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THE EFFECTS OF ISOMETRIC EXERCISE ON RESTING  
BLOOD PRESSURE: A HOME-BASED APPROACH

by  
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Thesis submitted  
for the Degree of Doctor of Philosophy

2014

## **ABSTRACT**

The main focus of this thesis was to develop an accessible home-based isometric exercise training (IET) protocol for the reduction of resting blood pressure (BP). Hypertension is estimated to affect nearly 30% of the world's population (WHO, 2012) and represents an inordinate health and economic burden worldwide. A growing body of research suggests that IET can lower resting BP. However, the majority of studies have utilised expensive and/or laboratory-based equipment, which may not be accessible to the general population. To this end, the studies within this thesis explored whether the novel isometric wall squat exercise could be prescribed for home-based training using relatively simple, inexpensive equipment. The first study determined a method for adjusting the wall squat intensity. It was found that knee joint angle reliably produced inverse relationships with heart rate (HR) and BP when individual bouts of wall squat exercise were completed ( $r$  at least  $-0.80$ ;  $P < 0.05$ ). Study 2 then established that these inverse relationships could be replicated from completing an incremental test ( $r$  at least  $-0.88$ ;  $P < 0.05$ ), from which wall squat training intensity could then be prescribed at an individualised knee joint angle ( $104 \pm 7^\circ$ ) to elicit a target training HR (95% peak HR:  $121 \pm 14$  beats $\cdot$ min $^{-1}$ ). Finally, using these methods, study 3 implemented a 4 week home-based isometric wall squat training protocol and found statistically significant and clinically relevant resting BP reductions (systolic BP:  $-4$  mmHg; diastolic BP  $-3$  mmHg; mean arterial pressure:  $-3$  mmHg). These results support the majority of previous research that has found reductions in resting BP following IET. Furthermore, the primary BP control mechanisms were also explored and the results suggested that a reduction in resting BP was potentially mediated by a decrease in resting cardiac output ( $-0.54 \pm 0.66$  L $\cdot$ min $^{-1}$ ), which may have been governed by a reduction in resting HR ( $-5 \pm 7$  beats $\cdot$ min $^{-1}$ ). The novel home-based IET protocol developed within this thesis may be more time and cost effective, which may ultimately increase the adherence to and efficacy of IET for the reduction of resting BP.

## **ACKNOWLEDGEMENTS**

I would like to take this opportunity to thank the following people for their support throughout this research.

To my supervisors, Dr Jonathan Wiles and Dr Damian Coleman, I would like to express my deepest thanks. I truly appreciate your guidance and knowledge throughout this process. You have both given your time and support so generously and for that I am very grateful.

To Dan Stretch and Dan Tolhurst, thank you for your invaluable technical assistance, advice and encouragement throughout my data collection.

To the Department of Sport Science, Tourism and Leisure and the Graduate School at Canterbury Christ Church University, thank you for the opportunity to conduct this research.

To all my participants, I would like to give you my special thanks. Without your dedication and enthusiasm the research in this thesis would not have been possible.

To my parents, Simon and Debbie, you have always been a constant source of support. Through your unconditional love and belief in me I have always felt like I could achieve anything. Without you, I would not be where I am today.

And finally, to my wife Rebecca, thanks to your unwavering encouragement and patience I have been able to complete my dream. It has not always been an easy ride but you've always been there. I quite simply could not have completed this journey without you. I look forward to our next big adventure!

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**WORD COUNT: 88,861**

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## ABBREVIATIONS

AAMI	Association for the Advancement of Medical Instrumentation
ACE	Angiotensin converting enzyme
ACSM	American College of Sports Medicine
ANOVA	Analysis of variance
ANCOVA	Analysis of covariance
ANS	Autonomic nervous system
ARB	Angiotensin receptor blockers
ATP	Adenosine triphosphate
AV	Atrioventricular
BP	Blood pressure
BHS	British Hypertension Society
CCBs	Calcium channel blockers
CI	Confidence interval
CV	Coefficient of variation
CVD	Cardiovascular disease
DBP	Diastolic blood pressure
ECG	Electrocardiograph
EMG	Electromyography
EMG <sub>peak</sub>	Peak electromyography
HR	Heart rate
HR <sub>max</sub>	Maximum heart rate
HR <sub>peak</sub>	Peak heart rate
HRM	Heart rate monitor
HRV	Heart rate variability
IET	Isometric exercise training
IHG	Isometric handgrip
INC	Incremental test
LSD	Least significant difference
MAP	Mean arterial pressure
MCID	Minimal clinically important difference
MSNA	Muscle sympathetic nerve activity
MVC	Maximal voluntary contraction
NICE	National Institute for Health and Care Excellence
Q̇	Cardiac output
RPD	Rate of perceived discomfort
RPE	Rate of perceived exertion
SA	Sinoatrial
SBP	Systolic blood pressure
SV	Stroke volume
T	Training session



TBPR	Target blood pressure range
THRR	Target heart rate range
TPR	Total peripheral resistance
$\dot{V}O_2$	Oxygen uptake
$\dot{V}O_{2\max}$	Maximal oxygen uptake
WHO	World Health Organization

### **SYMBOLS**

$\Delta$	Delta (change)
----------	----------------

## **CHAPTER 1: INTRODUCTION AND LITERATURE REVIEW**

### **1.1 Contextualising hypertension**

High blood pressure (BP), also known as hypertension, is estimated to affect nearly 30% of the world's population (WHO, 2012). Hypertension is the leading global risk for mortality and was estimated to have caused 7.5 million deaths worldwide in 2004, which accounts for 12.8% of all global deaths (WHO, 2009). In the UK, the prevalence of high BP was 23.4% in 2008, which was lower in comparison to the whole of Europe (29.3%) (WHO, 2014). The lowest prevalence of raised BP was in the Americas (23.0%), including the USA (15.6%), and the most prevalent region was Africa (36.8%) (WHO, 2014). In 2010, hypertension was reported to be the second leading risk factor in UK, which accounted for approximately 9% of disease burden (Murray et al., 2013). Hypertension is defined as systolic blood pressure (SBP)  $\geq$  140 mmHg and/or diastolic blood pressure (DBP)  $\geq$  90 mmHg (Williams et al., 2004). Hypertension is a major challenge for public health as it is one of the most prevalent and powerful risk factors that contributes to a number of diseases including coronary heart disease (MacMahon et al., 1990; Escobar, 2002), stroke (Cressman and Gifford, 1983; MacMahon et al., 1990), heart failure (Kannel and Belanger, 1991), peripheral vascular disease (Makin et al., 2001) and chronic kidney disease (Klag et al., 1996). Not only are these diseases the leading causes of mortality, morbidity and disability, but a large financial burden exists due to the concomitant medical expenditures (Hodgson and Cai, 2001) and this costs the global economy billions of dollars each year (Gaziano et al., 2009). In the UK alone, the cost of antihypertensive drug therapies was approximately £1 billion in 2006 (National Institute for Health and Care Excellence (NICE), 2011). Further to this, it was reported that the total cost of hypertension in the United States was \$46.4 billion in 2010 (Go et al., 2014), which highlights the substantial economic impact of high BP. In 2025 the number of adults with high BP is projected to increase by approximately 60%, so that in total 1.56 billion people will have hypertension worldwide (Kearney et al., 2005), further emphasising the significant public health burden that hypertension represents. Therefore any method that might help prevent and control high BP is of great importance.

The clinical goal of any antihypertensive therapy is to reduce resting BP to a target level (SBP < 140 mmHg; DBP < 90 mmHg), which will ultimately be associated with a reduction in cardiovascular morbidity and mortality (Chobanian et al., 2003). The two main types of intervention commonly used to treat and/or prevent hypertension are pharmacological therapy and lifestyle modification.

#### ***1.1.1 Pharmacological therapies for the treatment of hypertension***

Pharmacological therapies, also known as antihypertensive drug treatments, are offered to: 1) people under 80 years with BP  $\geq$  140/90 mmHg who have target organ damage, established cardiovascular disease (CVD), renal disease, diabetes, or 10-year cardiovascular risk > 20%, and 2) people of any age with BP  $\geq$  160/100 mmHg (NICE, 2011). Worldwide there are six main pharmacological agents used to lower BP in hypertensive populations; diuretics,  $\beta$ -blockers, calcium channel blockers (CCBs), angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs) and  $\alpha$ -blockers (Chobanian et al., 2003; Williams et al., 2004; Mancia et al., 2007). The Blood Pressure Lowering Treatment Trialists' Collaboration (2003) performed a prospective overview of randomised trials that investigated the effects of different BP lowering regimens on serious cardiovascular events. In placebo-

controlled trials during follow up, the mean BP in the ACE inhibitor treatment group was 5.4/2.3 mmHg lower than the placebo group from a baseline mean of 140/81 mmHg (SBP/DBP respectively). Also, the mean BP in the calcium antagonist treatment group was 8.4/4.2 mmHg lower than the placebo group during follow up from a baseline mean of 148/75 mmHg (SBP/DBP respectively). Such reductions in BP with ACE inhibitors and calcium antagonists are associated with a significant reduction in the relative risk of total major cardiovascular events by 22% and 18%, respectively (Blood Pressure Lowering Treatment Trialists' Collaboration, 2003).

Despite the proven efficacy of antihypertensive pharmacological therapies for reducing CVD and mortality (Chobanian et al., 2003), their effectiveness is inconsistent and it has been reported that up to 50% of medicated hypertensives fail to achieve their recommended target BP (Brown, 1997; Hajjar and Kotchen, 2003). Adherence to drug treatment can be low due to many factors such as the undesirable deleterious side effects of medication (Chobanian et al., 2003) along with the cost (Vawter et al., 2008), to name a few. Odell and Gregory (1995) carried out a retrospective analysis of hypertension care at an internal medical clinic (Salt Lake City, USA) and found that the first year of a patient's treatment costs \$947 (~£579; XE, 2014); 80% of which was linked to drug related costs. Not surprisingly, it has been suggested that due to the inadequacy and limitations of antihypertensive drug treatments, the use of lifestyle modifications is essential (Millar et al., 2007).

### ***1.1.2 Lifestyle modifications for the prevention and treatment of hypertension***

Lifestyle modifications, previously termed non-pharmacological therapies, are recommended as an initial therapy for people who have BP  $\geq$  140/90 mmHg without other risk factors and for people taking antihypertensive medication as an adjunctive therapy (NICE, 2011). A wide range of lifestyle modifications have been shown to successfully lower SBP including weight reduction (5-10 mmHg reduction per 10kg weight loss), Dietary Approaches to Stop Hypertension (DASH) eating plan (8-14 mmHg reduction), dietary sodium restriction (2-8 mmHg reduction), physical activity (4-9 mmHg reduction), and alcohol reduction (2-4 mmHg reduction) (Williams et al., 2004). Lifestyle modifications also have the additional benefits of being relatively cheap (Pescatello et al., 2004), whereas, pharmacological therapies, as indicated in section 1.1.1 (page 1), cost economies billions each year (Elliott, 2003). It must be noted that whilst lifestyle modifications, such as physical activity, are less costly (Pescatello et al., 2004), common exercises modalities currently prescribed to control resting BP (aerobic/resistance) do typically incur some associated cost, such as equipment and/or gymnasium memberships (Millar, Paashuis and McCartney, 2009b), which is a known barrier to participation (Belza et al., 2004; Allison et al., 2005; Lascar et al., 2014).

Lifestyle modifications are not only important for the treatment of hypertension but also for its prevention (Appel, 2003a; Appel et al., 2003b), particularly as the associated risk of CVD begins to appear from BP levels as low as 115/75 mmHg, SBP/DBP respectively (Lewington et al., 2002). Additionally, a person aged 55 years has a 90% residual lifetime risk of developing high BP (Vasan et al., 2002). Therefore merely waiting for hypertension to develop and then treating the problem is injudicious (Vasan et al., 2002). As Stamler (1998) succinctly articulates, dealing with hypertension in such a way is "late, defensive, mainly reactive, time-consuming, associated with side effects... , costly, only partially

successful, and endless” (p. 879). Therefore the logical conclusion is that lifestyle modifications aimed at normotensive individuals are essential for maintaining the ideal level of BP.

One particular lifestyle modification that has received a large amount of interest is physical activity. The WHO defines physical activity as “any bodily movement produced by skeletal muscles that requires energy expenditure – including activities undertaken while working, playing, carrying out household chores, travelling, and engaging in recreational pursuits” (WHO, 2015). Exercise is a subcategory of physical activity and is described as planned, structured and repetitive activity that aims to maintain or improve physical fitness (WHO, 2015). It is important to differentiate between physical activity and exercise as these terms describe different concepts (Caspersen, Powell and Christenson, 1985), however some authors’ use these terms interchangeably without clearly delineating a difference (Blair, LaMonte and Nichaman, 2004). Furthermore, the term training is often used in the literature and is described as a programme of exercise designed to improve physical fitness (Kent, 2006). Therefore, when discussing previous research within this thesis, the terminology employed by the author will be utilised.

Traditionally aerobic exercise is the type of physical activity recommended for the prevention and treatment of hypertension (Pescatello et al., 2004). Aerobic exercise principally comprises of rhythmical contractions that alter both the muscle length and joint angle with little change in tension (Mitchell and Wildenthal, 1974; Fadel, Smith and Gallagher, 2004). Aerobic exercise prescribed for the reduction of resting BP typically includes activities such as walking, running and cycling and is completed for at least 30 minutes most days of the week (Pescatello et al., 2004; Williams et al., 2004). Regular aerobic exercise has been demonstrated to help to prevent (Paffenbarger et al., 1983; Blair et al., 1984) and treat (Fagard, 2001; Whelton et al., 2002) hypertension as well as having a positive impact on several other CVD risk factors (Cornelissen and Fagard, 2005). Further to this, it has also been recommended that aerobic exercise should be supplemented by dynamic resistance exercise (Pescatello et al., 2004), which involves concentric and/or eccentric contractions that change both the length and tension of the muscle (Cornelissen and Smart, 2013). Indeed, previous meta-analyses have shown that dynamic resistance exercise produces modest reductions in resting SBP and DBP (Kelley and Kelley, 2000; Cornelissen et al., 2011; Cornelissen and Smart, 2013).

Despite the established value of exercise, the positive beneficial effects are only gained if the recommended exercise programme prescribed is rigidly adhered to and completed. Unfortunately it is estimated that 50% of adults who start an exercise program will drop out within the first 6 months and after 24 months only 20% will continue to exercise (Dishman, 1994); therefore methods to increase adherence are of great importance. One barrier to physical activity and exercise commonly reported is lack of time (Trost et al., 2002; Lascar et al., 2014), which is particularly pertinent to aerobic exercise as guidelines recommend  $\geq 3$  hours per week (Pescatello et al., 2004). It has been demonstrated that adherence levels are raised when shorter bouts of exercise are prescribed opposed to longer bouts (Jakicic et al., 1995) presumably as less pressure is placed on a person’s time commitments. Therefore developing a short duration exercise regime to assist in the treatment and prevention of hypertension would be potentially very beneficial. An exercise mode which may help to resolve this time related barrier is isometric exercise, which typically only requires  $< 1$  hour of training a week (Owen, Wiles and Swaine, 2010).

## 1.2 Isometric exercise training for the reduction of resting blood pressure

Isometric, or static, exercise is a mode of resistance training that principally involves a sustained contraction with the muscle exerting a force with little or no change in muscle length and joint angle (Fadel, Smith and Gallagher, 2004; Lind, 2011; Cornelissen and Smart, 2013). Isometric muscle contractions form an integral part of many daily activities such as grasping, lifting, holding and pushing heavy objects (Lind, 1970; Lind, 2011) along with contractions against immovable, fixed objects (Mitchell and Wildenthal, 1974). Traditionally isometric exercise training (IET) has not been recommended as a mode of exercise for the reduction of resting BP (Owen, Wiles and Swaine, 2010; Cornelissen and Smart, 2013). The exaggerated pressor response experienced during acute bouts of isometric exercise (Mitchell and Wildenthal, 1974) (see section 1.3.1, page 6, for further details) has often been cited as ‘proof’ for its opposed use in special populations (Millar, Paashuis and McCartney, 2009b), such as those with hypertension or heart disease (Araújo et al., 2011). Furthermore, there is a paucity of studies exploring the effects of IET on resting BP compared to the wealth of data available for aerobic exercise (Kelley and Kelley, 2010). Indeed, recent meta analyses exploring the effects of IET on resting BP had  $\leq 5$  studies that met the inclusion criteria (Kelley and Kelley, 2010; Owen, Wiles and Swaine, 2010; Cornelissen et al., 2011; Cornelissen and Smart, 2013), whereas meta-analytic research on the effects of aerobic exercise included a total of 72 studies (Cornelissen and Fagard, 2005). As well as reducing BP, it is well documented that there are numerous health benefits that can be derived from partaking in regular aerobic exercise (Fletcher et al., 2001), however there is limited research and knowledge on the health benefits on IET (Kelley and Kelley, 2010). As isometric exercise is a relatively unknown quantity in comparison to aerobic exercise it is often overlooked. However, the body of research suggesting that IET has an important role to play in the reduction of resting BP is growing, particularly over the past 10 years and should not be discounted.

Two landmark studies instigated the initial interest in isometric exercise as a potential method to lower resting BP. The first study by Kiveloff and Huber (1971) found that 5 to 8 weeks of maximal whole body, short duration isometric contractions of the extremities, neck, abdomen, and buttocks simultaneously could reduce both resting SBP and DBP in hypertensive individuals. However, the whole body isometric muscle contraction protocol did not change BP or heart rate (HR) in normotensive participants. Buck and Donner (1985) studied the effect that regular exposure to isometric exercise has on BP in 4,273 men and discovered a reduced incidence of hypertension among men who had jobs involving moderate or heavy occupational isometric activity. Since these two seminal studies, there has been an increasing body of research developing demonstrating that short duration IET can effectively lower resting BP in both normotensive and hypertensive individuals (Wiley et al., 1992; Ray and Carrasco, 2000; Howden et al., 2002; Taylor et al., 2003; Peters et al., 2006; McGowan et al., 2007a; 2007b; Millar et al., 2008; Devereux, Wiles and Swaine, 2010b; Wiles, Coleman and Swaine, 2010; Baross, Wiles and Swaine, 2012; Badrov et al., 2013a; 2013b; Millar et al., 2013a).

The reductions in resting BP found with IET are similar in magnitude, if not greater, to those produced with pharmacological therapies (Millar, Swaine and McGowan, 2012) and lifestyle modifications, particularly aerobic exercise and dynamic resistance training (Cornelissen and Smart, 2013; Millar et al., 2013b). Further to this, isometric training halves the time commitment required to train compared to

aerobic exercise training (Millar et al., 2013a). Indeed, a meta-analysis of controlled trials of IET studies has recently shown that both SBP and DBP can be reduced with less than 60 minutes of isometric exercise a week (Owen, Wiles and Swaine, 2010). To this end, isometric training has previously been identified as a time efficient method for reducing resting BP (Stiller-Moldovan, Kenno and McGowan, 2012), which may help to break down an important barrier to exercise and increase adherence (Millar, Paashuis and McCartney, 2009b; Carlson et al., 2014). Furthermore, isometric training, such as handgrip exercise, can be performed quickly, easily and in any location (Ray and Carrasco, 2000) and unlike other exercise modes commonly prescribed, such as aerobic exercise, IET requires very little adjustment to a person's daily routine (Millar, Paashuis and McCartney, 2009b). It is suggested that such qualities may help to enhance compliance to prescribed training interventions, which in the long term will increase the likelihood of a positive clinical outcome (Ray and Carrasco, 2000).

While isometric exercise has been proven to be effective for the reduction of resting BP, its application is somewhat limited currently as the majority of training studies have involved the use of expensive and/or laboratory-based equipment; this will be explored further in section 1.5.1c (page 24). As already identified, the cost of exercise, such as facilities and equipment, is a known barrier to physical activity and exercise (Belza et al., 2004; Allison et al., 2005; Lascar et al., 2014), as well as the time commitment required to undertake exercise (Troost et al., 2002; Lascar et al., 2014) due to the concomitant travel to and from the facility, such as a laboratory (see section 1.1.2, page 2). Any travel required supersedes the beneficial short duration nature of isometric exercise itself. Therefore the majority of isometric protocols currently documented are neither cost nor time effective, which as Millar, Paashuis and McCartney (2009b) highlight are factors that could reduce an isometric therapy's effectiveness for altering BP. In order to make IET more readily available, a home-based training regime using inexpensive, simple equipment may be more appropriate. Exercise that is low-cost and requires minimal supervision may help with the adoption and maintenance of regular exercise (Jette et al., 1999), and thus could increase the efficacy of IET. Furthermore, an accessible home-based programme would allow exercise to be completed at an individual's convenience and in the privacy and comfort of their home (Jette et al., 1999), enabling exercise to be more easily integrated into a person's daily routine and also diminishing the burden of travel (Steele et al., 2008); thus helping to reduce some of the obstacles known to negatively impact on engagement with regular exercise (Jette et al., 1999). To this end, this thesis will attempt to design an inexpensive home-based IET protocol for the reduction of resting BP.

The proceeding sections of this chapter will review the nature of isometric exercise studying the literature related to both the acute responses and chronic adaptations. For the purpose of this thesis an acute response will be described as the physiological reaction that occurs in the body during an individual bout of exercise and a chronic adaptation will be defined as the physiological alteration that occurs over time due to the repeated exposure to bouts of exercise training (Kent, 2006). A sound understanding of the acute responses to isometric exercise is necessary as it is the repeated exposure to these short term responses that provides the physiological training stimulus from which a reduction in resting BP can occur (Wiles, 2008a; Devereux, 2010a); this will be explored in section 1.3 (page 6). Further to this, the findings of previous IET studies will be examined to highlight the longer term physiological adaptations previously reported, such as a reduction in resting BP, and explore the possible physiological mechanisms responsible for such chronic adaptations; this will be discussed in section 1.4 (page 11). This information

will also allow the identification of the mechanisms that require further investigation. Furthermore, the protocols previously utilised to prescribe IET will be critically evaluated in section 1.5 (page 20) to determine which programme variables influence the acute cardiovascular response and ultimately produce the most optimal chronic BP adaptations. Careful evaluation of this information will help to inform the design and implementation of the home-based IET protocol to be used within this thesis, which will be discussed in the final section 1.6 (page 36).

