PEH was observed over this time period, BP had not returned to baseline values, indicating that a longer time collection period could be used to fully assess the acute BP response, however the practicalities of this remain a challenge.

HIIT has been shown to be safe in patients with CVD, however due to the structured nature of HIIT untrained patients should initially be supervised (Kessler et al., 2012). Higher levels of motivation are required in HIIT to meet the target intensity, this may put some individuals off participation, however continuous exercise has been anecdotally noted to be boring and varied intensities may be more motivating (Kessler et al., 2012). Using a mode of exercise with high impact forces such as running could result in HIIT
being unsuitable for patients with orthopaedic problems, however this could be negotiated by using a non-weight-bearing exercise such as cycling.

Future studies should address both the long term implications of a HIIT training programme on BP, and the long term effect of antihistamines on PEH and BP. The study design should include a larger sample size, a control group and assessment of PEH in ADL (through either simulated ADL or ambulatory BP monitoring). An accurate method of measuring the concentration of blood histamine levels and measurement of cardiovascular parameters associated with PEH will assist further understanding of the complex mechanisms causing PEH. The effect of the duration of the high intensity bouts on PEH should also be investigated to assist in optimal exercise prescription, whilst further analysis of population sub-groups will enable identification of individuals for whom HIIT will be the optimal exercise intervention in the treatment of hypertension and CVD.
CHAPTER 6: CONCLUSION

We observed a similar magnitude of PEH in a young normotensive sample to previous studies. When total work done was matched, HIIT caused a similar drop in BP to continuous exercise. Interval training should be considered for patients with hypertension/CVD because it is shown to be more efficient in improving VO$_{2\text{max}}$ and other markers of health than continuous training.

Antihistamines taken at the recommended daily dosage reduced the size of PEH in both continuous and interval exercise bouts by a clinically significant amount. Further research is required to determine the clinical implications of the interaction between antihistamines and PEH when prescribing antihistamines for patients using exercise as an intervention for hypertension and CVD.
REFERENCE LIST


Forjaz, C. et al. 1998a. Post-exercise changes in blood pressure, heart rate and rate pressure product at different exercise intensities in normotensive humans. *Brazilian Journal of Medical and Biological Research* 31(10), pp. 1247-1255.


Background of the study

This study is aiming to look at the post-exercise hypotension (PEH) after exercise. PEH is a phenomenon where blood pressure is lowered after exercise. This fall in blood pressure has also been associated with an increase in plasma (blood) volume which may lead to increases in exercise performance and increases in VO$_{2\text{max}}$ (a main determinant of aerobic performance). Additionally, the use of exercise to lower blood pressure is important in the treatment of hypertension (high blood pressure), which affects ~31% of the UK population.

Achieving high exercise intensity within training sessions, as seen in interval training, seems to be associated with optimising the development of cardiovascular fitness but the effect of interval exercise on the PEH and on hypertension generally is less clear because a comparison between different interval sessions has not yet been made. As such this study will look at the differences in PEH between interval training and continuous endurance training.

An additional aim of the study is to investigate how antihistamine tablets influence the PEH response. Past research has suggested that the use of antihistamines reduces this post-exercise drop in blood pressure but this effect has not been investigated in interval exercise. Antihistamines are routinely taken as a remedy for hay fever or allergies and, as such, they are widely available and generally considered to be very safe. They are not known to adversely influence physical or mental performance. Past research into PEH has used antihistamines in a higher dosage than is seen when they are taken as a remedy, so it is unclear whether routine dosages of antihistamines may also influence the blood pressure in recovery form exercise.

Therefore the aims of the study are:
- a) to compare the recovery of blood pressure between interval and continuous exercise sessions;
- b) to investigate how this response is affected with the use of antihistamines.

What would happen if you agree to take part?

1. Some preliminary measurements and tests will be taken before testing to ensure you are suitable for the protocols and for use as data. This will include your height, weight, resting electrocardiogram (ECG), resting blood pressure and VO$_{2\text{max}}$. The VO$_{2\text{max}}$ test will involve an incremental increase in intensity until exhaustion, performed on a cycle ergometer (exercise...
bike). This test will give the information needed to determine the intensity of the subsequent interval and continuous sessions.