### **1.3 Understanding the acute responses to isometric exercise as a prerequisite to blood pressure adaptation**

This section will review the current understanding of the responses to an acute bout of isometric exercise. Isometric exercise is known to produce distinct physiological responses, such as an exaggerated pressor response (Mitchell and Wildenthal, 1974) and mechanical compression of the blood vessels (Lind, 2011). These responses are thought to be mediated by three neurogenic control mechanisms; central command, the exercise pressor reflex and the arterial baroreflex (Smith, Mitchell and Garry, 2006). However, the exact underlying cellular events of these mechanisms remains unknown, particularly in relation to the exercise pressor reflex, and this continues to be an active area of research (Mitchell and Smith, 2008). Despite this fact, an understanding of the general role of these responses and control mechanisms is fundamental within the context of this thesis, as the acute responses define the physiological stimulus during IET and are thus inextricably linked to any chronic adaptations produced (Wiles, 2008a), such as a reduction in resting BP. An understanding of the acute responses is paramount when discussing the potential mechanisms that bring about chronic BP adaptations and will ultimately inform the design of the IET protocol to be used within this thesis.

#### ***1.3.1 The acute cardiovascular responses to isometric exercise***

It is widely acknowledged throughout the literature that isometric exercise is characterised by a pressor response, marked by a pronounced increase in SBP and DBP, with a modest increase in HR (mild tachycardia) (Martin et al., 1974; Lind, 2011). Thus isometric exercise puts a pressure load on the heart (Laird, Fixler and Huffines, 1979). Mean arterial pressure (MAP) is a function of both cardiac output ( $\dot{Q}$ ) and total peripheral resistance (TPR); ( $MAP = \dot{Q} \times TPR$ ), where  $\dot{Q}$  is a result of HR and stroke volume (SV) ( $\dot{Q} = HR \times SV$ ) (Hietanen, 1984). When an isometric muscle contraction is initiated, BP is thought to rise due to an increase in HR and a subsequent rise in  $\dot{Q}$  (Rowell and O'Leary, 1990). Several studies have shown that the pressor response produced by isometric exercise is mediated by an increase in  $\dot{Q}$  with little or no contribution from TPR (Martin et al., 1974; Shepherd et al., 1981; Bezucha et al., 1982). The increase in  $\dot{Q}$  is primarily thought to be due to an increase in HR (Lind and McNicol, 1967; Bezucha et al., 1982; Friedman, Peel and Mitchell, 1992), since SV tends to decrease or remain relatively unchanged from levels of rest during isometric exercise (Lind et al., 1964; Martin et al., 1974), which is presumably due to an impaired venous return (MacDougall et al., 1985). Upon the cessation of a sustained isometric contraction both BP and HR have been shown to return to control values within a few minutes without any rebound effect (Lind et al., 1964; Hietanen, 1984). Thus although isometric exercise may produce a pronounced BP response, the pressure load on the heart is minimal due to the fact isometric exercise contractions typically last for approximately 2 minutes, as will be identified in section 1.5.4 (page 30), and after this time BP values return to baseline rapidly.

### ***1.3.2 Acute local circulation response to isometric exercise***

It is well known that during a muscular contraction, the intramuscular blood vessels dilate as a greater quantity of blood is required by the contracting muscles (Lind and McNicol, 1967). However, during isometric exercise there is a certain degree of inflow obstruction (Martin et al., 1974). Hietanen (1984) explains that during a static contraction the active muscle fibres within their connective tissue sheaths stiffen and swell, which in turn raises the intramuscular pressure (Rowell, 1993). The contracting muscle mechanically squeezes the intramuscular blood vessels and causes compression. Lind et al. (1964) describe this as a throttling of muscle's blood vessels. Blood is hindered from entering the arteries and pushed out of the veins (Hietanen, 1984). Thus the increased flow of blood through the dilated blood vessels is opposed (Lind and McNicol, 1967; Martin et al., 1974). The dilation of the blood vessels is not adequate enough to overcome the intramuscular mechanical compression and thus there is an insufficient amount of blood delivered to perfuse the contracting muscle (Lind and McNicol, 1967). The marked rise in BP during isometric exercise, mediated by HR and subsequently  $\dot{Q}$ , may be viewed as an obligatory response physiologically designed to improve blood flow to the exercising muscle to try to overcome the mechanical compression and offset the inflow obstruction (Lind et al., 1964; Martin et al., 1974). This mechanical hindrance to muscle blood flow has often been considered the most important special aspect of isometric exercise (Mitchell and Wildenthal, 1974).

### ***1.3.3 Mechanisms that control the acute response to isometric exercise***

The autonomic nervous system (ANS) plays an important role in producing the appropriate pressor response to exercise (Mitchell, 1990). Exercise induced changes in the autonomic neural outflow occur in order to maintain adequate perfusion of the exercising muscle to meet the metabolic demands (Fadel, Smith and Gallagher, 2004). When exercise is performed there is an increase in sympathetic nervous system activity and a decrease in the parasympathetic nervous system activity (Mitchell, 1990). Several investigations have attempted to elucidate the possible neural mechanisms responsible for the regulation of the parasympathetic and sympathetic systems that evoke the cardiovascular responses to sustained isometric muscle contractions. It is commonly believed that the initiation and maintenance of the pressor response is resultant from a net combination of multiple separate and distinct neurogenic control mechanisms working in concert with one another (Fadel, Smith and Gallagher, 2004; Smith, Mitchell and Garry, 2006). Neural signals for three mechanisms originate from the brain (central command), the skeletal muscle (exercise pressor reflex), and the aorta and carotid artery (arterial baroreflex) (Smith, Mitchell and Garry, 2006).

#### ***1.3.3a The role of central command during isometric exercise***

In one mechanism, efferent neural activity descending from a higher central area of the brain is thought to be responsible for initiating the cardiovascular and hemodynamic changes (Mitchell, 1990). Signals from this central area activate the motor cortex (Franke, Boettger and McLean, 2000), which is responsible for the recruitment of motor units (Mitchell, 1990) to initiate and control the execution of the isometric contraction. In a parallel fashion, signals from the higher brain centres also activate the cardiovascular control areas located in the medulla (Mitchell, 1990), which control autonomic neural outflow (Franke, Boettger and McLean, 2000). This in turn adjusts the amount of efferent activity of the parasympathetic



and sympathetic nervous systems to both the heart and blood vessels (Mitchell, 1990). The autonomic adjustments make elicited changes in HR and BP that are proportional to the intensity of the exercise (Smith, Mitchell and Garry, 2006), primarily initiating an increase in HR through withdrawal of vagal tone (Freyschuss, 1970). This central control mechanism was originally termed 'cortical irradiation' by Krogh and Lindhard (1913) but is now widely accepted as 'central command' (Mitchell, 1990). It is thought that central command serves as a feed forward mechanism (Mitchell, 1990).

### *1.3.3b The role of the exercise pressor reflex during isometric exercise*

There is also a peripheral reflex control mechanism, which is often termed the 'exercise pressor reflex' (Mitchell, Kaufman and Iwamoto, 1983; Kaufman and Hayes, 2002). Mitchell, Kaufman and Iwamoto (1983) broadly define the exercise pressor reflex as "all the cardiovascular changes reflexly induced from contracting skeletal muscle that are responsible for the increase in arterial pressure" (p. 229). In this mechanism, it is proposed that changes in autonomic nerve activity are initiated in the contracting skeletal muscle by stimulating two types of afferent nerve endings; mechanical and metabolic (Mitchell, 1990).

Firstly, myelinated Group III muscle afferents transmit neural impulses to the cardiovascular control areas related to mechanical activity such as stretch, contraction or pressure (Kaufman et al., 1983; Mitchell, 1990; Gladwell and Coote, 2002). These are commonly known as 'mechanoreceptors' and are known to be activated abruptly at the onset of a muscle contraction (Gladwell and Coote, 2002; Fisher and White, 2004). It is thought that these neural impulses may reach the cardiovascular control areas almost simultaneously with the signals sent from central command (Mitchell, 1990). These neural impulses provide information regarding the mass of the skeletal muscle involved and the type and intensity of the muscle contraction (Mitchell, 1990).

Secondly, unmyelinated Group IV muscle afferents are excited by metabolic and chemical changes and transmit neural impulses to the cardiovascular control areas (Kaufman et al., 1983; Mitchell, 1990; Gladwell and Coote, 2002) and are commonly known as 'metaboreceptors' (Fisher and White, 2004). These afferents are activated when there is a mismatch between the blood flow and metabolism in the working skeletal muscle (Mostoufi-Moab et al., 1998), such as when blood flow is restricted so that the washout of metabolites is reduced (Rowell and O'Leary, 1990). The metabolite-sensitive nerve endings are stimulated by the consequent increased accumulation of metabolites (Mostoufi-Moab et al., 1998), such as lactic acid (Rotto and Kaufman, 1988), hydrogen ions (Victor et al., 1988), arachidonic acid (Rotto et al., 1990), potassium (Rybicki, Waldrop and Kaufman, 1985), adenosine (Costa and Biaggioni, 1994) and deprotonated phosphate (Sinoway et al., 1994). It is likely that one, or more, of these substances will increase the discharge rate of the metaboreceptors (Rotto and Kaufman, 1988), which will initiate sympathetic nerve activity directed to the exercising muscle (Victor et al., 1988); this will consequently lead to an increase in BP, HR and  $\dot{Q}$ . However, these neural impulses are somewhat delayed due to the time required for the accumulation of metabolites in the contracting muscle (Kaufman et al., 1983; Mark et al., 1985). These Group IV muscle afferents therefore discharge minimally at the onset of a muscle contraction but increase in activity steadily until exercise is terminated (Fadel, Smith and Gallagher, 2004).

It must be noted that although Group III and IV muscle afferents predominately respond to mechanical and metabolic stimulation, respectively, these muscle afferents show a degree of polymodality and are capable of responding to both stimuli (Kaufman et al., 1983). It is thought that the exercise pressor reflex serves as a feedback control (Mitchell, 1990).

#### *1.3.3c The role of the arterial baroreflex during isometric exercise*

The third mechanism that mediates the cardiovascular and hemodynamic adjustments to exercise is the 'arterial baroreflex'. The arterial baroreflex originates from the afferent fibres in the carotid sinus and aortic arch and play a pivotal role in the rapid reflex adjustments that occur with acute cardiovascular stress (Fadel, Smith and Gallagher, 2004). The carotid and aortic baroreflexes function as mechanoreceptors and report changes in a negative feedback control system that regulates BP on a beat-to-beat basis (Fadel, Smith and Gallagher, 2004). Autonomic neural outflow is reflexly altered and HR, SV and peripheral resistance are adjusted accordingly (Fadel, Smith and Gallagher, 2004). Changes in arterial BP cause a conformational change in the baroreceptors themselves and this in turn leads to adjustments in the afferent neuronal firing (Fadel, Smith and Gallagher, 2004).

At rest, with an increase in BP the arterial baroreceptors are stretched and begin to fire at an increased rate (Fadel, Smith and Gallagher, 2004). This results in a reflex mediated increase in parasympathetic nerve activity and a decrease in sympathetic nerve activity, which would consequently decrease HR (Fadel, Smith and Gallagher, 2004). However this appears to not occur during exercise as the large increase in BP persists and tachycardia ensues (Ludbrook, 1983). During fatiguing isometric exercise an abrupt increase in BP is elicited, which should cause the arterial baroreceptors to fire at an increased rate, however BP continues to rise until the end of the sustained contraction (Iellamo et al., 1994). Therefore it is thought that the arterial baroreceptor reflex could be modified during exercise (Ludbrook, 1983). Indeed, ample evidence exists elucidating that the baroreflex function is progressively 'reset' to a higher operating point from rest to exercise in direct relation to the exercise intensity to operate around the prevailing high BP (Fadel, Smith and Gallagher, 2004; Raven, Fadel and Ogoh, 2006). During isometric exercise, there is rightward shift of the baroreflex function curve along the pressure axis of the regression line relating to systolic arterial pressure and pulse interval (Iellamo et al., 1994).

It is thought that the feed-forward mechanism of central command is the primary regulator of resetting the arterial baroreflex and that the feedback mechanism of the exercise pressor reflex acts as a subserving modulator (Fadel, Smith and Gallagher, 2004; Raven, Fadel and Ogoh, 2006). Specific research related to isometric exercise by Iellamo et al. (1994) suggests that the modified operating point of the baroreflex during isometric handgrip (IHG) is a result of increased peripheral drive from chemoreflex stimulation from the working muscles. Later work by Iellamo et al. (1997) found that during dynamic one-legged knee extension movements, the two primary mechanisms of central command and muscle chemoreflexes work together to preserve the baroreflex sensitivity by 'resetting' the baroreceptor-cardiac response relationship, thus permitting the increase in HR and BP.

#### *1.3.3d Neurogenic cardiovascular control during isometric exercise*

It is important to note that the neurogenic control mechanisms are not mutually exclusive (Mitchell, 1990). All three neural mechanisms play an important role in the regulation of the cardiovascular

responses to exercise (Raven, Fadel and Ogoh, 2006). Due to the speed of the cardiovascular response at the onset of isometric exercise, it is thought that central command exclusively sets the basic patterns of effector activity (Rowell and O'Leary, 1990; Rowell, 1993). When a voluntary isometric muscle contraction begins, signals are received by the cardiovascular centres from the motor areas of the brain (Shepherd et al., 1981). As a result of these inputs to the cardiovascular centres, vagal activity to the heart decreases and thus initially increases HR (Martin et al., 1974). Seals, Chase and Taylor (1988) suggest that the initial pressor response is mediated by this tachycardia through an increase in  $\dot{Q}$ . This is supported by the fact that little or no increase in muscle sympathetic nerve activity (MSNA) occurred during the initial 1.5 minutes of IHG exercise (Seals, Chase and Taylor, 1988), which is a secondary indicator of chemosensitive muscle afferent nerve activation (Victor et al., 1988). It has also been suggested that the initial increase in HR is possibly due to mechanoreflexes sensing the increase in degree of activity at the contracting muscle (Martin et al., 1974; Shepherd et al., 1981; Rowell and O'Leary, 1990; Rowell, 1993).

After 2 or 3 minutes of exercise, it is thought that the cardiovascular responses are then modulated by 1) the exercise pressor reflex, via by chemosensitive and mechanosensitive afferent nerve endings, and 2) the arterial baroreflex, via by the mechanosensitive afferents within the carotid sinuses and aortic arch (Rowell and O'Leary, 1990). Indeed, Seals, Chase and Taylor (1988) reported that during the final minutes of IHG exercise, HR increased a little, if at all, and instead a progressive increase in MSNA occurred. It was proposed that an increased level of metabolites engaged the muscle chemoreflexes and thus produced greater increases in MSNA (Seals, Chase and Taylor, 1988). The stimulation of the metaboreceptors is delayed due to the aforementioned time required for the accumulation of metabolites in the contracting muscle (Kaufman et al., 1983; Mark et al., 1985). Once the metaboreceptors are stimulated this will cause an increase in sympathetic nerve activity (Victor et al., 1988), which elicits an increase in MAP (Franke, Boettger and McLean, 2000). Furthermore, as the arterial BP begins to increase, the mechanoreceptors of the carotid sinus and aortic arch become activated to further modulate the response (Shepherd et al., 1981) and the muscle chemoreflexes modify the operating point of the baroreflex (Iellamo et al., 1994; 1997).

It is clear that the alterations in autonomic outflow that occur from these three neurogenic control mechanisms mediate the hemodynamic and cardiovascular changes. As well as HR increasing, due to the decreased vagal activity of the heart, the increased sympathetic noradrenergic outflow causes increased cardiac contractility, changes in the diameter of resistance and capacitance vessels within peripheral tissue beds (e.g. splanchnic region, kidneys, skin, skeletal muscle) and a release of adrenaline from the medulla of the adrenal gland (Shepherd et al., 1981; Fadel, Smith and Gallagher, 2004; Smith, Mitchell and Garry, 2006). All of these changes result in adjustments of HR, SV and systemic vascular resistance, which in turn mediate appropriate alterations in MAP for the intensity and modality of the exercise (Fadel, Smith and Gallagher, 2004; Smith, Mitchell and Garry, 2006). These changes occur to increase the perfusion pressure to the contracting muscle in an attempt to overcome the mechanical hindrance to flow from the statically contracting muscle (Shepherd et al., 1981).

The information presented in this section provides an explanation of the acute responses produced during isometric exercise, which is prerequisite to designing an isometric training protocol aimed at lowering BP

and understanding the potential mechanisms that mediate chronic BP adaptations. It is feasible to suggest that the neural mechanisms that control the acute physiological responses may also play an integral role in determining the chronic BP adaptations that occur following repeated bouts of isometric training.

#### **1.4 The chronic adaptations following isometric exercise training**

Several studies have investigated the chronic adaptations following IET with particular reference to resting BP. The majority of this research has found that partaking in IET results in a reduction in resting BP (Millar et al., 2013b). Some of this research has also attempted to elucidate the potential mechanisms that govern such chronic BP adaptations, however the underlying regulatory pathways are not well understood and remain elusive due to the very limited evidence available (Millar et al., 2009b). This section will explore this existing research in an attempt to understand how isometric training produces reductions in resting BP, which will help inform the design of the home-based IET protocol to be used within this thesis and help to contextualise the findings of an intervention study.

##### ***1.4.1 Reductions in resting blood pressure following isometric exercise training***

As previously mentioned in section 1.2 (page 4), two landmark studies initially demonstrated that regular isometric exercise has the potential to lower resting BP (Kiveloff and Huber, 1971; Buck and Donner, 1985). Since these two seminal studies, there has been an increasing body of research that has investigated the effects of specific IET protocols on resting BP and a total of 16 studies have investigated the effects in normotensive, high-normal and hypertensive populations. The results of these studies are presented in Table 1.1 (pages 12-13). It can be seen that the majority of published results repeatedly demonstrate that a chronic adaptation to IET is a reduction in resting BP (Wiley et al., 1992; Ray and Carrasco, 2000; Howden et al., 2002; Taylor et al., 2003; Peters et al., 2006; McGowan et al., 2007a; 2007b; Millar et al., 2008; Devereux, Wiles and Swaine, 2010b; Wiles, Coleman and Swaine, 2010; Baross, Wiles and Swaine, 2012; Badrov et al., 2013a; 2013b; Millar et al., 2013a).

**Table 1.1.** Isometric exercise training protocols utilised for the reduction of resting blood pressure.

Author	Participants that completed training	Mode	Intensity	Duration	Frequency/Length	SBP change (mmHg)	DBP change (mmHg)	MAP change (mmHg)
Badrov et al. (2013a)	12 normotensive females	Unilateral handgrip (non-dominant hand)	30% MVC	Bouts: 4 x 2 min Rest: 4 min	3 times per week for 8 weeks	-6	not significant	not significant
	11 normotensive females	Unilateral handgrip (non-dominant hand)	30% MVC	Bouts: 4 x 2 min Rest: 4 min	5 times per week for 8 weeks	-6	not significant	not significant
Badrov et al. (2013b)	12 medicated hypertensive males (6) & females (6)	Bilateral handgrip	30% MVC	Bouts: 4 x 2 min Rest: 1 min	3 times per week for 10 weeks	-8	-5	-6
Baross, Wiles and Swaine (2012)	10 unmedicated high-normal males	Double-leg extension	70% HR <sub>peak</sub> (~8% MVC)	Bouts: 4 x 2 min Rest: 2 min	3 times per week for 8 weeks	not significant	not significant	not significant
	10 unmedicated high-normal males	Double-leg extension	85% HR <sub>peak</sub> (~14% MVC)	Bouts: 4 x 2 min Rest: 2 min	3 times per week for 8 weeks	-11	not significant	-5
Devereux, Wiles and Swaine (2010b)	13 normotensive males	Double-leg extension	95% HR <sub>peak</sub> (~24% MVC)	Bouts: 4 x 2 min Rest: 3 min	3 times per week for 4 weeks	-5	-3	-3
Howden et al. (2002)	8 normotensive males (6) & females (2)	Double-arm flexion	30% MVC	Bouts: 4 x 2 min Rest: 3 min	3 times per week for 5 weeks	-12	not significant	not reported
	9 normotensive males (7) & females (2)	Double-leg extension	20% MVC	Bouts: 4 x 2 min Rest: 3 min	3 times per week for 5 weeks	-10	not significant	not reported
McGowan et al. (2006)	17 medicated hypertensives	Unilateral handgrip (non-dominant hand)	30% MVC	Bouts: 4 x 2 min Rest: 4 min	3 times per week for 8 weeks	not reported	not reported	not significant
McGowan et al. (2007a)	11 normotensive males (8) & females (3)	Unilateral handgrip (non-dominant hand)	30% MVC	Bouts: 4 x 2 min Rest: 4 min	3 times per week for 8 weeks	-5	not significant	not reported
McGowan et al. (2007b)	9 medicated hypertensive males (7) & females (2)	Unilateral handgrip (non-dominant hand)	30% MVC	Bouts: 4 x 2 min Rest: 4 min	3 times per week for 8 weeks	-9	not significant	not reported
	7 medicated high-normal males (5) & females (2)	Bilateral handgrip	30% MVC	Bouts: 4 x 2 min Rest: 1 min	3 times per week for 8 weeks	-15	not significant	not reported
Millar et al. (2008)	25 normotensive males (14) & females (11)	Bilateral handgrip	30-40% MVC	Bouts: 4 x 2 min Rest: 1 min	3 times per week for 8 weeks	-10	-3	not reported
Millar et al. (2013a)	13 medicated hypertensive males (11) & females (2)	Unilateral handgrip (non-dominant hand)	30% MVC	Bouts: 4 x 2 min Rest: 4 min	3 times per week for 8 weeks	-5	not significant	-3

**Table 1.1.** continued. Isometric exercise training protocols utilised for the reduction of resting blood pressure.

Author	Participants that completed training	Mode	Intensity	Duration	Frequency/ Length	SBP change (mmHg)	DBP change (mmHg)	MAP change (mmHg)
Peters et al. (2006)	10 unmedicated hypertensive males (8) & females (2)	Bilateral handgrip	50% MVC	Bouts: 4 x 45 sec Rest: 1 min	3 times per week for 6 weeks	-13	not significant	not reported
Ray and Carrasco (2000)	9 normotensive males & females	Unilateral handgrip (dominant arm)	30% MVC	Bouts: 4 x 3 min Rest: 5 min	4 times per week for 5 weeks	not significant	-5	-4
Stiller-Moldovan, Kenno and McGowan (2012)	11 medicated hypertensive males (7) & females (4)	Bilateral handgrip	30% MVC	Bouts: 4 x 2 min Rest: 1 min	3 times per week for 8 weeks	not significant	not significant	not significant
Taylor et al. (2003)	9 medicated hypertensive males (5) & females (4)	Bilateral handgrip	30% MVC	Bouts: 4 x 2 min Rest: 1 min	3 times per week for 10 weeks	-19	not significant	-11
Wiles, Coleman and Swaine (2010)	11 normotensive males	Double-leg extension	75% HR <sub>peak</sub> (~10% MVC)	Bouts: 4 x 2 min Rest: 2 min	3 times per week for 8 weeks	-4	-3	-3
	11 normotensive males	Double-leg extension	95% HR <sub>peak</sub> (~21% MVC)	Bouts: 4 x 2 min Rest: 2 min	3 times per week for 8 weeks	-5	-3	-3
Wiley et al. (1992)	8 high-normal	Unilateral handgrip (dominant arm)	30% MVC	Bouts: 4 x 2 min Rest: 3 min	3 times per week for 8 weeks	-13	-15	not reported
	10 high-normal	Bilateral handgrip	50% MVC	Bouts: 4 x 45 sec Rest: 1 min	5 times per week for 5 weeks	-10	-9	not reported

Statistically significant reductions in resting SBP have been commonly found in the majority of IET studies ranging from -4 to -19 mmHg, except for three studies (Ray and Carrasco, 2000; Baross, Wiles and Swaine, 2012; Stiller-Moldovan, Kenno and McGowan, 2012) in which no SBP reductions were detected. Reductions in resting DBP have been less frequently detected with several studies finding no significant reduction in DBP (Howden et al., 2002; Taylor et al., 2003; Peters et al., 2006; McGowan et al., 2007a; 2007b; Baross, Wiles and Swaine, 2012; Stiller-Moldovan, Kenno and McGowan, 2012; Badrov et al., 2013a; Millar et al., 2013a). Failure to detect significant DBP differences may be due to the fact that DBP has a smaller range compared to SBP (Peters et al., 2006). Furthermore, changes in DBP may be more difficult to detect due to the relatively small participant numbers studied ( $\leq 17$ ) (Howden et al., 2002; Taylor et al., 2003; Peters et al., 2006; McGowan et al., 2007a; 2007b; Baross, Wiles and Swaine, 2012; Stiller-Moldovan, Kenno and McGowan, 2012; Badrov et al., 2013a; Millar et al., 2013a), which consequently provides a low statistical power (Kelley and Kelley, 2010). For small changes in BP to be identified, alterations must occur in nearly all participants and the variability of the measure must stay low (Peters et al., 2006). In those studies that have reported reductions in resting DBP, the changes have ranged between -3 and -15 mmHg.

While the magnitude of resting BP reductions found within the IET literature have been varied, two recent review articles have highlighted that even small reductions in resting BP are clinically relevant (Millar et al., 2013b) and could lead to significant reductions in morbidity and mortality related to hypertension (Lawrence et al., 2014). Indeed, a reduction in resting SBP or DBP as small as 2 mmHg is suggested to have a clinically significant benefit, such as reduced risk of coronary heart disease, stroke and mortality (Cook et al., 1995; Neaton et al., 1995 cited in Stamler, 1997). To this end Millar et al. (2013b) reviewed the response rates from both published and unpublished studies and estimated that such a beneficial reduction is attained in 60% to 90% of normotensive and unmedicated hypertensive individuals (Peters et al., 2006; McGowan et al., 2007a; Millar et al., 2008) and 50% to 83% of medicated hypertensive participants (McGowan et al., 2006; McGowan et al., 2007b; Millar et al., 2007; Stiller-Moldovan, Kenno and McGowan, 2012; Badrov et al., 2013b). Millar et al. (2013b) stated that the majority of IET studies have failed to report this statistic, which is surprising as the ultimate goal of any antihypertensive therapy is to lower cardiovascular related morbidity and mortality (Chobanian et al., 2003).

A further point of interest is the fact that MAP has not been reported for a large number of studies, which is surprising as MAP represents the average pressure in the arteries during a cardiac cycle (Darovic, 2002). Significant reductions in MAP that were reported lie between -3 and -11 mmHg. Further to this, of all the research presented, only three studies found significant reductions in all 3 BP parameters (SBP, DBP and MAP) (Devereux, Wiles and Swaine, 2010b; Wiles, Coleman and Swaine, 2010; Badrov et al., 2013b). Finally, it is also worth noting that contrary to the majority of IET research, some IET interventions have found no significant differences in any BP parameters (Baross, Wiles and Swaine, 2012; Stiller-Moldovan, Kenno and McGowan, 2012). Also McGowan et al. (2006) found no change in MAP following IET, but did not report SBP or DBP.

From the data presented, it can be seen that the magnitude of the resting BP reductions is quite varied between studies and it is suggested that this is due to differences in the IET prescription adopted; this will

be discussed in section 1.5 (page 20). Regardless of this it is suggested that future research should look to address the concerns regarding small sample sizes (Millar et al., 2013b) and also include a measure of average pressure in a cardiac cycle, MAP. Finally, it is of the utmost importance that future IET studies include the clinical relevance of reported BP reductions, as this is ultimately the goal of any antihypertensive therapy.

#### ***1.4.2 The physiological mechanisms that govern adaptations to resting blood pressure following isometric exercise training***

Mean arterial pressure is primarily determined by  $\dot{Q}$  and TPR (Hietanen, 1984), as previously discussed in section 1.3.1 (page 6), and therefore reductions in BP following IET must consequently be due to adjustments in either one or both of these variables (Wiley et al., 1992; Pescatello et al., 2004; Millar et al., 2013b). It is probable that a reduction in TPR would be the primary mechanism by which resting BP is lowered as  $\dot{Q}$  does not typically decrease following exercise training (Pescatello et al., 2004); despite this fact a change in  $\dot{Q}$  cannot be overlooked (Wiley et al., 1992). As  $\dot{Q}$  and/or TPR are likely to play such a prominent role in the regulation of chronic BP reductions, it is surprising to find that only two studies have currently measured these two variables pre- and post-IET (Devereux, Wiles and Swaine, 2010b; Wiles, Coleman and Swaine, 2010). Devereux, Wiles and Swaine (2010b) found significant reductions in SBP, DBP and MAP after 4 weeks double-leg extension training at 95%  $HR_{peak}$ , yet these BP reductions occurred in the absence of any statistically significant changes in  $\dot{Q}$  ( $-0.2 \text{ L}\cdot\text{min}^{-1}$ ) or TPR ( $-0.3 \text{ mmHg}\cdot\text{mL}^{-1}\cdot\text{min}^{-1}$ ). Furthermore, Wiles, Coleman and Swaine (2010) also found significant reductions in all resting BP parameters following 8 weeks of isometric double-leg extension training at 95%  $HR_{peak}$ , but again found no statistically significant changes in  $\dot{Q}$  ( $0.2 \text{ L}\cdot\text{min}^{-1}$ ) or TPR ( $-0.7 \text{ mmHg}\cdot\text{mL}^{-1}\cdot\text{min}^{-1}$ ). The lack of significant findings for  $\dot{Q}$  or TPR could be due to the relatively small participant numbers studied and therefore it would be beneficial to analyse these variables utilising a larger sample size.

To date the underlying mechanisms that modulate a reduction in resting BP following IET are not well understood and remain elusive due to the limited evidence available (Millar et al., 2009b) and the conflicting results that have been found. Several different regulatory pathways have been explored, which include endothelial function (McGowan et al., 2007a; 2007b; Badrov et al., 2013a), oxidative stress (Peters et al., 2006), autonomic function (Ray and Carrasco, 2000; Taylor et al., 2003; Wiles, Coleman and Swaine, 2010; Stiller-Moldovan, Kenno and McGowan, 2012; Badrov et al., 2013a; Millar et al., 2013a) and structural vasculature adaptations (Baross, Wiles and Swaine, 2012). These mechanisms would likely modulate a change in  $\dot{Q}$  and/or TPR to produce a reduction in BP, although a direct causal link has not often been made. The preceding sections will provide a brief overview of the current mechanistic research that may suggest an adaptation to TPR or  $\dot{Q}$  will occur following IET; this will be discussed in sections 1.4.2a (page 15) and 1.4.2b (page 18), respectively. This knowledge will provide a valuable insight into the regulatory pathways that may potentially mediate an alteration to either TPR and/or  $\dot{Q}$  and ultimately produce a reduction in resting BP. This information will also help inform the design of the home-based IET protocol to be used within this thesis.



#### *1.4.2a Mechanisms that may alter total peripheral resistance following isometric training to reduce resting blood pressure*

Total peripheral resistance is dependent on the viscosity of the blood, vessel length, and lumen size (Tortora and Derrickson, 2012). However of these three factors, reductions in TPR are mainly attributable to changes in vessel diameter following training (Pescatello et al., 2004). There are a range of mediating influences that may lead to alterations in TPR, such as neurohumoral (improved endothelial function and decreased sympathetic nervous activity) and structural adaptations (vascular remodelling) (Pescatello et al., 2004).

An important training adaptation that reduces TPR, and consequently BP, is an improvement in endothelial-dependent vasodilation (Pescatello et al., 2004). Hypertension is associated with endothelial dysfunction (Bian, Doursout and Murad, 2008), which is accompanied by greater vascular tone and less vasodilator function (Pescatello et al., 2004). McGowan et al. (2007b) found that after hypertensive participants completed 8 weeks of IHG training resting SBP reduced and this was associated with localised improvements in nitric oxide dependent vasodilation. The physiological stimulus that produces such adaptations from isometric training is believed to be shear stress (Tinken et al., 2010), which occurs through the pressor response experienced in this form of exercise (Ray and Carrasco, 2000). Further to this McGowan et al. (2006a) proposed that impairment in endothelium-dependent vasodilation may also be related to increases in oxidative stress. Indeed, Peters et al. (2006) found that SBP significantly lowered following 6 weeks of IHG training with hypertensive participants and this was regulated by favourable changes in markers of oxidative stress.

While improvements in endothelial function may bring about a reduction in TPR, and consequently BP, when studying hypertensive participants, this may not be the case for all populations. When normotensive participants completed 8 weeks of unilateral IHG training, resting SBP reduced but there was no improvement in endothelial function (McGowan et al., 2007a), which suggests that this may not be the mediating factor in this population, and thus TPR may not alter. Green et al. (2004) proposed that exercise training in healthy participants may not induce improvements as the endothelial function is normal already, whereas benefits may be more probable in those with antecedent endothelial dysfunction, such as those with hypertension. Further to this Green et al. (2004) also suggests that exercise involving larger muscle groups, such as the legs, may be more likely to produce systemic changes in endothelial function through greater levels of shear stress, which presumably occurs as a greater pressor response is experienced (Mitchell et al., 1980; Seals et al., 1983; Lewis et al., 1985; Iellamo et al., 1999; Franke, Boettger and McLean, 2000; Gálvez et al., 2000); this will be discussed further in section 1.5.2 (page 25).

The aforementioned studies by McGowan and colleagues examined the effects of IET on the larger conduit artery endothelial function (McGowan et al., 2007a; 2007b). Additionally, hypertension is also associated with the narrowing of the smaller resistance vessels (Oparil, Zaman and Calhoun, 2003). A recent study by Badrov et al. (2013a) found that 8 weeks of IHG lowered resting SBP in a normotensive population alongside improvements in the resistance vessel vasculature. However, a caveat to this finding was that a significant reduction in SBP was recorded after 4 weeks but resistance vessel endothelial function remained unchanged. Thus while, improved resistance vessel endothelial function may provide

an alternative mechanism to explain the reductions in resting BP in a normotensive population, it would appear that this is not a key mechanism (Badrov et al., 2013a).

Hypertension is also associated with an autonomic imbalance (Brook and Julius, 2000), which is predominately characterised by less cardiac parasympathetic inhibition (Julius, 1991) and/or excessive increases in sympathetic outflow to the heart and peripheral circulation (Grassi, Bertoli and Seravalle, 2012). Increased sympathetic nerve activity, along with a subsequent noradrenaline increase, causes vasoconstriction consequently increasing TPR (Pescatello et al., 2004) and presumably BP. While this may be the case, few IET studies have actually explored the neural modulation of vascular tone in an attempt to explain the possible BP reduction mechanisms (Millar et al., 2013b). Taylor et al. (2003) found that following 10 weeks of IHG there was a significant reduction in both resting SBP and MAP in hypertensive participants, as well as a change in ANS activity that modulates BP, such that sympathetic activity decreased and parasympathetic modulation increased. It was particularly pertinent that the low frequency component of SBP variability reduced, as this is thought to indicate alterations in the efferent sympathetic regulation of the peripheral vasculature (Pagani et al., 1997). Such an alteration in the peripheral sympathetic vasoconstrictor activity may serve to reduce resting BP (Millar et al., 2013b), presumably through a reduction in TPR. Conversely, Ray and Carrasco (2000) found that DBP and MAP reduced in a normotensive population following 5 weeks of IHG without changes in MSNA. This suggested that a reduction in efferent sympathetic outflow to the skeletal muscle is not a prerequisite to lowering BP in this population (Ray and Carrasco, 2000). However, compared to a hypertensive population, the normotensive individuals studied did not have an elevated resting MSNA level initially (Millar et al., 2013b), which likely limited the capacity for this variable to be altered with training.

Finally, it has also been proposed that structural adaptations occur after IET, such as increased lumen diameter (Millar et al., 2007). Baross, Wiles and Swaine (2012) found that participants with high-normal BP levels initially attained significant reductions in SBP and MAP following 8 weeks of high intensity isometric double-leg extension training. This BP reduction was accompanied by localised vascular adaptations comprising of increased resting femoral artery diameter, blood flow, blood velocity, and vascular conductance (Baross, Wiles and Swaine, 2012). Such vascular remodelling is likely to lower TPR and consequently lead to alterations in BP; however this has not been studied with normotensive participants and remains to be elucidated.

The above evidence suggests that IET will lower TPR to mediate the reduction in BP with participants that have high-normal BP (Baross, Wiles and Swaine, 2012) or are hypertensive (Taylor et al., 2003; Peters et al., 2006; McGowan et al., 2007b). The same BP reduction mechanisms have not been evident when a normotensive population has been studied despite resting BP still being lowered (Ray and Carrasco, 2000; McGowan et al., 2007a). Green et al. (2004) suggest that healthy individuals may have a differential mechanistic response due to the fact that a normal vascular function is already evident. For these individuals, a higher training volume may be necessary to bring about the same beneficial effects, which may involve prescribing exercises that utilise a larger muscle mass to induce greater levels of systemic shear stress (Green et al., 2004).

#### *1.4.2b Mechanisms that may alter cardiac output following isometric training*

The majority of IET studies have mainly focussed on mechanisms that would mediate a reduction in TPR to lower resting BP. However, as discussed, these potential mediating factors were not always present despite reductions in BP still being found, which suggests that alternative mechanisms may be present and indeed Wiley et al. (1992) advises that a change in  $\dot{Q}$  cannot be overlooked. As  $\dot{Q}$  is the result of HR multiplied by SV (Smith and Fernhall, 2011), a change in one or both of these variables would mediate an alteration in  $\dot{Q}$ . Only two studies estimated SV pre- and post-IET, but no changes were found alongside a reduction in BP (Devereux, Wiles and Swaine, 2010b; Wiles, Coleman and Swaine, 2010). Indeed, SV does not typically alter following strength training (Fleck, 2003) and thus the main variable likely to alter  $\dot{Q}$  is HR, which has been found to reduce following strength training (Fleck, 2003) and isometric double-leg extension training (Devereux, Wiles and Swaine, 2010b; Baross, Wiles and Swaine, 2012). Such a change in HR would be typically mediated by alterations of both autonomic branches, which would present as an increase in parasympathetic activity and a decrease in the sympathetic activity (Fleck, 2003), however autonomic function was not recorded by Devereux, Wiles and Swaine (2010b) or Baross, Wiles and Swaine (2012).

Taylor et al. (2003) found that following 10 weeks of IHG there was a significant reduction in both resting SBP and MAP in medicated hypertensive participants alongside changes in ANS activity, as measured by traditional spectral heart rate variability (HRV) analysis. Specifically, an increase was found in the high frequency component of HRV, which is suggested to be a marker of efferent vagal modulation (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996), however no significant change in HR was found following IHG training. Similarly Millar et al. (2013a) recorded reductions in SBP and MAP following 8 weeks IHG training in medicated hypertensive participants and this was combined with alterations in nonlinear HRV measures, which reflected improvements in sympathovagal interactions, but no change in HR was found. These two studies suggest that cardiac neural adaptations occur in hypertensive individuals following IET that may modulate the reduction in resting BP. However, Stiller-Moldovan, Kenno and McGowan (2012) also studied medicated hypertensive participants and found no such improvements in HRV following IHG training, as well as no significant changes in resting BP or HR. It was postulated that maximum autonomic improvements may have already been experienced due to the fact that the majority of the participants were taking ACE inhibitor or  $\beta$ -blockers (Stiller-Moldovan, Kenno and McGowan, 2012), which are known to improve autonomic function (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996). Further to this, no change in autonomic regulation or HR has been associated with reductions in BP when normotensive participants have completed both IHG training (Badrov et al., 2013a) and double-leg extension training (Wiles, Coleman and Swaine, 2010).

From the research presented it would appear that it is unlikely that IET results in any significant improvements in HR and autonomic function in both well-controlled medicated hypertensive and normotensive participants (Badrov et al., 2013a), which suggests that other mechanisms may be responsible for resting BP adaptations. However, it should be acknowledged that changes to HR and autonomic function may not have been found in these studies due to several issues. First of all, while

HRV has been widely accepted as a tool to quantify cardiac autonomic regulation in both health and disease (Billman, 2011; Billman, 2013), several different methodologies have been developed (Lombardi and Stein, 2011). As a result of this previous IET research has utilised a range of techniques to study HRV, such as time-domain, frequency-domain and non-linear analysis (Taylor et al., 2003; Wiles, Coleman and Swaine, 2010; Stiller-Moldovan, Kenno and McGowan, 2012; Badrov et al., 2013a; Millar et al., 2013a), which could have led to the ambiguous results reported. For example, the traditional spectral measures of HRV, as used by Wiles, Coleman and Swaine (2010), may not be sensitive enough to detect small changes in neurocardiac modulation when only modest reductions in resting BP are produced (Millar et al., 2013a) and therefore it may have been more appropriate to use an alternative HRV technique. Secondly, agreement regarding the precise autonomic underpinnings for many HRV parameters has not been reached (Lombardi and Stein, 2011). Indeed, the concept that certain frequency components of spectral analysis reflect particular divisions of the ANS (high frequency: parasympathetic; low frequency: sympathetic) is controversial and remains the subject of debate (Billman et al., 2015). Indeed, accumulating evidence suggests that this concept over simplifies the complex interactions between the divisions of the ANS and as such the high/low frequency data cannot not accurately reflect sympatho-vagal balance (Billman, 2013). Furthermore, previous IET studies have overlooked some components of HRV, such as the very low frequency range. This is likely due to the fact that the physiological interpretation of this variable still remains largely unknown (Xhyheri et al., 2012) despite limited findings that suggest this may be linked with sympathetic nervous system activity (ChuDuc, NguyenPhan and NguyenViet, 2013). Finally, previous IET studies investigating medicated hypertensive and normotensive participants have utilised relatively small sample sizes ( $\leq 17$ ), which could also explain the lack of significant changes in HR and autonomic function. As such, it has been emphasised that there is a substantial need for methodological improvements in HRV measurement (Heathers, 2014) and until such developments are made the value of this measure is questionable. Therefore due to the ambiguous results reported and the methodological limitations outlined, HRV was not measured in studies of this thesis.

In summary, several mechanisms have been proposed in an attempt to explain how BP reduces with IET but this research is ambivalent. The exact physiological mechanisms that modulate an alteration in TPR and/or  $\dot{Q}$  to produce an adaptation to resting BP are still unknown and it appears that the mechanistic pathways are multi-factorial. Studies that have investigated  $\dot{Q}$ , TPR, SV and HR utilised a relatively small sample size, which is a limiting factor that should be considered in future work (Millar et al., 2013b). Of the research discussed, the primary mediating variable for hypertensive individuals appears to be TPR; however this may not be the case for a normotensive population as the same mechanistic adaptations have not been found. An adjustment to  $\dot{Q}$  is a viable method by which BP could be reduced and such an adaptation cannot be disregarded. Finally, when designing IET it appears that it may be more beneficial to utilise exercise of a larger muscle mass as this may induce systemic changes to endothelial function, which may reduce resting BP to a greater extent. Therefore, with these points considered, it would be useful to study  $\dot{Q}$ , TPR, SV and HR pre- and post-IET whilst utilising a larger sample size and exercise mode of a greater muscle mass in order to reduce BP and tease out the primary BP reduction mechanisms.

## **1.5 The physiological effect of programme variables upon the acute and chronic cardiovascular response to isometric exercise training**

As outlined in the previous section 1.4.1 (page 11), IET has been shown to successfully reduce resting BP, however differences in the magnitude of these reductions has been reported as well as variation in the mechanisms responsible for such reductions. This is likely due to the fact that a wide variety of training prescriptions have been adopted differing in terms of isometric contraction style, exercise mode, training impulse (intensity, duration and frequency) and intervention length (see Table 1.1, pages 12-13). There are currently no established IET guidelines (Millar, Swaine and McGowan, 2012) and previous protocols appear to be selected based on past success (Ray and Carrasco, 2000). Due to this fact, the optimal prescription for home-based IET remains unclear.