2. In the following four weeks you will be asked to take part in the four additional sessions. These will be ordered randomly but are given below:

   Two 35 minutes continuous exercise bouts (one with, and one without Loratadine) at a moderate intensity (70% VO$_{2\text{max}}$) with a 3 minutes warm-up and 2 minutes cool-down (50% VO$_{2\text{max}}$).

   Two interval sessions (one with, and one without Loratadine) of 3 minutes at 50% VO$_{2\text{max}}$ followed by 4x (4 min at 85% VO$_{2\text{max}}$, 3 min at 50% VO$_{2\text{max}}$) and then a final 2 minutes at 70% and 2 minutes at 50% VO$_{2\text{max}}$.

   Each of the four 35 minute sessions will be preceded by 10 minutes of semi-supine (lying down) rest during which time we will take baseline measurements. Following the 35 minutes you will be asked to rest for a further 60 minutes before returning to the exercise bike for 10 more minutes of very easy cycling (30% VO$_{2\text{max}}$).

3. The procedures for each of these 35-minute bouts will include assessment of heart rate, blood pressure and respiratory gases during exercise. In addition we will also measure core body temperature for the whole trial using a sterilised rectal temperature probe. This is a standard procedure for measuring core temperatures and has been used many times in the Exercise Physiology Laboratories. After instruction you will be asked to insert the rectal probe in private. The probe itself is very small in diameter (the size of a computer mouse wire) and will not cause any discomfort. After the exercise, we will assess blood pressure, and heart rate for a 60-min recovery period during which you will be asked to sit quietly and relax. We will take a capillary blood sample midway and at the end of the exercise bouts to establish blood lactate concentration. We will take less than 0.05 millilitres of blood in making these measures (you have a blood volume of at least 4 litres).

4. Before all tests we will ask you to complete a questionnaire to check your suitability to perform exercise. We want you to prepare similarly for each of the four exercise sessions, to avoid caffeine in any food or drink in the 3-hours. You must not consume alcohol in the 24-hrs before tests.

5. For each of the interval or continuous bouts, you must consume a 500ml drink of water one hour before you begin the exercise bout.

6. When you are due to perform the antihistamine exercise bouts, you must take one tablet at each of the following times in the lead up to the exercise test. Each tablet should be taken with a small drink of water. On the day of the exercise test, you should consume the 500ml drink of water with the tablet.
   - 49 hours before
   - 25 hours before
   - 1 hour before

**Are there any risks?**

There is a very minor chance that you may feel unwell during or after the exercise bouts, however we have chosen exercises which reduce the likelihood of this happening.

The antihistamine medication is a routine over-the-counter remedy which is considered to be very safe, provided that you have met the inclusion criteria of the study (see the ‘participant consent form’).
It is important that you identify any changes in your health or in your ability to do exercise before you perform exercise.

**Exclusion criteria from the study**

You should not participate in this study if:

- You experience asthma, eczema or hay fever
- Regularly take antihistamines (e.g. allergy medication, Zantac etc.)
- You have been told by your doctor that you:
  - Are lactose intolerant
  - Should not take antihistamine medication
  - Have any kidney disease
- Are currently taking any medication other than the contraceptive pill
- Are currently pregnant

**Your rights**

Joining this study does not mean that you give up any legal rights. In the very unlikely event of something going wrong during the evaluation, Cardiff Metropolitan fully indemnifies its staff, and participants are covered by its insurance.

**What happens to the results of the study?**

The results will be coded so that the names are removed and you will not be identifiable in the results. The results may be published but no description of individual participants will be provided.

**Are there any benefits of taking part?**

Yes, you will find out your resting heart rate and blood pressure and you will find out your VO$_{2\text{max}}$, all of which are good indicators of your health and fitness. You will also be taking part in an innovative study.

**What happens next?**

With this information sheet you should have been given a participant consent form that you will need to fill out and hand in, to confirm that you are willing to take part in the study.