An understating of these programme variables is prudent as it is the manipulation of these factors that will ultimately determine the isometric training stimulus and consequent BP adaptations produced. Evidence suggests that the acute pattern of cardiovascular response may be affected by the isometric contraction style performed (e.g. constant force, constant EMG (electromyography) or constant position) (see section 1.5.1, page 20). Further to this, several programme variables are thought to affect the magnitude of the acute response, such as exercise mode (muscle mass) (see section 1.5.2, page 25), intensity (see section 1.5.3, page 28) and duration (see section 1.5.4, page 30). Finally, reductions in BP may also be a function of training frequency and intervention length, which will ultimately affect the amount of time that an individual is exposed to the training stimulus (Badrov et al., 2013a); see sections 1.5.5 (page 31) and 1.5.6 (page 32) respectively. Further to this a wide variety of participants have been studied differing in terms of initial BP classification and age, which may also have affected the BP results produced; these will be discussed in sections 1.5.7a (page 33) and 1.5.7b (page 35) respectively.

The proceeding sections will therefore look to review each of these programme variables. Where relevant, the current literature will be examined in relation either the acute responses to a single bout of isometric exercise and/or the chronic adaptations produced from repeated exposure to the IET stimulus. From this critical evaluation, the most effective IET protocol can be identified and subsequently utilised within the home-based programme of this thesis.

### ***1.5.1 Styles of isometric contraction previously utilised within isometric exercise training protocols***

There are various different styles of isometric contraction that can be completed (Lind, 2011), however this aspect has not received a great deal of attention within the IET literature. Traditionally, isometric contractions are performed at a percentage of an individual's maximal voluntary contraction (MVC) (Lind, 2011). Indeed, this is the isometric contraction style most commonly utilised in IET protocols designed for the reduction of resting BP (Wiley et al., 1992; Ray and Carrasco, 2000; Howden et al., 2002; Taylor et al., 2003; McGowan et al., 2006; Peters et al., 2006; McGowan et al., 2007a; 2007b; Millar et al., 2008; Stiller-Moldovan, Kenno and McGowan, 2012; Badrov et al., 2013a; 2013b; Millar et al., 2013a). Prior to training, a MVC is completed to determine a participant's maximal instantaneous force. Isometric exercise training is then completed at a specific percentage of this MVC (%MVC) for a fixed period of time (Lind, 2011). This style of isometric contraction has previously been termed a constant force task as the participant is required to maintain a target force (Hunter et al., 2002).

While the vast majority of IET research has prescribed constant force isometric contractions, a few more recent studies utilised an alternative style in which training was completed at a participant-specific EMG activity value that equated to a percentage of their peak HR ( $HR_{peak}$ ) (Devereux, Wiles and Swaine, 2010b; Wiles, Coleman and Swaine, 2010; Baross, Wiles and Swaine, 2012). In these studies participants were required to perform an initial MVC assessment from which the corresponding peak EMG activity ( $EMG_{peak}$ ) was calculated. Subsequently an incremental isometric test was completed, which was comprised of five work stages of gradually increasing intensity (10, 15, 20, 25, and 30%  $EMG_{peak}$ ) (Wiles et al., 2008b). Due to the linear relationship established between EMG activity and HR, it was possible to interpolate the EMG value required to elicit a specific HR target during training. Completing isometric exercise in this manner has previously been termed a constant EMG task as an individual is required to sustain a predetermined EMG activity value (Franke, Boettger and McLean, 2000).

While both styles of isometric contraction have been used to successfully lower resting BP when included within an IET protocol, these two methods produce a distinct pattern of acute cardiovascular response (Schibye et al., 1981; Franke, Boettger and McLean, 2000) (see section 1.5.1a, page 21). Such differences could have important implications on the training stimulus produced, which may alter the efficacy of the IET protocol. Further to this, it should be pointed out that another style of isometric contraction exists in which a given joint angle is held while supporting an inertial load; this has been described as a constant position task (Hunter et al., 2002). Although this isometric contraction style has not previously been utilised within an IET programme aimed at reducing resting BP, this method provides an alternative means by which isometric exercise could be prescribed. Therefore it is also important to consider the acute cardiovascular response to a constant position isometric contraction, which has again been shown to produce a different pattern compared to constant force tasks (Hunter et al., 2002; 2008; Rudroff et al., 2011) (see section 1.5.1b, page 22).

### *1.5.1a The acute cardiovascular responses to isometric exercise performed at constant force vs. constant EMG*

The acute cardiovascular responses to a constant force (%MVC) isometric contraction are well documented within the literature. The majority of research reports that HR and BP develop a steady-state after a few minutes when performed at non-fatiguing intensities (<15% MVC) (Lind and McNicol, 1967; Mitchell and Wildenthal, 1974), however both HR and BP continuously increase during fatiguing contractions (> 15% MVC) (Lind et al., 1964; Seals et al., 1983; Friedman, Peel and Mitchell, 1992; Seals, 1993; Smolander et al., 1998; Franke, Boettger and McLean, 2000). As EMG activity has been found to simultaneously increase with HR and BP during constant force work, it has been proposed that the increase in cardiovascular response is likely due to an increase in central command (Schibye et al., 1981). Additional motor unit recruitment is required in order to maintain the desired force output as the muscle begins to fatigue (St Clair Gibson, Lambert and Noakes, 2001). Such an increase in the activity of the motor cortex would concomitantly stimulate the cardiovascular control centre in a parallel fashion (Franke, Boettger and McLean, 2000) causing a rise in HR and BP due to increased central command.

A few studies have also looked to explore the cardiovascular responses to constant EMG isometric contractions and compare these acute responses to those achieved during constant force tasks. In a study by Schibye et al. (1981) participants were required to perform static single-leg extension exercise for 5

minutes using two different isometric contraction styles. First of all, participants held the isometric contraction at a constant force of 20% MVC. Then for the second contraction, participants held the contraction at a constant EMG value, which corresponded to the EMG value obtained during first 5 seconds of the constant force contraction. There was a significant increase in HR and BP for both experimental conditions; however the percentage increases were approximately 50% lower during constant EMG contractions. This finding was supported by the later work of Franke, Boettger and McLean (2000) in which isometric leg contractions held at a constant EMG again attenuated the upward drift in the cardiovascular responses. During constant EMG contractions no additional motor units can be recruited as EMG activity is maintained at the same value, which causes the force output to decline with fatigue (Schibye et al., 1981). As EMG activity is thought to reflect central command (Mitchell et al., 1981; Schibye et al., 1981), it is reasonable to assume that a more consistent level of central drive would be maintained throughout the constant EMG isometric contraction, which would likely cause the cardiovascular response to be attenuated. Any increases in HR and BP are therefore likely to be attributable to other control mechanisms such as the exercise pressor reflex through stimulation of the metaboreceptors (Schibye et al., 1981). Furthermore, the increase in HR and BP may be greater during a constant force task as the tension (%MVC) is consistently higher (Schibye et al., 1981), which may reduce blood flow to a greater extent (Lind and McNicol, 1967) and therefore increase the accumulation of metabolites (Rowell and O'Leary, 1990) consequently activating the metaboreceptors (Mostoufi-Moab et al., 1998) to produce an increase in the cardiovascular response.

From the research presented it is suggested that performing isometric exercise at a constant EMG attenuates the upward drift and elicits a much steadier cardiovascular response compared to constant force isometric exercise (Schibye et al., 1981; Franke, Boettger and McLean, 2000). Due to this fact Wiles et al. (2008b) proposed that prescribing isometric exercise at a constant EMG allows a more accurate IET prescription and accompanying cardiovascular stress compared to constant force work, which is necessary to ensure participants exercise at appropriate and safe levels during training (Wiles et al., 2005). Wiles and colleagues went on to successfully reduce resting BP through the implementation of an IET protocol that utilised constant EMG contractions (Devereux, Wiles and Swaine, 2010b; Wiles, Coleman and Swaine, 2010; Baross, Wiles and Swaine, 2012). It remains to be established whether a constant force or constant EMG IET protocol is more effective for producing chronic BP reductions as a study directly comparing the two methods has not been completed to date.

#### *1.5.1b The acute cardiovascular responses to isometric exercise performed at constant force vs. constant position*

Constant position isometric contractions have not previously been utilised within an IET protocol designed to produce chronic BP adaptations, however this contraction style provides an alternative method that could potentially be used to prescribe isometric exercise. Several studies have explored and compared the acute responses to constant force and constant position isometric contractions, which provide a valuable insight into the likely training stimulus that could be produced.

It has previously been reported that participants find constant position contractions more difficult to perform than at a constant force, which is reflected in the contraction duration when both are sustained to fatigue (Enoka et al., 2011). In a seminal study by Hunter et al. (2002), participants completed both a

force task, which required an elbow flexor contraction to be maintained at a constant force of 15% MVC, and a position task in which the elbow joint was maintained at a constant position (90°) while supporting a load equivalent to 15% MVC; both tasks were held indefinitely until fatigue. The duration of the force task (1402 ± 728 seconds) was double the time of the position task (702 ± 582 seconds). Indeed, the time to task failure is typically longer for a constant force task for low intensity contractions (≤ 30% MVC) (Hunter et al., 2002; Maluf et al., 2005b; Rudroff et al., 2005; 2007; Hunter et al., 2008). In general it has also been reported that the cardiovascular response increases over time during both constant force and constant position tasks, as well as producing an increase in EMG activity (Hunter et al., 2002; Rudroff et al., 2005; 2007; Hunter et al., 2008). As previously outlined in section 1.5.1a (page 21), this is presumably to maintain the desired force output as the muscle begins to fatigue (St Clair Gibson, Lambert and Noakes, 2001), which would concomitantly activate the cardiovascular control centre in a parallel fashion causing the rise in HR and BP (Franke, Boettger and McLean, 2000). However, the position task has been accompanied by a more rapid increase in the cardiovascular response (HR and/or MAP) (Hunter et al., 2002; 2008; Rudroff et al., 2011), which is likely due to the faster increase in EMG activity that has also been reported (Maluf et al., 2005b; Hunter et al., 2008; Rudroff et al., 2011). This suggests an earlier, more rapid motor unit recruitment occurs during constant position tasks (Maluf et al., 2005b; Hunter et al., 2008; Rudroff et al., 2011) that would presumably also concurrently activate the cardiovascular control centre faster (Franke, Boettger and McLean, 2000). It has been postulated that the differences in motor unit behaviour between these two tasks is possibly attributable to increased sensitivity of the stretch reflex during low intensity constant position contractions (Maluf and Enoka, 2005a).

The constant force and constant position tasks require varying levels of compliance and stability (Maluf and Enoka, 2005a). When performing an isometric contraction at a constant force the load is of low compliance as the participant pushes against a rigid restraint and thus alterations in the limb position are limited (Enoka et al., 2011). Whereas a constant position contraction involves a more compliant, unstable load (Maluf and Enoka, 2005a; Enoka et al., 2011), which can result in small limb movements (Enoka et al., 2011). It is suggested that in order to manage the different mechanical properties of the tasks, the motor system may compensate (Barry and Enoka, 2007). Indeed, contractions with compliant loads have resulted in an augmented stretch reflex (Akazawa, Milner and Stein, 1983; Perreault et al., 2008) and it is suggested that this serves to assist in the accurate control of the limb position during the unstable condition and is likely to be responsible for the more rapid recruitment of motor units during position constant tasks (Maluf and Enoka, 2005a). Due to the associated adjustments, it is proposed that the position task would also likely involve greater increases in descending drive and peripheral feedback (Mottram et al., 2005), which would consequently explain the more rapid HR and BP increases. Indeed, any increase in motor unit recruitment may also subsequently increase the cardiovascular response (particularly HR) through central command, as the cardiovascular control centres are activated in a parallel fashion with the motor cortex (Franke, Boettger and McLean, 2000). Further to this, it has also been proposed that a greater activation of motor units may also augment the exercise pressor reflex response through greater activation of the group III and IV muscle due to increased mechanical and/or chemical stimulation (Gálvez et al., 2000). Certainly, muscle metabolites may accumulate more rapidly during the position task due to the faster motor unit recruitment (Baudry et al., 2009), which could



consequently lead to greater activation of the afferent nerve fibres and thus an increase in BP (Rowell and O'Leary, 1990).

Taking the cited research into consideration it appears that constant position isometric contractions produce a less stable cardiovascular response compared to constant force tasks, and by association constant EMG tasks, due to the greater increases in HR and BP. Accordingly, this suggests that constant position exercise may therefore provide a less accurate training prescription than constant EMG isometric exercise. However, Wiles et al. (2008b) acknowledge that a rise in the cardiovascular parameters, such as that experienced during constant force and constant position work, could be an important factor to induce training effects. Indeed, if HR and BP were to rise at an increased rate during constant position exercise, this may prove to be a beneficial aspect of the isometric training as the level of cardiovascular stimulus required may be attained more rapidly and thus training will be completed at the necessary intensity for longer; which could lead to greater BP adaptations. It remains to be seen whether constant position IET can produce chronic adaptations to resting BP, however this isometric contraction style is arguably the most accessible style of isometric contraction and as such a viable method that should be explored in future research.

#### *1.5.1c The impact of contraction style on the isometric exercise training equipment selection*

When looking to design an inexpensive home-based IET protocol it is also pertinent to discuss the potential ramifications that isometric contraction style has on the exercise equipment selected for training. The majority of IET studies that lowered resting BP using either constant force or constant EMG contractions have involved the use of expensive and/or laboratory-based equipment. In order to precisely prescribe constant force a dynamometer is usually necessary (Lind, 2011), which is a piece of equipment that measures the force output when an individual pushes/pulls against a dynamometer attachment (Murray et al., 2007). Indeed the majority of constant force IET studies have used a programmable digital handgrip dynamometer (Ray and Carrasco, 2000; Taylor et al., 2003; McGowan et al., 2007a; 2007b; Badrov et al., 2013a; 2013b; Stiller-Moldovan, Kenno and McGowan, 2012; Millar et al., 2013a). This digital handgrip device has visual and audible instructions, which guides the individual through a complete IHG exercise session (Abe and Bisognano, 2011) and can therefore be used without supervision (Millar et al., 2009b). However, while this device has the potential to be used in the home, it is currently on the market in the UK from £299 to £449 (Zona Health, 2014). It is suggested that this financial outlay would be too expensive for many individuals and therefore this device may be inaccessible to a large proportion of the general population. Further to this, previous IET studies that have prescribed constant EMG contractions required the use of EMG equipment as well as a isokinetic dynamometer (Devereux, Wiles and Swaine, 2010b; Wiles, Coleman and Swaine, 2010; Baross, Wiles and Swaine, 2012). This equipment is expensive, usually laboratory-based and requires detailed knowledge due to the complicated measurement techniques (Murray et al., 2007) and is therefore not appropriate for home-based IET.

One study endeavoured to implement constant force IHG exercise in a cost effective home-based training regime. Millar et al. (2008) investigated the effectiveness of an inexpensive (~\$2) spring-loaded IHG device, which was successfully used to reduce resting BP. Whilst this hand-held device did provide a convenient alternative to the expensive handgrip dynamometer, due to its simplicity the IHG training could not be set to a precise intensity and thus the accuracy of the training prescription was severely

compromised. Training was completed at an approximate resistance level between 30-40% MVC and therefore intensity could not be rigorously controlled, which is fundamental in the safe prescription of isometric exercise (Wiles et al., 2005).

Finally, while constant position contractions have not previously been applied within an IET protocol to lower resting BP, the equipment typically required is quite simplistic in comparison as an inertial load is required to be supported and maintained at a constant joint angle (Hunter et al., 2002). The inertial load could either be an external weight or the participant's body weight, and the joint angle could be measured using a goniometer, which is a piece of equipment that is inexpensive and easy to use (Reese and Bandy, 2010). However, as alluded in the previous section 1.5.1 (page 20), constant position tasks have not previously been prescribed within an IET programme designed to reduce resting BP, despite the fact that this isometric contraction style may provide a simple, inexpensive alternative that could be utilised within home-based training.

### ***1.5.2 Modes of exercise previously utilised within an isometric training programme***

For the purpose of this thesis the term 'mode' is used to refer to the type of exercise performed (Kent, 2006). The most common mode previously utilised within isometric training for the reduction of resting BP is IHG exercise; both unilateral IHG (Wiley et al., 1992; Ray and Carrasco, 2000; McGowan et al., 2006; McGowan et al., 2007b; Badrov et al., 2013a; Millar et al., 2013a) and bilateral IHG (Wiley et al., 1992; Taylor et al., 2003; Peters et al., 2006; McGowan et al., 2007b; Millar et al., 2008; Stiller-Moldovan, Kenno and McGowan, 2012; Badrov et al., 2013b). During unilateral IHG training contractions are either performed with the dominant or non-dominant arm for all repeated sets, whilst during bilateral IHG training sets are performed with alternate hands. Other isometric training modes employed include arm flexion (Howden et al., 2002) and double-leg extension (Howden et al., 2002; Devereux, Wiles and Swaine, 2010b; Wiles, Coleman and Swaine, 2010; Baross, Wiles and Swaine, 2012). The mode of exercise selected consequently affects the muscle mass involved in the isometric contraction (Millar et al., 2013b). Indeed, handgrip exercise utilises the smaller forearm muscles (Mitchell et al., 1980), whereas leg extensions primarily involve the larger quadriceps muscle (Delavier, 2010). The majority of research suggests that the size of the active muscle mass affects the magnitude of the acute cardiovascular response (Mitchell et al., 1980; Seals et al., 1983; Lewis et al., 1985; Iellamo et al., 1999; Franke, Boettger and McLean, 2000; Gálvez et al., 2000) (see section 1.5.2a, page 25), which also has the potential to influence the subsequent chronic BP adaptations produced (Devereux, Wiles and Swaine, 2010b) as discussed in section 1.5.2b (page 27).

#### ***1.5.2a The effect of muscle mass on the acute cardiovascular response to isometric exercise***

The effect of muscle mass on the cardiovascular response to isometric exercise has been a controversial topic in the past as conflicting results have been reported (Fisher and White, 2004), however there is a growing body of research suggesting that muscle mass is an important contributor. One of the earliest studies to report this finding was conducted by Mitchell et al. (1980) in which separate isometric contractions were performed with the fingers (digits II and II), forearm (handgrip) and thigh (knee extensions) at 40% MVC for 2 minutes. When the HR and BP responses were compared between the three isometric tasks it was found that the exercise with the largest muscle mass of the thigh produced the

greatest cardiovascular response, followed by the exercises with the smaller forearm muscles and then lastly the smallest finger muscles. Subsequent research has supported this notion and also found that the cardiovascular response is greater for isometric contractions of a larger muscle mass when performed at the same relative intensity as a smaller muscle mass (Seals et al., 1983; Lewis et al., 1985; Iellamo et al., 1999; Franke, Boettger and McLean, 2000; Gálvez et al., 2000). Further to this, it has also been reported that there is a direct relationship between the cardiovascular response produced and the absolute force generated by the muscle mass (Mitchell et al., 1980; Seals et al., 1983).

Several studies have explored the mechanisms that produce a muscle mass dependent cardiovascular response. It has been hypothesised that isometric contractions of a greater muscle mass would require an increased central and peripheral drive (Mitchell et al., 1980; Gálvez et al., 2000). When an isometric contraction of a large muscle mass is initiated it is reasonable to expect that a greater number of motor units will be activated (Gálvez et al., 2000). Consequently, the cardiovascular control centres will be stimulated in parallel fashion with the motor cortex (Franke, Boettger and McLean, 2000), thus producing a larger increase in the cardiovascular response through greater central command (Gálvez et al., 2000). Further to this, it is also possible that the increased motor unit recruitment will also enhance the exercise pressor reflex due to either a greater physical deformation that will stimulate the mechanoreceptors (Gálvez et al., 2000) and/or increased metabolite production activating the metaboreceptors (Iellamo et al., 1999). The latter proposal is supported by the work of Seals (1989) who found a greater pressor response and MSNA (an indicator of chemoreflex activation) during two-arm IHG exercise (larger mass) compared to one-arm (smaller mass) performed at 30% MVC for 2.5 minutes. Finally, Iellamo et al. (1999) also found that baroreflex sensitivity was reduced during isometric leg extension exercise compared to handgrip contractions. It was proposed that the arterial baroreflex was 'reset' to a higher operating point permitting the rise in HR (Iellamo et al., 1994). It therefore appears likely that the enhanced cardiovascular response to isometric exercise of a larger muscle mass is regulated by several neural control mechanisms.

When considering the research that has explored the effects of muscle mass on the cardiovascular response to isometric exercise it is important to note that the majority of studies compared different muscle groups, such as the forearm and quadriceps. Some muscle groups not only differ in terms of the size of the muscle mass but also possibly the muscle fibre structural characteristics, such as orientation, thickness and curvature (Rowell, 1993). This may produce differences in the intramuscular pressure and blood flow when isometric contractions of different muscle groups are compared at the same relative intensity (Mitchell et al., 1980), which would likely affect the cardiovascular response produced. For example, Lind and McNicol (1967) studied forearm blood flow during IHG contractions performed at different intensities (5%, 10%, 15%, 20%, 30% MVC) and reported that blood flow was highest at 30% MVC and lowest at 5% MVC. Conversely, Sjøgaard et al. (1988) found that blood flow was highest in the quadriceps during knee extension exercise performed at an intensity of 5% MVC and lower during higher intensities (15%, 25%, 50% MVC). Taken together these studies suggest that blood flow in the quadriceps may be reduced compared to that of the forearm when both isometric contractions are performed at the same relative intensity, such as 30% MVC. This is thought to be due to differences in muscle fibre arrangement that cause higher intramuscular pressure in the quadriceps (Rowell, 1993). It is plausible to suggest that the reduced quadriceps blood flow is likely to cause a greater accumulation of

metabolites compared to the forearm, which would increase metaboreceptor activation and produce a greater cardiovascular response. Thus whilst the actual muscle mass itself may affect the cardiovascular response produced, it is also important to consider the role of the muscles structural characteristics. Taking this research into consideration, it may be advantageous to design a home-based training protocol with an isometric exercise mode that utilises the quadriceps in order to produce an enhanced cardiovascular stimulus.

#### *1.5.2b The effects of isometric exercise training muscle mass on the chronic adaptations to resting blood pressure*

It has previously been proposed that the rate of BP reduction following IET is dependent on the mode of exercise selected and size of the contracting muscle mass (Devereux, Wiles and Swaine, 2010b). Indeed it is feasible to expect that the enhanced acute cardiovascular response produced during isometric exercise of a larger muscle mass, as outlined in the preceding section 1.5.2a (page 25) may provide a greater training stimulus from which chronic BP adaptations can occur. To date only one study has utilised two different modes of isometric training from which the effects of muscle mass on BP reductions can be explored. Howden et al. (2002) compared the effects of 5 weeks isometric leg- and arm-training on resting BP and it was reported that both protocols produced similar significant reductions in resting SBP (arm: -12 mmHg; leg: -10 mmHg). This may suggest muscle mass is not a determinant of the magnitude of BP reductions, however it is important to note that training was not completed at the same relative intensity; arm training was completed at 30% MVC, whereas leg training was only completed at 20% MVC. From this finding it was proposed that there is an inverse relationship between the intensity of isometric exercise and the size of the muscle mass recruited (Lawrence et al., 2014), suggesting that isometric training utilising a larger muscle mass could be completed at a lower relative intensity to produce similar reductions in resting BP. This notion is supported by the fact that double-leg extension exercise has generally been performed at a lower intensity than handgrip exercise, as seen in Table 1.1 (pages 12-13). For example, in the study by Wiles, Coleman and Swaine (2010) isometric double-leg extension training was carried out at ~21% MVC, whereas unilateral handgrip exercise in the study by McGowan et al. (2007a) was performed at 30% MVC yet the reductions in SBP were similar (-5.2 mmHg and -4.9 mmHg, respectively). This suggests that although the relative intensities of the two exercise modes were different, they may have induced a similar training stimulus for BP adaptations to occur. As isometric contractions of a larger muscle mass produce a greater acute cardiovascular response (see section 1.5.2a, page 25), it is possible that leg extensions can be performed at a lower relative intensity compared to IHG exercise to produce a similar central and peripheral drive and consequent cardiovascular response. Thus, it is suggested that IET utilising the quadriceps can be performed at a lower relative exercise intensity (% MVC) than forearm training to bring about a similar training stimulus and BP adaptation, which may be advantageous for those with a limited exercise capacity. However it remains to be established whether IET of a larger muscle mass can produce greater chronic adaptations to resting BP.

### ***1.5.3 Exercise intensity of isometric exercise training***

Throughout this thesis intensity will relate to the effort required (Kent, 2006). Isometric training studies that utilised constant force contractions most typically used intensities in the range of 10-50% MVC, with 30% MVC being the most common (Millar et al., 2009a). Whereas constant EMG isometric training studies set the intensity at a range of target HR values from 70% to 95%  $HR_{peak}$ , which equated to approximately 8 to 24% MVC (Devereux, Wiles and Swaine, 2010b; Wiles, Coleman and Swaine, 2010; Baross, Wiles and Swaine, 2012). It is well documented that the acute cardiovascular response produced during isometric exercise corresponds to the intensity of the work being performed (Lind et al., 1964; Iellamo et al., 1999; Gálvez et al., 2000); this literature will be reviewed in section 1.5.3a (page 28). Furthermore, research suggests that the rate and magnitude of chronic BP adaptations may be affected by the intensity of IET prescribed (Baross, Wiles and Swaine, 2012), which will be discussed in section 1.5.3b (page 29).

#### ***1.5.3a The effect of intensity on the acute cardiovascular response to isometric exercise***

Within this section of the thesis studies that utilised constant force isometric contractions will be discussed, as it appears that no research has directly compared the acute cardiovascular responses to constant EMG tasks performed at different intensities. It is well documented that the magnitude of the acute cardiovascular response to isometric exercise is related to the intensity (% MVC) of the static contraction (Lind et al., 1964; Iellamo et al., 1999; Gálvez et al., 2000), where an increase in isometric intensity is subsequently matched by an increase in HR and BP (Mitchell, 1990; Gálvez et al., 2000). Blood pressure is thought to increase in an attempt to overcome the mechanical compression of the blood vessels by the statically contracting muscle in order to maintain blood flow (Lind et al., 1964; Martin et al., 1974). Therefore it is likely that the magnitude of the response is related to the ability of the blood flow to either meet the metabolic requirements of the active muscle or remove the substances produced (Lind et al., 1964).

During non-fatiguing contractions performed at low intensities (< 15% MVC) the magnitude of the cardiovascular changes are small (Lind and McNicol, 1967) as limited mechanical interference occurs. After several minutes, the blood flow through the muscles is at a sufficient level to meet the metabolic requirements so that a steady state is attained and the contraction can be maintained for long periods of time without further hemodynamic changes (Lind and McNicol, 1967; Martin et al., 1974). However, during fatiguing isometric contractions (> 15% MVC) unremitting mechanical restrictions occur due to the increased muscle fibre recruitment (Hietanen, 1984) and blood flow is insufficient to meet the muscles metabolic requirements (Lind and McNicol, 1967). Such a mismatch between blood flow and metabolism may cause an accumulation of metabolites (Rowell and O'Leary, 1990), which activate the metaboreceptors (Mostoufi-Moab et al., 1998) leading to a consequent steady increase in BP due to a greater exercise pressor reflex. The tension exerted is suggested to be directly related to an increase in BP and a decrease in contraction time due to fatigue (Lind and McNicol, 1967). For example, an isometric contraction completed at 20% MVC can be maintained for approximately 10 to 13 minutes, at 30% MVC for 4 to 6 minutes and at 50% MVC for 1 to 2 minutes (Lind et al., 1964; Lind and McNicol, 1967). Finally, an isometric contraction performed at 100% MVC can only be held for a few seconds (Lind, 2011). During such a strong muscular contraction, the intramuscular blood vessels could be squeezed so

tightly that blood flow becomes totally blocked leading to ischemic conditions, which causes the highest BP values to be reported (Hietanen, 1984). Thus, it is suggested that the intensity of the isometric contraction affects the blood flow and consequently the BP response produced (Lind and McNicol, 1967). However, it is important to consider that the intensity at which blood flow is hindered may also differ depending on the muscle being contracted due to differences in the muscle's structural characteristics (Rowell, 1993), as previously discussed in section 1.5.2a (page 25).

Other research has put forward alternative explanations for the differing cardiovascular responses between isometric contractions performed at low and high intensities. These theories are similar, if not the same, to those discussed in section 1.5.2a (page 25) in relation to muscle mass. Gálvez et al. (2000) proposed that isometric contractions that involve a greater level of force will consequently activate a greater number of motor units, which will lead to greater activation of both central command and the exercise pressor reflex (through the mechanoreceptors) to stimulate the cardiovascular control centres.

In summary, the research discussed suggests that isometric exercise performed at a higher intensity may cause greater hindrance to muscle blood flow and/or increased activation of motor units. Consequently, the exercise pressor reflex and central command may be stimulated to a greater extent producing large increases in HR and BP. Based on this idea, IET should be performed at a high intensity to elicit a greater cardiovascular stimulus. While this may be the case, the isometric intensity also affects the duration that the contraction can be sustained (Lind et al., 1964; Lind and McNicol, 1967), which needs to be considered when designing an IET protocol to ensure an adequate duration to produce the optimal cardiovascular training stimulus for BP adaptations to occur; this will be discussed further in section 1.5.4 (page 30).

#### *1.5.3b The effect of isometric exercise training intensity on resting blood pressure reductions*

While it is thought that exercise intensity might be an important factor in the magnitude and rate of occurrence of chronic adaptations seen on the completion of isometric training (Baross, Wiles and Swaine, 2012) very few studies have explored this occurrence. Wiles, Coleman and Swaine (2010) prescribed isometric double-leg extension training at a constant EMG to elicit a target HR of either 75%  $HR_{peak}$  (~10% MVC) or 95%  $HR_{peak}$  (~21% MVC) and found that both intensities lowered resting BP following training. However, the SBP reductions were -3.7 mmHg in the low intensity group and -5.2 mmHg in the high intensity group suggesting that higher intensity work may bring about larger SBP reductions; DBP and MAP produced similar reductions in both groups (see Table 1.1, pages 12-13). Furthermore the reductions in resting BP, particularly SBP, appeared to occur in the first 4 weeks in the high intensity training group but took 8 weeks in the low intensity training group; although this finding was not statistically significant (Wiles, Coleman and Swaine, 2010).

A later study by Baross, Wiles and Swaine (2012) found that after 8 weeks of isometric double-leg extension training there were no significant changes in BP (SBP: -0.8 mmHg; DBP: 1.1 mmHg; MAP: 0.5 mmHg) in the low intensity group (70%  $HR_{peak}$ ; ~8% MVC) but there were significant changes in SBP (-10.8 mmHg) and MAP (-4.7 mmHg) in the high intensity group (85%  $HR_{peak}$ ; ~14% MVC). This finding suggests that there may be an intensity threshold at which BP adaptations occur (Millar et al., 2013b). Furthermore, Baross, Wiles and Swaine (2012) proposed that the combination of the powerful

pressor response and the high level of occlusion during high intensity isometric training may have a marked effect on blood flow, particularly on vascular shear stress, which will bring about localised vascular adaptations (Baross, Wiles and Swaine, 2012) and consequently reduce resting BP. From the findings of these studies it is suggested that home-based IET should utilise relatively high intensity isometric exercise, such as that set at 95% HR<sub>peak</sub>, to elicit a greater cardiovascular stimulus for BP reductions to occur.

#### ***1.5.4 Duration of isometric exercise training sessions and the effects on the acute cardiovascular response***

Duration is defined as the amount of time a training session lasts (Kent, 2006). A typical isometric training session is comprised of periods of exercise and rest. The contraction duration sustained at a given isometric exercise intensity is typically 2 minutes (Millar et al., 2009a). These bouts of exercise are then interspersed with rest periods from 1 to 5 minutes. This cycle of exercise and rest is generally repeated four times to complete a training session. The total time an isometric training session lasts is approximately 12 to 14 minutes, which consists of 8 minutes effective isometric exercise (Araújo et al., 2011).

The duration of the sustained isometric contraction has been found to affect both the pattern and magnitude of the cardiovascular responses produced (Lind et al., 1964; Lind and McNicol, 1967; MacDougall et al., 1992), which appears to be interlinked with the isometric contraction style and intensity, as previously discussed in section 1.5.3a (page 28). When non-fatiguing constant force isometric contractions (< 15% MVC) are performed BP and HR initially increase and then develop a steady-state after a few minutes, whereas during more intense isometric contractions (>15% MVC) these variables continue to increase throughout the exercise duration until muscle fatigue prohibits the contraction (Lind and McNicol, 1967). While this is also the case for constant EMG isometric contractions the cardiovascular response is somewhat attenuated in comparison (Schibye et al., 1981; Franke, Boettger and McLean, 2000). Furthermore, the isometric intensity (% MVC) will also affect the magnitude of cardiovascular response and the duration that the contraction can be sustained (Lind and McNicol, 1967). Indeed, a high intensity isometric contraction will produce a greater cardiovascular response but can only be maintained for limited duration (Lind et al., 1964). Therefore when designing an IET protocol the intricate relationship between duration and intensity must be balanced in order to attain the optimal cardiovascular stimulus whilst also ensuring that the training prescribed is achievable and also limits the pressor response experienced to ensure that safe BP levels are maintained.

The most common duration prescribed for IET is four 2 minute contractions separated by several minutes of rest; however there is limited justification for its use. A recent study by Millar, MacDonald and McCartney (2011) investigated the acute cardiovascular responses to different IHG protocols by altering the contraction and rest period frequency and duration. In the study, three different handgrip protocols were examined each at 30% MVC, which is the intensity most commonly utilised: 1) four 2 minute contractions each separated by 1 minute of rest, 2) eight 1 minute contractions each separated by 30 seconds of rest, and 3) sixteen 30 second contractions each separated by 15 seconds of rest. There was also a sham control group performing four 2 minute contractions at 3% MVC each separated by 1 minute of rest. Following protocol 1 there were the largest increases in SBP, HR and cardiac autonomic response,

which demonstrate that the contraction and/or rest period frequency and duration had a significant effect on the exercise pressor reflex. Millar, MacDonald and McCartney (2011) speculate that this is due to the fact that protocol 1 would have increased intramuscular pressure and decreased skeletal muscle blood flow for a longer period of time leading to a greater accumulation of metabolites, thus increasing metaboreflex stimulation. Isometric contractions of longer durations (2 minutes) produced the largest sympathetic stimulus, which may be an important factor in maximizing IET reductions in BP. While this seems plausible, no research has actually prescribed different exercise durations within an IET study to directly compare the effects on the chronic BP adaptations.

From the research discussed it is suggested that home-based IET should comprise of isometric contractions that are 2 minutes in duration interspersed with periods of at least 1 minutes rest. It is important to note that all participants completed all the study protocols outlined by Millar, MacDonald and McCartney (2011) including the procedure that consisted of the longest contraction duration of 2 minutes. Further to this, isometric training studies that have utilised a protocol including a 2 minute contraction duration have not reported that any training session were incomplete (Wiley et al., 1992; Howden et al., 2002; Taylor et al., 2003; McGowan et al., 2006; 2007a; 2007b; Millar et al., 2008; Devereux, Wiles and Swaine, 2010b; Wiles, Coleman and Swaine, 2010; Baross, Wiles and Swaine, 2012). Thus, an isometric contraction of 2 minutes appears to be a realistic and attainable exercise duration to be included within an IET protocol that will subsequently elicit a sufficient cardiovascular stimulus to attain chronic adaptations to BP.

#### ***1.5.5 Frequency of isometric exercise training sessions and the effects on chronic blood pressure adaptations***

Frequency refers to the number of times a week that training is undertaken (Kent, 2006). Generally training sessions are performed 3 times a week (Wiley et al., 1992; Howden et al., 2002; Taylor et al., 2003; McGowan et al., 2006; Peters et al., 2006; McGowan et al., 2007a; 2007b; Millar et al., 2008; Devereux, Wiles and Swaine, 2010b; Wiles, Coleman and Swaine, 2010; Baross, Wiles and Swaine, 2012; Stiller-Moldovan, Kenno and McGowan, 2012; Badrov et al., 2013a; 2013b; Millar et al., 2013a) with at least 24 hours between each session (Devereux, Wiles and Swaine, 2010b; Wiles, Coleman and Swaine, 2010; Baross, Wiles and Swaine, 2012). Only a handful of studies have utilised alternative training frequencies, which consisted of 4 (Ray and Carrasco, 2000) and 5 (Wiley et al., 1992; Badrov et al., 2013a) times per week. With training duration and frequency considered together, IET studies typically involve less than 60 minutes of exercise per week (Owen, Wiles and Swaine, 2010). The frequency of IET will ultimately determine the amount of time that an individual is exposed to the training stimulus, which may have important implications on the chronic BP adaptations produced.

Badrov et al. (2013a) looked to determine whether training frequency influenced the magnitude of BP reductions. In this study participants were assigned to complete unilateral IHG training (4 x 2 min contractions with 4 minutes rest between) every 3 days or every 5 days for 8 weeks. Equivalent reductions in SBP were found regardless of training frequency, suggesting that this is not an important determinant of the magnitude of SBP adaptations. As lack of time is a known barrier to physical activity and exercise (Troost et al., 2002; Lascar et al., 2014) it would be beneficial to utilise an IET protocol that has a reduced time commitment. Thus, if the same BP adaptations can be gained when utilising a protocol



that requires only 60 minutes training per week (3 sessions) compared to 100 minutes (5 sessions), then this should be prescribed in an attempt to increase exercise adherence. Although it is also acknowledge that conversely increasing frequency may enhance the formation of an exercise habit and, potentially, facilitate adherence (Tappe et al., 2013). However, this concept requires further exploration in relation to IET specifically. It is also important to note that Badrov et al. (2013a) reported that those assigned to train 5 times a week produced significant SBP reductions after only 4 weeks with no further reductions thereafter, while BP reductions were not apparent until week 8 in those participants that trained 3 times per week. It was therefore suggested that higher frequency training may have a temporal effect on BP adaptations (Badrov et al., 2013a). The effects of training intervention length will be explored further in the preceding section 1.5.6 (page 32).

#### ***1.5.6 Isometric exercise training intervention length and the associated chronic blood pressure adaptations produced***

The period of IET has lasted for a varying degree of time, from 4 to 10 weeks (Millar et al., 2013b) with the majority of studies utilising an 8 week intervention length (Wiley et al., 1992; McGowan et al., 2006; McGowan et al., 2007a; 2007b; Millar et al., 2008; Wiles, Coleman and Swaine, 2010; Baross, Wiles and Swaine, 2012; Stiller-Moldovan, Kenno and McGowan, 2012; Badrov et al., 2013a; Millar et al., 2013a). However, BP adaptations have been evident when shorter training interventions have been implemented, such as 4 weeks (Devereux, Wiles and Swaine, 2010b), 5 weeks (Wiley et al., 1992; Ray and Carrasco, 2000; Howden et al., 2002) and 6 weeks (Peters et al., 2006). Further to this, some studies that prescribed IET for longer lengths (8-10 weeks) found significant reductions in resting BP after only 4-6 weeks (Wiley et al., 1992; Taylor et al., 2003; Badrov et al., 2013a).

It would appear that significant BP reductions were possible after a shorter intervention length in some IET studies due to modifications in the training prescription, such as utilising a larger muscle mass, increasing intensity and increasing frequency. Indeed, rather than prescribing the traditional forearm handgrip exercise, Howden et al. (2002) and Devereux, Wiles and Swaine (2010b) instead utilised the larger muscle mass of the quadriceps during double-leg extension exercise to produce significant reductions in resting BP after training was completed 3 times a week for 4-5 weeks. Other studies kept the traditional handgrip exercise but have instead set the intensity higher at 50% MVC (Wiley et al., 1992; Peters et al., 2006), rather than at the traditional 30% MVC, to produce BP reductions after 5-6 weeks. Finally, some studies have manipulated the frequency of training so that exercise is completed 5 times a week (Wiley et al., 1992; Ray and Carrasco, 2000; Badrov et al., 2013a), as opposed to the more common frequency of 3 times a week, in order to produce BP adaptations after 4-5 weeks. As previously discussed in sections 1.5.2 (page 25), 1.5.3 (page 28) and 1.5.5 (page 31) respectively, such alterations to these factors may increase the magnitude of, or amount of exposure to, the acute cardiovascular response and subsequently increase the training stimulus, which may induce chronic BP adaptations at a faster rate. However, as suggested in section 1.5.5 (page 31), it may not be as desirable to alter the frequency of IET as this would consequently increase the time commitment required, which is a known barrier to physical activity and exercise (Trost et al., 2002; Lascar et al., 2014), and may decrease adherence to the prescribed IET programme. Thus in order to produce BP reductions at an increased rate, after a shorter

intervention length, it appears that it may be beneficial to prescribe an exercise mode that utilises a larger muscle mass and this should be completed at a relatively high but sustainable intensity.

### ***1.5.7 Participants involved in isometric exercise training studies***

Not only have a wide variety of training protocols been implemented to explore the effects of IET on resting BP, but also a wide variety of participants have been selected to complete the designed studies, which may have affected the overall BP outcome. First of all the resting BP classification of participants has varied greatly with normotensive, high-normal and hypertensive (medicated and unmedicated) individuals all being studied, which is strongly suggested to affect the likely BP adaptations produced (Stiller-Moldovan, Kenno and McGowan, 2012; Badrov et al., 2013a). Further to this, a diverse age range has been investigated, such as younger (< 45 years), middle-aged (45 to 60 years) and older (> 60 years) adults, which could influence a participant's acute responses and chronic adaptations to IET due to age related physiological differences (Baross, Wiles and Swaine, 2012). As both initial BP levels and age have been suggested to affect the chronic BP adaptations produced following IET, these factors will be discussed in the proceeding sections 1.5.7a (page 33) and 1.5.7b (page 35) respectively.

It is also important to note that male participants have been more commonly studied. In the research that presented data for participant sex, a quarter of the participants were female out of the 246 that completed training and only one of these studies used solely female participants (Badrov et al., 2013a). However, this is likely due to the fact that BP has been shown to be greatly affected by the menstrual cycle (Dunne et al., 1991). Finally, as previously highlighted in section 1.4.1 (page 11) the vast majority of this research has been conducted on a small-scale with a relatively small number ( $\leq 17$ ) of participants recruited for each training group (Wiley et al., 1992; Ray and Carrasco, 2000; Howden et al., 2002; Taylor et al., 2003; McGowan et al., 2006; Peters et al., 2006; McGowan et al., 2007a; 2007b; Devereux, Wiles and Swaine, 2010b; Wiles, Coleman and Swaine, 2010; Baross, Wiles and Swaine, 2012; Stiller-Moldovan, Kenno and McGowan, 2012; Badrov et al., 2013a; 2013b; Millar et al., 2013a). Peters et al. (2006) elucidate that this may limit the ability for the results to be generalised. The largest number of participants recruited for a training group was 25 participants (Millar et al., 2008). Therefore it appears there is a need for larger scale IET intervention studies (Millar et al., 2013b).

#### ***1.5.7a The influence of initial resting blood pressure on the chronic adaptations to isometric exercise training***

It is suggested that a participant's initial BP classification may affect the degree to which resting BP is lowered following IET (Baross, Wiles and Swaine, 2012). Several studies that used hypertensive (Taylor et al., 2003; Peters et al., 2006; McGowan et al., 2007b; Millar et al., 2013a) or high normal (Wiley et al., 1992; McGowan et al., 2007b; Baross, Wiles and Swaine, 2012) participants found greater reductions in BP (SBP: -5 to -19 mmHg; DBP: -5 to -9 mmHg) compared to studies that used normotensive participants (SBP: -4 to -10 mmHg; DBP: -3 to -5 mmHg) (Ray and Carrasco, 2000; McGowan et al., 2007a; Millar et al., 2008; Devereux, Wiles and Swaine, 2010b; Wiles, Coleman and Swaine, 2010). Ray and Carrasco (2000) believe that greater reductions in resting BP after completing IET may be found in individuals with hypertension due to the fact that this population has an initial higher level of BP to start, and thus have a greater capacity for reductions (Stiller-Moldovan, Kenno and McGowan, 2012; Badrov et

al., 2013a). Indeed, research completed by Millar et al. (2007) found that medicated hypertensive participants with a higher initial resting SBP value produced greater rates of BP decline ( $r = -0.67$ ) following 8 weeks of IHG training.