**How your privacy is protected**

Careful steps will be taken to ensure that you are not identifiable. The results will be coded and locked away. Consent forms will be kept for 10 years and then destroyed because it is a requirement of Cardiff Met.

**Further Information**

If you have any other further queries then please contact:

Michael G Hughes
Email: MGHughes@cardiffmet.ac.uk

The following forms are to be used for all participants.

- The participant consent form, along with the Physical Activity Readiness Questionnaire (PAR-Q) that accompanies this explanation will be given in the first visit.
- The Test Preparation form will be given before each of the four main test sessions.
PARTICIPANT CONSENT FORM

Reference Number:

Participant name or Study ID Number:

Title of Project: The Effect Of Intensity On Post-Exercise Hypotension

Name of Researchers: Dr Michael Hughes

Participant is to complete this section: Please place initials in each box.

1. I can confirm that I have fully read and understand the information sheet for the research. I have had time to process the information and have asked all the questions I feel are necessary and I have had these questions answered satisfactorily.

2. I fully understand that I have volunteered for this study and that I am able to withdraw at any time, without giving any reasons.

3. I understand the following criteria must be **TRUE** to allow for to my involvement in the study:
   - I am not currently taking antihistamines (e.g. allergy medication)
   - I have never been told by my doctor that I:
     - Am lactose intolerant
     - Should not take antihistamine medication
   - I am not currently taking any other medication other than the contraceptive pill
   - I am not currently pregnant.

4. I understand that all information gained from this study will be kept confidential and no one except the researchers will have access to the information.

5. I therefore agree to take part in the above study.

Print name of Participant
_______________________________________
Date

Signature of Participant
_______________________________________

Signature of researcher
_______________________________________
Date
Appendix B- Test preparation questionnaire

Additionally, please answer the following questions, adding detail in the space provided

a) Are there any changes to your health or suitability for exercise (i.e., injury) since your last test?

b) Have you eaten in the last 3 hours? (Give details if so)

c) Have you exercised in the last 24 hours? (If so give details)

d) Are you currently performing your typical amount of exercise training?

e) Does your participation in today’s test conform to the guidelines given at the start of the study regarding caffeine (none in last 3 hours) / alcohol consumption (none in last 24 hours)?

f) For the continuous and interval sessions, have you consumed a 0.5 litre volume of fluid 30 minutes before arriving at the laboratory?

When you have answered these questions and you are happy with the explanations given, you can sign below if you consent to participate in the tests.

I have read this form and understand the test procedures that I will perform. I consent to participate in the test.

Signed ______________________ Date ________________

Name (print) __________________
Appendix C - Power outputs taken from VO$_{2\text{max}}$ test

An example of the VO$_{2\text{max}}$ achieved by a subject in the graded exercise test and how this then determines the respective power outputs for the interval and continuous sessions.

<table>
<thead>
<tr>
<th>VO$_2$ Peak =</th>
<th>51.6</th>
</tr>
</thead>
<tbody>
<tr>
<td>PO at peak (watts) =</td>
<td>300</td>
</tr>
</tbody>
</table>

**Intensities**

<table>
<thead>
<tr>
<th>% of VO$_2$ Max</th>
<th>Corresponding PO (watts)</th>
</tr>
</thead>
<tbody>
<tr>
<td>40%</td>
<td>115.9</td>
</tr>
<tr>
<td>50%</td>
<td>150.3</td>
</tr>
<tr>
<td>70%</td>
<td>219.3</td>
</tr>
<tr>
<td>85%</td>
<td>271</td>
</tr>
</tbody>
</table>
Appendix D- Comparison of VO\(_2\) and HR during continuous and interval exercise

Exercise intensity as a % of VO\(_{2\text{max}}\) (mean) throughout the continuous and interval sessions, both with and without antihistamines. Variation in exercise intensity can be seen in the interval sessions, with peaks and troughs representing the high intensity exercise bouts and the active recovery periods.

Mean heart rate throughout continuous and interval bouts, with and without antihistamines, as with % VO\(_{2\text{max}}\) the differing intensities with HIIT can be seen.