Furthermore Baross, Wiles and Swaine (2012) believe that the mechanisms responsible for lowering BP could be different for participants who have normal BP due to the fact that hypertension is associated with endothelial dysfunction. As previously discussed in section 1.4.2a (page 16), when studying a hypertensive population BP reductions were associated with improvements in localised endothelial-dependent vasodilation (McGowan et al., 2007b) and autonomic function (Taylor et al., 2003; Millar et al., 2013a), but this association was not found for the BP reductions that occurred with a normotensive population (Ray and Carrasco, 2000; McGowan et al., 2007a; Wiles, Coleman and Swaine, 2010; Badrov et al., 2013a). This difference may have occurred due to the fact that endothelial function is already normal in healthy participants (Green et al., 2004), as is probably also the case for autonomic function. As the mechanisms that lower resting BP may be different for normotensive and hypertensive participants, it is therefore likely that the magnitude of BP changes for each group may be consequently affected.

Conversely, Stiller-Moldovan, Kenno and McGowan (2012) found no reductions in resting BP in hypertensive participants following IET, however these individuals were successfully medicated and had resting BP values within the normal range (resting BP:  $\sim 115/68$  mmHg). Therefore antihypertensive pharmacological therapies may affect the capacity of IET to lower resting BP in those medicated for hypertension (Stiller-Moldovan, Kenno and McGowan, 2012). For example, in the study by Stiller-Moldovan, Kenno and McGowan (2012) the majority of participants were taking ACE inhibitor and/or  $\beta$ -blockers, which have been shown to improve autonomic function (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996; Kontopoulos et al., 1997). Therefore participants may have already gained the maximum improvements in autonomic function from these pharmacological therapies and consequently may have been unable to improve further through IET (Stiller-Moldovan, Kenno and McGowan, 2012).

Therefore, while IET may be the most beneficial and applicable to those individuals with hypertension, it is suggested that normotensive participants should be studied first when establishing an IET protocol (Badrov et al., 2013a) due to the fact that these populations may produce a different mechanistic response (Baross, Wiles and Swaine, 2012) and also that antihypertensive medications may alter the effectiveness of IET to modify BP (Stiller-Moldovan, Kenno and McGowan, 2012). It is also important to highlight that IET has often not been recommended for a hypertensive population in the past due to the fact that isometric exercise produces a pronounced pressor response (Mitchell and Wildenthal, 1974), which was formerly highlighted in section 1.3.1 (page 6). The percentage change in a hypertensive individual's acute BP response is no greater than that experienced in a normotensive person (Ewing et al., 1973). However, as hypertensive individuals already have a high baseline BP level to start with, isometric exercise could result in extremely high BP values being attained while working at a relatively modest workload (Ewing et al., 1973); which could cause excessive strain on the heart (Greer, Dimick and Burns, 1984). Despite this initial concern regarding the acute increase in BP, it appears that no adverse events have actually been reported in any IET studies of both normotensive and hypertensive populations (Kelley and Kelley, 2010; Araújo et al., 2011; Millar et al., 2013b). Indeed, a group of authors who have collectively

completed over 25,000 IET sessions stated that “there had been no reports of lasting physical impairments or significant unfavourable clinical events during or resulting from isometric exercise training” (Millar et al., 2013b; p. 351). Thus it appears that IET is a well-tolerated procedure. However, while this may be the case, it would be a prudent precaution to study a normotensive population first when designing a new home-based IET protocol, as implied by Badrov et al. (2013a), in order to explore the magnitude of BP change and ensure that safe BP levels are attained. Exposing hypertensive individuals to a novel IET procedure without prior knowledge of the likely pressor response would be irresponsible.

#### *1.5.7b The effects of participant age on the blood pressure adaptations to isometric exercise training*

Research investigating the BP adaptations to IET have studied participants of a wide variety of ages and have found differing BP changes between groups, particularly with respect to SBP. Studies using younger adults (< 45 years) have found resting SBP changes between -4 to -13 mmHg (mean SBP reduction: -8 mmHg) (Wiley et al., 1992; Howden et al., 2002; McGowan et al., 2007a; Devereux, Wiles and Swaine, 2010b; Wiles, Coleman and Swaine, 2010; Badrov et al., 2013a). Studies of middle-aged adults (45 to 60 years) have found reductions in resting BP of -11 and -13 mmHg (mean SBP reduction: -12 mmHg) (Peters et al., 2006; Baross, Wiles and Swaine, 2012). Finally, research using older adults (> 60 years) have found BP reductions from -5 to -19 mmHg (mean SBP reduction: -11 mmHg) (Taylor et al., 2003; McGowan et al., 2007b; Millar et al., 2008; Badrov et al., 2013b; Millar et al., 2013a). It therefore appears that middle-aged and older individuals ( $\geq 45$  years) present a greater capacity for BP reductions. There are several physiological changes that occur with age such as reduced endothelial-dependent vasodilation (Brandes, Fleming and Busse, 2005), increased oxidative stress (Kregel and Zhang, 2007), loss of large atrial compliance (Gates and Seals, 2006) and decreased baroreflex sensitivity (Monahan et al., 2001). Furthermore, ageing is also associated with increases in sympathetic nervous system activity and plasma noradrenaline (Seals and Esler, 2000). It is suggested that such physiological changes that occur with age could influence a participant’s acute responses and chronic adaptations to IET (Baross, Wiles and Swaine, 2012). While the most direct application of IET is in middle-aged and older populations due to the increase in BP with age (Pescatello et al., 2004), it has been advised that it may be best to establish a new IET protocol with a younger more homogenous sample, as indicated by Badrov et al. (2013a) in order to reduce the effect of any potential confounding factors. Once the basic pattern of cardiovascular response and adaptation has been clearly established, the application of this novel home-based IET protocol can be investigated in future research with older populations.

#### *1.5.8 Summary of the isometric exercise training programme variables previously prescribed*

From the research presented it can be clearly seen that a wide variety of IET protocols have been utilised with the aim of reducing resting BP. Currently no guidelines exist from which a new inexpensive home-based programme can be designed. However, based on the current literature it is suggested that to bring about optimal BP adaptations at an increased rate an IET prescription should include: 1) an exercise mode that utilises a larger muscle mass, such as the quadriceps, 2) relatively high intensity exercise, and 3) four 2 minute contractions with at least a 1 minute rest in between. Such factors may increase the magnitude of the acute response to consequently increase the training stimulus and bring about chronic BP adaptations at a faster rate. Further to this, it would seem beneficial to utilise a shorter training frequency, such as 3 times a week, to minimise the participants time commitment and hopefully increase adherence to the

prescribed programme (DeMichele et al., 1997). While it seems relatively logical that these parameters should be utilised within a home-based IET protocol, the selection of an isometric contraction style is a little less clear as this is a concept that has remained relatively unexplored in the IET literature. Both constant force and constant EMG contraction styles have been included within IET protocols and have both been found to reduce resting BP. However, both contraction styles require the use of expensive and/or laboratory-based equipment, which is not suitable for home-based training. Contrary to this, constant position isometric contractions have not previously been applied within training for the reduction of resting BP, although may possibly be most suitable when prescribing home-based exercise due to the potential use of simple, inexpensive equipment.

## **1.6 Developing home-based isometric exercise training using the isometric wall squat**

Based on all of the research currently presented, this thesis will ultimately look to explore a potential new inexpensive, home-based IET programme for the reduction of resting BP. While some research has endeavoured to prescribe IHG training in the home (Millar et al., 2008; Badrov et al., 2013a; Millar et al., 2013a), these studies were only part home-based as out of the 3 training days per week, 2 days were completed while supervised at a University and 1 day was completed independently at home. Further to this the exercise mode prescribed utilised the smaller forearm muscle. As previously discussed in section 1.5.2 (page 25), it would appear to be more beneficial to use an exercise mode that requires a larger muscle mass, such as the quadriceps. To date, one constant force (Howden et al., 2002) and three constant EMG studies (Devereux, Wiles and Swaine, 2010b; Wiles, Coleman and Swaine, 2010; Baross, Wiles and Swaine, 2012) have utilised the larger leg muscles by prescribing double-leg extension exercise, however these protocols required the use of an expensive isokinetic dynamometer. It is instead proposed that the isometric wall squat, which is a simple alternative leg exercise, could be utilised within a home-based training regime.

### ***1.6.1 Introducing the isometric wall squat exercise***

An isometric wall squat requires a squat to be performed with the back resting against a wall (Escamilla et al., 2009a; 2009b) (see Figure 1.1). The wall aids balance during the exercise and also provides support for some of the individual's body weight (Sisto and Malanga, 2006). Participants are traditionally required to hold a squat position at approximately 90-110° with the thighs parallel to the floor, vertical lower legs and knees positioned above the ankle (Escamilla et al., 2009a; 2009b). However the wall squat can be performed with a variety of different techniques, such as positioning the feet further away from the wall or moving them closer (Escamilla et al., 2009a; 2009b), which would consequently alter the knee joint angle. The main active muscles during the wall squat are the quadriceps (Escamilla et al., 2009a; 2009b), which stabilise the knee to hold the static position against the force of gravity. The wall squat requires a great amount of knee extensor torque as the trunk is erect against the wall and a line of force is produced down the centre of mass, which limits the ability of the hip extensors, such as the hamstrings, to contribute (Escamilla et al., 2009a). The use of the wall squat as a strength training exercise (Hazeldine, 1990), a test of static muscular endurance (Tomchuk, 2011) and a knee rehabilitation exercise (Bevilaqua-Grossi et al., 2005) are well documented. However, isometric wall squat exercise has not been previously utilised as part of a home-based training protocol to lower resting BP.



**Figure 1.1.** The isometric wall squat exercise

It is suggested that the wall squat may be suitable for home-based training as it is a simple exercise to perform that requires minimal equipment, so it is therefore both economical and accessible. The wall squat may provide an alternative to laboratory-based double-leg extension exercise that has successfully reduced BP (Howden et al., 2002; Devereux, Wiles and Swaine, 2010b; Wiles, Coleman and Swaine, 2010; Baross, Wiles and Swaine, 2012). Although the two exercises are inherently different, they both mainly utilise the leg extensor muscles. However, it has been suggested that squat based exercises, such as the parallel squat, place less stress on the knee joint compared to the leg extension (Signorile et al., 1994).

### ***1.6.2 Prescription of isometric wall squat exercise for home-based training***

There are several factors that need to be explored before isometric wall squat exercise can be utilised within a home-based training programme designed for the reduction of resting BP. These include the contraction style to be utilised (see section 1.6.2a, page 37), the method for adjusting and prescribing the exercise intensity (see sections 1.6.2b and 1.6.2c, page 39), the potential acute cardiovascular responses that will be produced (see section 1.6.2d, page 40) and the protocol of an exercise session (see section 1.6.2e, page 43). These factors will be discussed in the sections that follow with the aim of highlighting any issues that need to be explored when developing and implementing a home-based isometric wall squat training protocol. This information will consequently inform the design of the studies to be carried out within this thesis.

#### ***1.6.2a Exploring suitable contraction styles for isometric wall squat exercise***

As previously discussed in section 1.5.1 (page 20), IET designed for the reduction of resting BP has typically been performed at constant force, which involves participants completing isometric work at a percentage of their MVC against the resistance of a dynamometer (Lind, 2011). However, a dynamometer does not appear to have been previously used to measure the MVC of an isometric wall squat exercise. A

dynamometer designed for this purpose would possibly involve a wall squat being performed against a shoulder harness that was fixed to a strain gauge and secured to a platform on the floor, as utilised when measuring an MVC of a parallel squat (Behm, Power and Drinkwater, 2003). The individual could then statically contract the quadriceps, which would push the shoulders up against the pads and measure the force output. It would then be possible to complete an MVC and perform wall squat training at percentage of this MVC. However, while this is a plausible method, this would likely involve the use of expensive and/or laboratory-based equipment, which would contradict the simple nature of the isometric wall squat exercise and may impose barriers, such as the cost of exercise (Belza et al., 2004; Allison et al., 2005; Lascar et al., 2014) and transportation (Belza et al., 2004). Furthermore, since working to percentage MVC is reported to cause HR to constantly increase throughout the exercise duration (Lind et al., 1964; Seals et al., 1983; Seals, 1993; Smolander et al., 1998; Friedman, Peel and Mitchell, 1992; Franke, Boettger and McLean, 2000) it is desirable that future developments involving isometric training prescription allow intensity to be more precisely controlled (Wiles et al., 2008b) and monitored to ensure safe levels of physiological stress are maintained (Wiles et al., 2005). This is particularly pertinent for home-based exercise prescription in which participants will be training unsupervised.

To this end, other IET studies have prescribed isometric exercise at a constant EMG value (Devereux, Wiles and Swaine, 2010b; Wiles, Coleman and Swaine, 2010; Baross, Wiles and Swaine, 2012), as previously outlined in section 1.5.1 (page 20). In these studies participants were required to complete a pre-training incremental test in order to establish a linear relationship between EMG activity and HR (Wiles et al., 2008b). From which it was then possible to calculate a participant specific EMG value that should be maintained during a training session in order to elicit a specific target HR, which ranged from 70% to 95%  $HR_{peak}$  (Devereux, Wiles and Swaine, 2010b; Wiles, Coleman and Swaine, 2010; Baross, Wiles and Swaine, 2012). Performing isometric exercise at a constant EMG value has been shown to produce an attenuated cardiovascular response in comparison to constant force contractions (Schibye et al., 1981; Franke, Boettger and McLean, 2000). However, while prescribing this isometric contraction style produces a cardiovascular response that can be more precisely controlled and monitored, its application for home-based training is somewhat limited as EMG is a complicated and expensive measure (Murray et al., 2007).

Although constant force and constant EMG contractions have previously been utilised within IET protocols, it is clear to see that both styles have their potential drawbacks for home-based isometric wall squat training. It is instead proposed that isometric wall squat exercise would be more suitably aligned with the isometric contraction style termed constant position, in which a given joint angle is maintained while supporting an inertial load (Hunter et al., 2002). Indeed the isometric wall squat exercise typically requires a participant to keep the knee joint at a prescribed angle while supporting an inertial load, their body mass, using the quadriceps. This is a novel mode that has not been previously used within an IET programme aimed at reducing resting BP and may provide a more accessible home-based method as measuring the knee joint angle to set the wall squat position would require inexpensive and easy to use equipment, such as a goniometer (Reese and Bandy, 2010).

### *1.6.2b Establishing a method for adjusting constant position isometric wall squat intensity via knee joint angle*

For constant position isometric wall squat exercise to be utilised as part of a home-based training programme aimed at reducing resting BP, a suitable method for prescribing and adjusting exercise intensity must be established. It is proposed that wall squat exercise intensity could be altered by manipulating the knee joint angle because as knee flexion increases during squatting exercise, the quadriceps present higher EMG activity (Escamilla, 2001; Kvist and Gillquist, 2001; Bevilacqua-Grossi et al., 2005), which is a known marker of isometric exercise intensity (Devereux, Wiles and Swaine, 2011). It is suggested that the greater quadriceps EMG activity with knee flexion is likely required to increase knee extensor torque in order to maintain static equilibrium. As knee flexion increases the feet are positioned further away from the wall and the back is moved down the wall. This would consequently increase the moment arm, which is the distance between the line of action of the force (the individual's line of gravity) and the axis of rotation (knee joint) (McGinnis, 2013). As the magnitude of torque is equal to the force multiplied by the moment arm (McGinnis, 2013), any increase in the moment arm would subsequently increase the torque generated by the weight of the individual. Thus, to offset this gravitational torque and maintain the required static wall squat position the quadriceps must produce an equal and opposite knee extensor torque, as per Newton's third Law of Motion (McGinnis, 2013), which would consequently increase the EMG activity. However, while EMG activity may be an indicator of isometric exercise intensity, it is not suitable for home-based training, due to the associated expense and therefore an alternative measure must be established.

It is proposed that HR could instead be used as an indication of isometric exercise intensity as Wiles et al. (2008b) previously found that HR and BP increased with greater EMG activity during isometric double-leg extension exercise. Such an increase in the cardiovascular response with EMG activity is likely due to greater central command (Franke, Boettger and McLean, 2000) and/or the exercise pressor reflex (Gálvez et al., 2000), as previously outlined in section 1.5.2a (page 25). Therefore it is hypothesised that wall squats performed in a position with a greater degree of knee flexion will produce an augmented cardiovascular response, due to an increase in EMG activity, and thus reflect an increase in intensity. Heart rate is a much cheaper and simpler variable to measure compared to EMG activity and can be more easily utilised when training at home. Due to this fact HR is the most widely used indication of intensity for aerobic exercise (Achten and Jeukendrup, 2003). Further to this setting training at a precise target HR is a useful indication of overall stress (Jeukendrup and VanDiemen, 1998), which may help to optimise adaptations and avoid over training (Achten and Jeukendrup, 2003). Thus establishing the relationship between the cardiovascular response and knee joint angle for the isometric wall squat exercise is a key element that will be explored in this research.

### *1.6.2c The prescription of constant position isometric wall squat exercise intensity using an incremental test*

If a relationship does indeed exist between HR and the wall squat knee joint angle, and this can be established from an incremental test, then the methods of Wiles, Coleman and Swaine (2010), as outlined in section 1.5.1 (page 20), could be adapted to prescribe wall squat exercise intensity for home-based training. For example, participants could complete a pre-training incremental test involving several stages



of wall squat exercise performed at increasing levels of knee flexion. Knee joint angle would then be plotted against HR for each incremental stage so that it would be possible to interpolate the knee joint angle required to elicit a specific HR value. Thus it is possible that home-based isometric training could be completed at an individualised wall squat position, set via knee joint angle, to elicit a precise target HR value. While setting wall squat intensity from an incremental test does appear to be a viable method, a key feature of the test designed by Wiles et al. (2008b) was that isometric exercise was performed at a constant EMG activity level to produce an attenuated 'steady-state' cardiovascular response at each incremental stage. Indeed, HR did not significantly alter during the last 30 seconds (90 vs. 120 seconds) of each incremental stage (100.5 vs. 100.7 beats·min<sup>-1</sup>;  $P > 0.05$ ) (Wiles et al., 2008b). Achieving a 'steady-state' is necessary to be able to prescribe intensity from an incremental test (Kraemer, Fleck and Deschenes, 2012). It is unknown whether wall squat exercise performed at a constant position will produce a 'steady-state', however the likely pattern of acute cardiovascular response will be discussed in proceeding section 1.6.2d (page 40).

Utilising an incremental test to prescribe isometric wall squat exercise intensity may provide a safer, more appropriate method, compared to performing a MVC, as maximal levels are reached gradually. This is an important feature to consider as it is known that isometric contractions can produce a powerful pressor response and cause substantial and sudden circulatory stress (Fisher et al., 1973). Therefore performing abrupt isometric exercise, such as a MVC test, is not recommended particularly for patients with CVD (Fisher et al., 1973). However, an incremental test is designed to progressively increase intensity from resting levels and provide gradational stress to a participant (Wasserman et al., 1999). Indeed, it has been found that an incremental isometric test produces a gradual increase in BP with each exercise stage until peak values are attained (Wiles et al., 2008b). Whereas a MVC involves recruiting as many muscle fibres as possible (Knuttgen and Kraemer, 1987) and therefore applies maximum stress to the participant from the onset. Indeed, when performing a 100% MVC, BP has been shown to produce an extreme response in the first 3 seconds (MacDougall et al., 1992). As previously alluded to, this considerable cardiovascular stress may not be suitable for special populations (Mitchell and Wildenthal, 1974). Further to this, there is also some concern with regards to injury, as performing a maximal strength test can also place great stress on the muscles, connective tissue and joints (Baechle, Earle and Wathen, 2008). Therefore this may not be suitable for those individuals who are untrained or inexperienced (Baechle, Earle and Wathen, 2008) as this could cause muscle soreness or injury (Braith et al., 1993). With these points considered, prescribing isometric wall squat intensity from an incremental test may provide a more appropriate and safer method than those previously advocated in the literature.

#### *1.6.2d Predicting the possible acute cardiovascular response to constant position isometric wall squat exercise*

It is pertinent to discuss the likely cardiovascular response to constant position isometric wall squat exercise, as producing an attenuated 'steady-state' is a prerequisite of any incremental test (Kraemer, Fleck and Deschenes, 2012). As previously highlighted in section 1.5.1b (page 22) it appears that a constant position task, such as the wall squat, could cause the cardiovascular response to increase at a more rapid rate than constant force contractions (Hunter et al., 2002; 2008; Rudroff et al., 2011) due to the unstable nature of the task which causes heightened sensitivity of the stretch reflex (Maluf and Enoka,

2005a). Thus at a first glance it would appear that constant position isometric contractions may produce a cardiovascular response that cannot be controlled precisely. However, while this research does provide an interesting insight into the cardiovascular responses to constant position work, any potential inferences to the isometric wall squat exercise need to be made with caution. There are several factors that may influence the pattern of cardiovascular response, such as the contraction duration, exercise type (single vs. multi joint) and position restraints; these factors will be discussed in the following paragraphs.

First of all, the aforementioned research studied fatiguing contractions of a prolonged duration ( $\geq 5$  minutes 25 seconds), whereas the proposed duration for the current study is a finite time of 2 minutes. Constant position contractions performed indefinitely until fatigue may produce a different pattern of cardiovascular response due to the fact that muscle recruitment will likely increase over time to maintain the force output (St Clair Gibson, Lambert and Noakes, 2001), which could potentially lead to increases in the cardiovascular response through greater central command (Franke, Boettger and McLean, 2000), as discussed in section 1.5.1b (page 22). Conversely, shorter duration constant position contractions may not induce such fatigue associated increases in motor unit recruitment and thus produce an attenuated cardiovascular response in comparison. Using the results from the constant position research discussed, it is difficult to infer whether the first few minutes produced an attenuated response in comparison as the HR and/or MAP data were generally not presented in 30 second time periods (Hunter et al., 2002; Rudroff et al., 2005; Rudroff et al., 2007; Hunter et al., 2008) due to the lengthy nature of the contractions performed. To accurately analyse the cardiovascular response of a 2 minute wall squat in this research it would be beneficial to analyse the data at 30 seconds intervals, as done by Wiles et al. (2008b).

Further to this, for any given isometric task there are numerous possible muscle activation patterns that could be utilised to produce the desired outcome (van Bolhuis and Gielen, 1999) and the possibilities increase with a greater number of joints and muscles involved (Boyas, Maïsetti and Guével, 2009). The aforementioned constant position studies have typically utilised single-joint tasks that aimed to work a particular muscle or muscle group (Hunter et al., 2002; Maluf et al., 2005b; Rudroff et al., 2005; Enoka et al., 2011). Whereas squat based exercises are compound, multi-joint activities that utilise more than one muscle group over several joints (Fleck and Kraemer, 2004). Indeed, the isometric wall squat primarily utilises the quadriceps, as well as secondary muscles such as gluteus maximus and hamstrings (Contreras, 2014) to produce knee and hip extension to maintain the wall squat position (Escamilla et al., 2009a; 2009b). The triceps surae, hip adductors and abductors, abdominal muscles, and the back extensor muscles may also be potentially utilised, as with the traditional squat exercise (O'Shea, 1985; McCaw and Melrose, 1999; Delavier, 2010). It has been suggested that such multi-joint tasks, that involve several joints and muscles, may allow participants to develop several different patterns of muscular recruitment (McBride, Deane and Nimphius, 2007; Boyas, Maïsetti and Guével, 2009), which compared to single-joint tasks may delay the onset of localised fatigue and consequently attenuate the cardiovascular response produced.

During fatigue, there is a partial impairment of the motor system and the central nervous system may compensate by utilising the abundance of motor apparatus to maintain the required performance target (Kruger et al., 2007). During single-joint isometric position constant tasks, EMG activity has been found to increase (Hunter et al., 2002; Rudroff et al., 2005; 2007; Hunter et al., 2008), presumably to maintain

the required force output (St Clair Gibson, Lambert and Noakes, 2001). However, McBride, Deane and Nimphius (2007) speculated that muscle activity pattern strategies may be utilised by multi-joint tasks when the force producing capacity of the muscle is reduced. Related to the squat, the antagonist (hamstrings) or synergist muscles (triceps surae) may compensate when the agonist (quadriceps) cannot maintain the required force output (McBride, Deane and Nimphius, 2007). Boyas, Maïsetti and Guével (2009) explored the EMG activity among the synergist muscles (trunk and thigh muscles) involved in the maintenance of a multi-joint isometric constant position hiking task. While it was observed that EMG activity did increase during the task, as occurs with single-joint tasks, changes in the relative contribution among synergists was also observed. The ratio of EMG activity between the trunk and thigh muscles increased, which suggested that the trunk muscles played a greater contribution to hip flexion as time went on. Such modulation of the central nervous system may delay the decline in force output (Boyas, Maïsetti and Guével, 2009) and potentially reduce localised muscle fatigue. This may consequently decrease the metabolite accumulation that is associated with fatigue (Enoka and Duchateau, 2008) and thus modify feedback to the cardiovascular control centre from the group III and IV muscle afferents (Mitchell, 1990), which may attenuate the HR and BP response.

A final and important point to make is that in the single-joint studies the participant was restrained using straps to limit any unwanted movement (Hunter et al., 2002; Rudroff et al., 2005; Hunter et al., 2008) and provide stability (Rudroff et al., 2007), which would minimise any deviation from the precise exercise position presumably to isolate specific muscle groups. However with regards to the multi-joint wall squat, although the exercise position is set via the knee joint angle there are no direct restraints placed on the body. This is necessary to ensure the simplistic nature of the exercise is maintained for home-based training. Therefore slight changes in the body position can still occur that may alter the relative contribution of the muscles involved. For example, when performing a wall squat the back is positioned against the wall, however the location of the support force can be altered (Blanpied, 1999). Applying the support force at hip level increases the activation of the quadriceps, whereas if the support force is located at scapula level the activity of the gluteus and hamstrings muscle groups are increased (Blanpied, 1999). While instructions can be given to the participant to apply the support force at certain position, this change in body position can be extremely subtle and therefore difficult to detect by an investigator. Furthermore, as isometric exercise is known to cause muscular discomfort (Lind, 2011; Millar et al., 2013b), it is likely that the participants may endeavour to relieve this discomfort through such subtle changes in the exercise position. If such adjustments were to occur, this may reduce localised fatigue, which may attenuate the cardiovascular response as previously alluded to.

In light of the research presented it appears that a single-joint constant position task causes the cardiovascular response to increase throughout the isometric contraction duration. However, there are several highlighted limitations when applying this work to short duration, multi-joint isometric tasks and thus the likely cardiovascular response to the isometric wall squat exercise still remains elusive. It is plausible to suggest that the wall squat may utilise a multitude of different muscle recruitment strategies to maintain the desired exercise position due to its multi-joint and unrestrained aspects, which may reduce localised fatigue and attenuate the cardiovascular response similar to that of constant EMG isometric work. Thus it is possible that an attenuated or 'steady-state' response could be achieved and that the methods of Wiles et al. (2008b) could be applied to prescribe the wall squat intensity from an incremental

test. However, this remains to be established and is a fundamental element that will be explored in this thesis.

#### *1.6.2e The home-based isometric wall squat exercise training protocol*

If it is indeed possible to utilise constant position isometric wall squat exercise within an incremental test then home-based training could be prescribed at an individualised wall squat knee joint angle to elicit a precise target HR value, as previously outlined in section 1.6.2c (page 39). Previous studies that have utilised HR to set the isometric training intensity have used target values ranging from 70% to 95% of the  $HR_{peak}$  attained during the pre-training incremental test (Devereux, Wiles and Swaine, 2010b; Wiles, Coleman and Swaine, 2010; Baross, Wiles and Swaine, 2012). However, it is proposed that isometric wall squat exercise training should be prescribed at 95%  $HR_{peak}$  as it has been previously found that this higher isometric intensity can produce reductions in resting BP at an enhanced rate of 4 weeks (Devereux, Wiles and Swaine, 2010b). Within this study isometric exercise was completed 3 times per week for 4 weeks and each session was comprised of four 2 minute exercise bouts with 3 minutes rest in between. It is put forward that a shorter rest period, such as 2 minutes (Wiles, Coleman and Swaine, 2010), should be used in order to reduce the time commitment required, as this is a known barrier to physical activity and exercise (Trost et al., 2002; Lascar et al., 2014).

Due to the variable nature of HR (Scott, Randolph and Leier, 1989; Stanforth et al., 2000; Højgaard et al., 2005) it is important to set a target heart rate range (THRR) for training rather than selecting one single target value. Previous studies that have prescribed training intensity relative to a target HR required the average training HR value to be within  $\pm 5\%$  of the target (Devereux, Wiles and Swaine, 2010b; Wiles, Coleman and Swaine, 2010). For example, in the study of Wiles, Coleman and Swaine (2010) the mean target HR for the high intensity group was  $101 \text{ beats} \cdot \text{min}^{-1}$  and therefore the THRR was 95 to 105  $\text{beats} \cdot \text{min}^{-1}$ . If the actual training HR value were to fluctuate within this range between training sessions it could simply be viewed as natural variability, whereas if a HR were to fall outside this THRR this could be interpreted as a 'real' change (Eliaszewicz et al., 1994) potentially due to training adaptations. Consequently, the individual's training EMG value would be adjusted for the following IET session in an attempt to alter the HR value within the THRR and ensure an adequate cardiovascular stimulus was still attained. It was possible to use the  $\pm 5\%$  value in previous IET studies due to the fact that constant EMG isometric contractions were performed, which produce an attenuated response compared to constant force work (Schibye et al., 1981; Franke, Boettger and McLean, 2000) and therefore the magnitude of the HR response would be reduced so that  $\pm 5\%$  was a realistic THRR (J.D. Wiles, personal communication, October 2013). However, compared to the aerobic training THRRs, the  $\pm 5\%$  value used in the IET studies appears to be somewhat arbitrary and presents a smaller range. Indeed, the THRR used to determine the intensity levels for cardiorespiratory (aerobic) exercise for most adults is 10% (66-76% maximum heart rate ( $HR_{max}$ ) for moderate intensity) and/or 18% (77-95%  $HR_{max}$  for vigorous intensity) (Garber et al., 2011). It is proposed that a more precise method for determining the THRR should be used for IET, which considers the natural variability of HR; this is a key idea that will be explored within this thesis.

In review of the current literature and ideas presented, it is suggested that constant position wall squat exercise may provide a viable alternative isometric contraction style that could be utilised within a novel

home-based training programme designed to reduce resting BP. Such accessible and inexpensive IET may help to remove some of the key barriers to participation and adherence in order to provide an effective lifestyle modification for the prevention and/or treatment of hypertension. However, there are several highlighted issues that need to be explored before the constant position wall squat can be implemented within an IET programme, which mainly includes: 1) establishing the adjustment of knee flexion as a viable method for altering isometric wall squat intensity, and 2) determining the efficacy of utilising an incremental test for the prescription of wall squat intensity; these will be investigated within the studies of this thesis.

## **1.7 Executive summary**

Isometric training has been shown to reduce resting BP in both normotensive and hypertensive populations and there is an increasing amount of evidence to suggest that it is an effective non-pharmacological alternative for the prevention and treatment of hypertension, particularly as it is short in duration and easy to perform. However, the vast majority of training studies involved the use of expensive and/or laboratory-based equipment, which is neither time nor cost effective. These two factors may reduce the compliance to training and consequently the likelihood of BP reductions and a resultant positive clinical outcome. The isometric wall squat exercise has the potential to be prescribed within a home-based isometric training protocol as it is cheap and simple to perform; however the wall squat has never previously been utilised within a training regime aimed at reducing BP.

Previous IET studies have set intensity at either a constant force (traditional % MVC) or constant EMG, however these methods are not suitable for home-based training as they require complicated and/or expensive laboratory-based equipment. Thus, if IET is to be widely prescribed in the home, an alternative method for adjusting and monitoring intensity must be established. It is proposed that the isometric wall squat exercise could be prescribed at a constant position (knee joint angle), which has not previously been utilised within an IET study aiming to reduce resting BP. If adjusting the knee joint angle can indeed change the wall squat intensity and, furthermore, induce HR changes in a linear fashion during an incremental test, then the methods of Wiles et al. (2008b) can be utilised to set an individualised knee joint angle to elicit a target HR during training. Completing an incremental test may provide a more suitable method to determine exercise intensity for inexperienced individuals as maximal levels are reached gradually, compared to the traditional MVC test, placing less stress on the cardiovascular and musculoskeletal systems. However, for the wall squat to be utilised within an incremental test a steady-state HR response must be achieved at each work stage. The likely cardiovascular response of this position constant task is unknown and requires exploration.

Once a method for prescribing wall squat intensity has been established then a home-based training protocol can be created and implemented to elucidate the efficacy of using isometric wall squat exercise for the reduction of resting BP. While it is established that isometric training does induce positive BP adaptations the precise mechanisms that bring about such a change remain elusive. It is particularly interesting that a change in BP is governed by a change in TPR and/or  $\dot{Q}$  yet few studies have measured these variables. Moreover, those studies have had low statistical power due to small sample sizes and have consequently found no significant differences. Studying TPR and  $\dot{Q}$  using a larger sample size may help to improve the current understanding of the resting BP reduction mechanisms. Finally, it is prudent

to establish this novel home-based isometric wall squat training protocol with a younger normotensive population first in order to produce a safer, more homogenous response.

### **1.8 Research aims and objectives**

To conclude, the overall aim of this thesis is to investigate a new isometric exercise mode that can be implemented within an accessible home-based training protocol aimed at reducing resting BP and also enhance the understanding of the mechanisms that cause such a BP reduction.

Therefore the objectives of this thesis are:

1. To develop a method for adjusting isometric wall squat exercise intensity via knee joint angle.
2. To determine a method for prescribing home-based isometric wall squat exercise training and evaluate the efficacy of using an incremental test.
3. To explore the chronic cardiovascular adaptations to home-based isometric wall squat training, with particular emphasis placed on resting BP.
4. To elucidate the potential physiological mechanisms that induce BP adaptations with isometric training with specific focus on TPR and  $\dot{Q}$ .



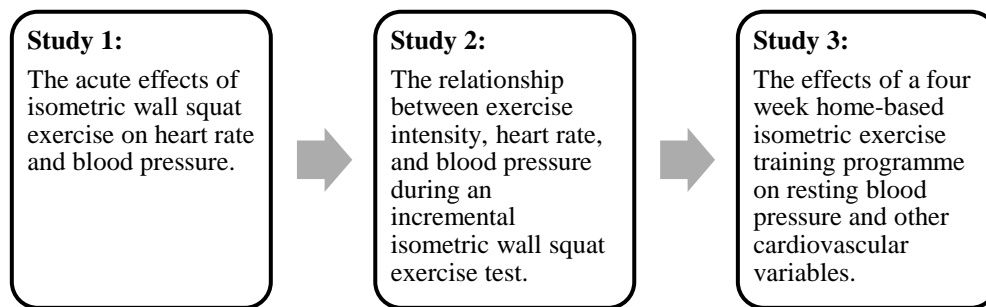
## CHAPTER 2: GENERAL METHODS

### 2.1 Introduction

This chapter will present the general methods used throughout the studies constituting this thesis to provide an understanding of the research approach used, participants studied and variables measured. Specific detail will be included regarding the measurement and recording of the following variables: blood pressure (BP), heart rate (HR), cardiac output ( $\dot{Q}$ ), total peripheral resistance (TPR), stroke volume (SV), isometric wall squat knee joint angle and rate of perceived discomfort (RPD). This chapter will also provide the necessary information regarding the validity and reliability of each variable.

### 2.2 The research approach

The research approach used in this thesis was experimental in nature and adopted a quantitative approach. Study 1 developed a method for adjusting isometric wall squat exercise intensity at a constant position, via knee joint angle. Further to this, the acute cardiovascular responses of HR and BP to isometric wall squat exercise were also explored to ascertain the suitability, reliability and safety of this exercise mode; the findings of study 1 will be presented in Chapter 3. Study 2 investigated the efficacy of using an incremental test to prescribe wall squat exercise intensity for training; this will be detailed in Chapter 4. Finally, study 3 was designed to provide an insight into the chronic BP adaptations following 4 weeks of home-based isometric wall squat training. Furthermore, several other cardiovascular variables ( $\dot{Q}$ , TPR, HR and SV) were also investigated to provide a possible explanation of the physiological mechanisms involved in producing chronic BP adaptations; the results of this final study will be presented in Chapter 5. Figure 2.1 illustrates the order that the studies within this thesis were carried out.



**Figure 2.1.** Schematic of the studies contained within this thesis.

All testing for studies 1 and 2 was carried out in a controlled environment in the Sport and Exercise Science Laboratory at Canterbury Christ Church University. Part of study 3 was also completed in the same laboratory; however the four week home-based training programme was completed in a location of the participant's choice. Testing procedures in all of the studies within this thesis were carried out by the same investigator. All studies were approved by the Canterbury Christ Church University Ethics Committee and all procedures were conducted according to the Declaration of Helsinki.



## **2.3 Participant information**

### ***2.3.1 Participant inclusion criteria***

Healthy males (aged  $29 \pm 7$  years) were recruited for each of the studies within this thesis. 'Healthy' was defined as those not suffering from any clinically diagnosed injury or disease that could conceivably affect their wellbeing during the testing period or the results obtained. Participants were also required to be non-smokers and not taking any medication that could influence their performance or cardiovascular function. All participants were screened before data collection using a standardised health and medical questionnaire (see Appendix 1, page 209) to self-report current health status; this was completed during the familiarisation process (see section 2.3.5, page 50). A further prerequisite of each study was that participants must not be classified as hypertensive. Participants with resting BP levels  $\geq 140$ mmHg SBP and/or  $\geq 90$ mmHg DBP were not allowed to partake, as levels above this range would be classified as hypertensive (Williams et al., 2004). Blood pressure was measured prior to data collection to confirm resting BP status using the protocol outlined in section 2.5.2 (page 52). Women were excluded from the study as BP has been shown to be greatly affected by the menstrual cycle (Dunne et al., 1991).

### ***2.3.2 Participant recruitment***

The majority of participants within the study were either members of staff or students from the Department of Sport Science, Tourism and Leisure at Canterbury Christ Church University. Some participants were also sourced from local sports clubs or from personal acquaintance. Participation was voluntary and included no monetary benefits, however feedback and advice regarding the health and fitness benefits of exercise were provided as an incentive. A number of participants volunteered for multiple studies.

To avoid any suggestion of coercion, the same recruitment process was followed for all prospective participants. All prospective participants were supplied with a participant information sheet and an informed consent form for the specific research that they wished to volunteer for. The participant information sheets for the three studies can be found in the Appendix (Appendices 2-4; pages 211-224). All three information sheets contained a written explanation of the studies nature and purpose, testing requirements and study procedures. Furthermore, any potential benefits, risks and the likelihood of some minor discomfort were also described. Participants were also given an informed consent form to read (see Appendix 5, page 225, for studies 1 and 2 and Appendix 6, page 227, for study 3). Once completed, the informed consent form highlighted that the participant had: 1) read and understood the participant information sheet and had the opportunity to ask questions, 2) understood that participation was voluntary, and 3) agreed to take part in the study. All participants were given approximately 1 week to read and digest the participant information sheet and informed consent form, after which time further contact was then made by the researcher. During this follow up call it was confirmed that the prospective participant had read the information provided and were satisfied regarding any queries that may have arisen. The participant was then asked whether they wished to participate in the study and, if so, arrangements were made for a familiarisation visit. During this familiarisation visit both the participant and researcher signed the informed consent form. At this point, it was again made clear that participation in the study was completely voluntary and that they were free to withdraw at any point without giving any

reason should they so desire. Participants were also reminded of the testing requirements, as outlined in section 2.3.4 (page 50).

### **2.3.3 Participant sample size**

The selection of a study sample size is an ethical issue due to several factors. Namely that if a sample size is too small a clear finding may not be produced, however if the sample size is conversely too large resources may be needlessly wasted (Hopkins, 2006). In order to calculate the sample size required for a study the following factors must be considered: 1) the smallest worthwhile effect that is to be detected, 2) the Type I and Type II error rates, 3) the study design (Hopkins, 2001). Reliability of the dependent variable is also important when estimating the study sample size. This is due to the fact that participant values are more reproducible if the reliability is high and thus it is more likely that any true changes in a variable will be detected. This also means that fewer participants are required to be recruited (Hopkins, 2001). For a longitudinal study with a crossover design the sample size required can be calculated using the following equation:

$$n = 16 (s^2/d^2)$$

where  $n$  is the total number of participants required for the study,  $s$  is the within-subject variation and  $d$  is the smallest worthwhile difference that is required to be detected (Hopkins, 2001). This equation gives a study power of 0.80 (equivalent to a Type II error rate of  $\leq 20\%$ ), with  $P = 0.05$  significance level (equivalent to a Type I error rate of 5%) (Hopkins, 2001). Thus, it can be understood that there is an 80% certainty of finding a statistically significant ( $P < 0.05$ ) worthwhile change.

This equation considers the most important type of reliability, which is the within-subject variation ( $s$ ) (Hopkins, 2000). The within-subject variation is the difference in a measured value of a participant from one measurement to another and is concerned with the reproducibility of a participant's values when later obtained on the same equipment by the same investigator (Hopkins, 2000). Any change recorded outside the within-subject variation is considered to be a 'real', significant change. The coefficient of variation (CV) can be used within the equation of sample size, which is the within-subject standard deviation expressed as a percentage of the mean value (Hopkins, 2001). For the purpose of sample size calculation for the studies within this thesis, reliability data from unpublished (see section 3.2.2, page 93) and published (Wiles, Coleman and Swaine, 2010) work previously conducted within the Department was utilised.

Further to this, the equation also considers the smallest effect worth detecting. It has often been suggested that the Cohen effect size statistic of 0.2 (Cohen, 1988) should be considered as the value for the smallest worthwhile effect (Batterham and Atkinson, 2005). However, using this value often results in an overly large estimated sample size in order to provide the power to detect the small effect (Batterham and Atkinson, 2005), which as discussed previously would ultimately incur an unnecessary, inefficient use of resources. Instead, in order to gain the most accurate predictions the value for the smallest worthwhile effect should ideally be based upon previous related studies that contain a similar intervention measuring the same outcome variables or alternatively the value could be derived from preliminary or pilot studies (Batterham and Atkinson, 2005). For the purpose of calculating the smallest worthwhile effect for the studies within this thesis, the data from unpublished (see section 3.2.2, page 93) and published (Wiles,

Coleman and Swaine, 2010) work previously conducted within the Department was utilised. In the studies in this thesis the value for the smallest worthwhile effect ( $d$ ) was entered as a proportion (expressed as a percentage) of the mean group score (Kirkland et al., 2008), so that the  $d$  value was in comparable units to  $s$  (CV expressed as a percentage). After the sample size calculations were completed, the estimates were inflated by 10 to 30% to allow for participant drop out (Hopkins, 2006).

#### **2.3.4 Testing requirements**

For the duration of each study, all participants agreed to maintain an abstinence from food 2 hours pretesting, from caffeine 4 hours pretesting, from alcohol 12 hours pretesting and were asked not to perform any strenuous exercise 24 hours pretesting, as these have been shown to influence HR and/or BP measurement(s) (Potter et al., 1986; Jansen and Lipsitz, 1995; Shapiro et al., 1996; James, 2004; Rezk et al., 2006). Furthermore, participants were required to maintain their regular dietary habits and level of physical activity throughout the testing period. These testing requirements were outlined in the participant information sheet and adherence to these conditions was verbally confirmed with each of the participants prior to the start of each session. None of the participants indicated that they had deviated from this protocol at any point.

#### **2.3.5 Familiarisation**

Before any familiarisation protocols were conducted participants completed a health and medical questionnaire in order to self-report their current health status (Appendix 1, page 209). Participants then completed and signed a written informed consent form (see Appendix 5, page 225, for studies 1 and 2 and Appendix 6, page 227, for study 3). At this point, it was made clear to the participants that they were free to withdraw from the study at any point should they so desire.

Once all paperwork had been completed, anthropometric measurements of stature and body mass were recorded to provide descriptive data of the participants; this data would also be entered into the Finometer BP and  $\dot{Q}$  measurement device and HR monitor, as outlined in sections 2.5.6 and 2.6.4 (pages 59 and 67, respectively). Stature was measured in centimetres (cm) using a telescopic measuring rod (Seca 220, Seca GmbH & Co. KG., Hamburg, Germany) and body mass was measured in kilograms (kg) using mechanical column scales (Seca 710, Seca GmbH & Co. KG., Hamburg, Germany). Also, the circumference of the participant's middle phalanx of the left middle finger and the left upper arm (greatest circumference whilst relaxed) were measured in centimetres (cm) using an ergonomic circumference measuring tape (Seca 201, Seca GmbH & Co. KG., Hamburg, Germany) to ensure the appropriate BP cuff sizes were used throughout testing, as outlined in section 2.5.3 and 2.5.6 (pages 54 and 59, respectively).

The participant's normotensive status (SBP < 140mmHg and/or DBP < 90mmHg) was then confirmed by taking a measurement of resting BP using an automated BP monitor (Dinamap Pro 200, GE Medical Systems, Tampa, Florida), as outlined in section 2.5.3 (page 54). After 10 minutes of rest in a seated position, three measurements of BP (SBP, DBP, MAP) were taken with 60 seconds between each measurement. The lowest of three measures (for each SBP, DBP, and MAP) were used for the purpose of BP classification (Devereux, Wiles and Swaine, 2010b; Wiles, Coleman and Swaine, 2010). All participants were made aware that if they were categorised as having high BP they would not be allowed

to take part in the study. It would then be strongly recommended to participants that they consult a qualified medical practitioner to have their BP status confirmed. In order to facilitate this process the participant would be issued with a standard letter detailing the measurement procedure and their BP results (Appendix 7, page 229).

Finally, the testing protocols and measurement procedures were verbally explained and demonstrated to the participants. Participants then performed each of the testing procedures to ensure that they were accustomed to the protocols and equipment before testing began.

## **2.4 Measurement of the studies variables**

Several different variables were manipulated and measured within the studies of this thesis. In the laboratory-based studies, 1 and 2, the participant's knee joint angle (independent variable) was manipulated during wall squat exercise in order to examine the acute responses and relationships with BP and HR (dependent variables). In study 3, these variables were once again manipulated and measured in the laboratory to prescribe wall squat training intensity, as well as the measurement of RPD (dependent variable). To monitor and adjust the participant's response to wall squat training in the home, the knee joint angle was assigned and altered using a 'Bend and Squat' device (see section 2.10.5, page 83) and HR and RPD were recorded. To determine and help explain the chronic adaptations to home-based wall squat training, HR and BP were measured at rest in the laboratory as well as  $\dot{Q}$ , TPR and SV. In the remaining sections of this chapter the equipment and methods used to measure these variables will be explained. A brief description of each variable and its measurement will be outlined as well as a detailed narrative of the measurement techniques used within this thesis. Furthermore relevant previous work related to the validity and reliability of each measure will be discussed. Validity is defined as "the extent to which measurements actually reflect the phenomena being studied" (p. 288) and reliability is defined as "the extent to which findings would be similar if the research were to be repeated" (p. 287) (Gratton and Jones, 2010).

## **2.5 Blood pressure (BP) measurement**

### ***2.5.1 Background information on blood pressure***

Blood pressure can be defined as the force exerted by the blood on the blood vessel walls (Tortora and Derrickson, 2012). There are three key BP values to consider. Systolic BP is the force that the blood exerts against the arterial walls during ventricular contraction and it is the highest pressure attained during systole in the cardiac cycle. Conversely, DBP is the force that the blood exerts on the arterial walls during ventricular relaxation and is the lowest BP measured throughout a cardiac cycle during diastole (McArdle, Katch and Katch, 2010; Tortora and Derrickson, 2012). Finally, MAP represents the average force of the blood on the arterial walls throughout a whole cardiac cycle (McArdle, Katch and Katch, 2010). Mean arterial pressure is not simply an average of SBP and DBP as the heart remains in diastole longer than systole. Mean arterial pressure can be approximately estimated using the equation:

$$\text{MAP} = \text{DBP} + \left[ \frac{1}{3} (\text{SBP} - \text{DBP}) \right]$$

(McArdle, Katch and Katch, 2010; Tortora and Derrickson, 2012).

Mean arterial pressure is often thought of as the ‘driving pressure’ (Smith and Fernhall, 2011). This is due to the fact that MAP represents the pressure gradient for the entire systemic circulation (Sherwood, 2014) and this is an important determinant of blood flow (Guyton and Hall, 2006). Indeed, the pressure gradient is the difference in pressure between two ends of the systemic circulatory system (Sherwood, 2014) and is the force that pushes blood through the blood vessel (Guyton and Hall, 2006). A second determinant of blood flow is vascular resistance, which is the impedance to flow represented by the blood vessels (Guyton and Hall, 2006). The relationship between flow, resistance and pressure can be described in a similar way to Ohm’s law for electrical circuits (Mayet and Hughes, 2003) and consequently blood flow can be calculated using the formula:

$$F = \frac{\Delta P}{R}$$

in which F represents the blood flow through the vessel,  $\Delta P$  the change in pressure between two ends of the blood vessel ( $P_1 - P_2$ ), and R the resistance to flow (Guyton and Hall, 2006). This relationship is sometimes referred to as Darcy’s Law (Mayet and Hughes, 2003), which is the hydraulic equivalent of Ohm’s Law (Levick, 1991). The equation can be rearranged and expressed in alternative algebraic forms, such that  $\Delta P = F \times R$ , and when applied to the whole systemic circulation gives the equation:  $MAP = \dot{Q} \times TPR$  (Sherwood, 2014). Thus, MAP is determined by both cardiac output and total peripheral resistance (Smith and Fernhall, 2011).

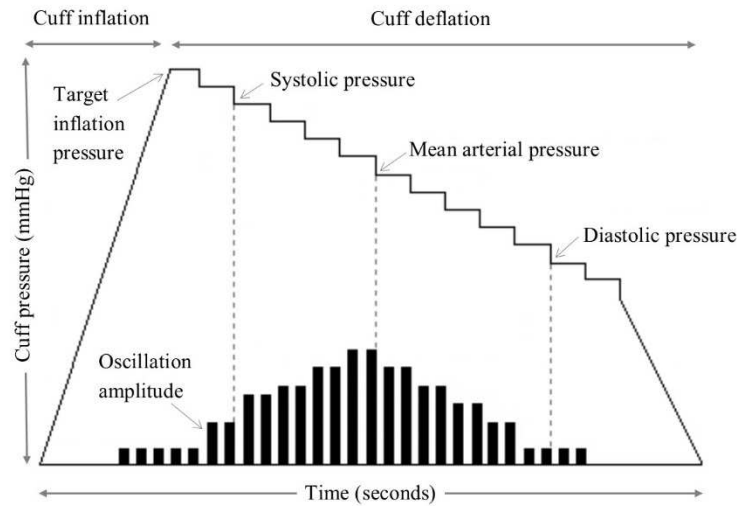
In a clinical setting the gold standard method used to measure BP is the auscultatory method, which typically involves the use of a mercury sphygmomanometer and the Korotkoff sound technique (Pickering et al., 2005). However, this procedure may often lead to the misclassification of BP from inaccuracies in the methods such as poor technique (Pickering et al., 2005). Due to this fact, the use of automated BP measurement devices is gradually increasing (Pickering et al., 2005). Typically, automated monitors indirectly measure BP by applying an upper arm cuff over the brachial artery that automatically inflates and deflates (O’Brien et al., 2001). Automated BP monitors use a variety of different methods to determine BP, with the majority using the oscillometric method (Ramsey, 1991). Automated BP devices are easy to use, require less training than auscultatory methods and reduce observer variability (Chang, Rabinowitz and Shea, 2003). However, only one or two individual measurements are typically recorded using both the auscultatory method and automated BP devices. Thus, a somewhat crude average BP level is attained, which is momentary and does not take into account the beat-to-beat variability of BP (Pickering et al., 2005). Thus a continuous measurement of BP is more desirable. The primary method utilised to measure BP in a continuous manner is through the invasive cannulation of the artery, which measures intra-arterial pressure (Truijen et al., 2012). However, due to the invasive nature of the procedure and the associated risks the application of this method is limited (Langewouters et al., 1998). An alternative non-invasive technique used to continuously measure BP is through finger cuff technology (Truijen et al., 2012) such as that utilised by the Finometer, which is the device used to measure BP during rest and exercise in the studies in this thesis. Resting BP was also measured using an automated device in order to initially confirm the participant’s normotensive status during the familiarisation session, as outlined in section 2.3.5 (page 50).

### ***2.5.2 Dinamap measurement of blood pressure***

Resting BP was measured noninvasively using an automated BP monitor (Dinamap Pro 200, GE Medical Systems, Tampa, Florida). The acronym Dinamap stands for 'Device for Indirect Noninvasive Automatic Mean Arterial Pressure'. The Dinamap measures BP using the oscillometric method, which is based on the principle that oscillations of the arterial wall are created as pulsatile blood flows through an artery (GE Healthcare, n.d.). The Dinamap consists of a monitor, air hose and pneumatic upper arm cuff. The upper arm cuff of the Dinamap contains a transducer that detects the oscillations of the arterial wall, which appear as tiny pulsations in cuff pressure.

To measure BP a cuff is placed around the upper arm and is inflated to a target pressure of 160 mmHg for adult participants (GE Medical Systems, 2002), which is normally high enough to occlude the underlying brachial artery. If the initial inflation is not adequate to occlude blood flow, the 'Systolic Search' feature of the Dinamap identifies the lack of SBP and immediately re-inflates the cuff to search at higher cuff pressures than the initial target to identify SBP. The maximum pressure allowed in the 'Systolic Search' is 290 mmHg, which is limited by the normal range for cuff pressures (GE Medical Systems, 2002). Once the target inflation pressure is established the arm cuff is incrementally deflated. The arm cuff is deflated in increments of 5 mmHg each time two pressure pulsations of relatively equal amplitude are detected; this is termed stepped-deflation (GE Medical Systems, 2002). The deflation rate depends on the frequency of the matched pulses and thus is based on the participant's HR. If however matched pulses are not detected within several seconds, the cuff is subsequently deflated to the next step (GE Medical Systems, 2002).

As the arm cuff is deflated and blood flow is increased, the amplitude of the pulsations begins to change, however the time interval between the pulsations remains the same as this is determined by the participant's pulse rate. The transducer in the upper arm cuff measures the amplitude of the pulsations and the subsequent cuff pressure. At each step of the deflation process a microprocessor stores the information related to the cuff pressure, matched pulse amplitude and time between successive pulses (GE Medical Systems, 2002). This microprocessor also controls the inflation and deflation of the cuff. Incremental deflation continues until DBP is determined or cuff pressure falls below 8 mmHg (GE Medical Systems, 2002). The inflation and deflation process to measure BP takes approximately 30 seconds. See Figure 2.2 for the Dinamap's BP determination sequence.



**Figure 2.2.** The blood pressure determination sequence of the Dinamap. Adapted from GE Healthcare (n.d.) and GE Medical Systems (2002). Systolic, mean and diastolic pressures are estimated by identifying the cuff pressures that correspond to certain oscillation amplitudes within the cuff during deflation.

Once DBP is determined the monitor finishes deflating the arm cuff to zero detected pressure and the stored data is then analysed. The pattern of change in pulsation amplitude is compared to cuff pressure and is analysed to determine BP using an algorithm. First of all, MAP is determined by the algorithm as the lowest cuff pressure at the point that the greatest pulsation amplitude (maximum oscillation) is detected (GE Healthcare, n.d.). The maximum and minimum MAP values detectable by the Dinamap are 15 and 215 mmHg, respectively (GE Medical Systems, 2002). Next SBP is determined by reviewing the oscillation data above MAP and is detected by the algorithm as the cuff pressure at which the pulsation amplitude is approximately 0.5 (GE Healthcare, n.d.). This corresponds to the onset of rapidly increasing pressure oscillations (Bogert and van Lieshout, 2005). The maximum and minimum SBP values detectable by the Dinamap are 30 and 245 mmHg, respectively (GE Medical Systems, 2002). Finally, DBP is determined by reviewing the oscillation data below MAP and is detected by the algorithm as the cuff pressure at which the pulsation amplitude is approximately 0.625 (GE Healthcare, n.d.). This corresponds to the onset of rapidly decreasing pressure oscillations (Bogert and van Lieshout, 2005). The maximum and minimum DBP values detectable by the Dinamap are 10 and 195 mmHg, respectively (GE Medical Systems, 2002). These points for SBP, DBP and MAP do not always occur during an exact stepped-deflation phase and thus the algorithm will interpolate cuff pressures and pulsation amplitudes between steps if necessary (GE Healthcare, n.d.). The front panel then displays the calculated SBP, DBP and MAP values (GE Medical Systems, 2002).

### ***2.5.3 Laboratory-based measurement of resting blood pressure using the Dinamap***

In the familiarisation session, the circumference of the participant's upper left arm was measured (greatest circumference whilst relaxed) in centimetres using an ergonomic circumference measuring tape (Seca 201, Seca GmbH & Co. KG., Hamburg, Germany) to select the proper arm cuff size. There were four BP

cuff sizes available for use with the Dinamap in the studies; cuff bladder dimensions were child (12-19 cm), small adult (17-25 cm), adult (23-33 cm) and large adult (31-40 cm) (Dura-Cuf, Critikon, models 2781, 2779R, 2774, and 2791 respectively, GE Healthcare, Buckinghamshire, United Kingdom). In the circumstance that the cuff sizes overlapped, the larger cuff size was chosen (GE Medical Systems, 2002). Once the correct cuff bladder size was selected, the cuff was connected to the air hose, which was attached to the front of the Dinamap monitor.

Before placement of the arm cuff, the participant was asked to remove all clothing that covers the left arm ensuring that a participant's sleeve was not rolled up presenting a tourniquet effect (Pickering et al., 2005). The participant was then seated in a comfortable position with the legs uncrossed and the back supported. The appropriate sized upper arm cuff was then snugly positioned on the bare upper left arm so that the arrow on the cuff marked 'artery' was aligned with the brachial artery (located by palpating the antecubital fossa) and the middle of the cuff was positioned level with the right atrium (Pickering et al., 2005). The left arm was then supported on a side table on the left hand side of the chair.

After a 10 minute seated rest, three consecutive measurements of BP were taken separated by a 60 second period, in accordance with BP measurement recommendations (Pickering et al., 2005). Each BP measurement was initiated manually using the 'Manual' mode of the Dinamap. The lowest of the three BP measurements (including SBP, DBP and MAP) were used for analysis, as done so by (Devereux, Wiles and Swaine, 2010b; Wiles, Coleman and Swaine, 2010).

#### ***2.5.4 Published data on the validity and reliability of the Dinamap measurement of blood pressure***

To validate the accuracy of an automated BP measuring device specific protocols were developed by the Association for the Advancement of Medical Instrumentation (AAMI, 1987) and the British Hypertension Society (BHS) (O'Brien et al., 1990). These guidelines are the original two protocols most widely accepted and had revisions made in 2002 by AAMI and 1993 by BHS (Pickering et al., 2005). Both guidelines have several requirements for evaluation with some similarities and some differences. Part of the accuracy criteria is the same for both guidelines stating that the mean difference between the BP device being assessed and the comparison device must be  $\pm 5$  mmHg or less, with a standard deviation  $\pm 8$  mmHg or less for both SBP and DBP (O'Brien et al., 1993b; White et al., 1993). Further to this the BHS guidelines use a grading system to rank accuracy from A (very good) to D (very poor). Blood pressure measurement devices must achieve a grade A or grade B for both SBP and DBP in order to be recommended for clinical use.

The operation manual for the Dinamap Pro Series (100 to 400) specifies that the BP values obtained using the Dinamap Pro monitor correspond to comparisons with intra-aortic values, which either meet or exceed the American National Standards Institute (ANSI)/AAMI SP-10 standards for accuracy (a mean difference of  $\leq 5$  mmHg, and a standard deviation of  $\leq 8$  mmHg) (GE Medical Systems, 2002), although no published studies are cited. Despite this declaration there have been some questions raised regarding the accuracy of the Dinamap BP technology (O'Brien and Atkins, 1997). O'Brien et al. (1993a) assessed the accuracy of the Dinamap 8100 according to both the BHS and AAMI protocols. It was found SBP and DBP were underestimated by 0.71 mmHg and 7.6 mmHg, respectively. The SBP meet the AAMI criteria (AAMI, 1987) and achieved a grade B for the BHS criteria (O'Brien et al., 1990). However, the DBP did



not meet the AAMI criteria and achieved only a grade D on the BHS criteria. Based on these findings O'Brien and Atkins (1997) recommended that the Dinamap 8100 should not be used when accurate BP measurements are required due to the erroneous DBP measurement. The inaccuracy has been attributed to flaws within the measurement device (O'Brien et al., 1993b). However, as Friedman (1997) articulates, O'Brien et al. (1993b) compared the Dinamap BP values to those measured using the auscultatory method, which is also an indirect measure of BP that is not a gold standard method for reference and has potential sources for measurement errors. Furthermore the Dinamap Pro manual (GE Medical Systems, 2002) specifically states that the accuracy of the monitor should not be verified using the auscultatory method due to the fact the technology and techniques differ. The oscillometric method used by the Dinamap measures the pressure oscillations that occur in a cuff during deflation, from which MAP corresponds to the point of maximal oscillation and SBP and DBP are subsequently estimated through an algorithm (Pickering et al., 2005). Alternatively the auscultatory method determines BP through audible sounds heard through a stethoscope that occur during cuff deflation, from which SBP corresponds to the first appearance of sound during cuff deflation and DBP corresponds to the last audible sound (Pickering et al., 2005); using this method MAP is usually estimated from the recorded SBP and DBP values. Thus the two methods use very different techniques to measure BP making direct comparisons difficult.

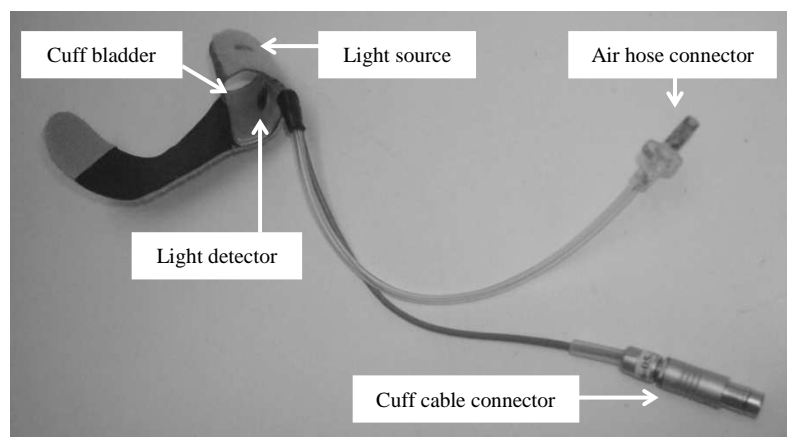
There are currently no publications that report the reliability of the Dinamap Pro 200 device. However, the reliability of the Dinamap Pro 200 for the measurement of BP was explored in the PhD thesis of Wiles (2008a) using ten healthy male participants. Blood pressure was measured on three separate occasions within a 1 week testing period. During each session, participants rested in a seated position for 15 minutes after which time BP was measured three times with 1 minute between each successive measurement. The within-subject variation was expressed as a coefficient of variation (CV) with 95% confidence intervals (CI). When the lowest BP value of each of the three trials were compared SBP produced a CV of 3.54% (CI: 2.47-4.95%), DBP produced a CV of 4.73% (CI: 3.29-6.62%) and MAP produced a CV of 2.83% (CI: 1.97-3.96%) (Wiles, 2008a). Thus it appears that the Dinamap reports reliable BP values over time. Indeed, Scott, Randolph and Leier (1989) suggest that a CV less than 10% should be considered good and a CV less than 20% should be considered acceptable. However, it is important to note that Atkinson and Nevill (2001) discourage the use of an arbitrary cut off point to accept an adequate level of reliability, such as a CV < 10%, as this makes no relation between the error recorded and use of the measurement tool. The reliability reported by previous research appears to be adequate for the detection of meaningful changes in BP when a relatively moderate sample size is utilised. This criterion will be utilised to determine the acceptable levels of reliability for all variables in the preceding sections.

### ***2.5.5 Finometer measurement of blood pressure***

The Finometer device (Finometer, model 1, Finapres Medical Systems BV, Amsterdam, The Netherlands) is the successor to the original Finapres (Schutte et al., 2003), which stands for FINGER Arterial PRESSure. The measurement of BP using the Finometer is based on the volume-clamp method invented by Peñáz (1973) together with the Physiological criteria developed by Wesseling et al. (1995b).

Using the Finometer, arterial pressure is measured using a small cuff that is placed around the finger, which contains an inflatable bladder (see Figure 2.3). The volume-clamp method is based on the dynamic pulsatile unloading of the finger arterial walls (Wesseling et al., 1995b; Imholz et al., 1998) and is

designed to keep the finger artery under the cuff at a constant (clamped) diameter in spite of any changes in arterial pressure that may occur during each heart beat (Bogert and van Lieshout, 2005; Truijen et al., 2012). An infrared photo-plethysmograph, consisting of light source (an infrared light emitting diode) and a light detector (an infrared sensing photo diode), is mounted inside the cuff to measure any changes in finger artery diameter (see Figure 2.3). The finger cuff is attached to a 'frontend' box, which is a small box attached to the wrist enclosing a fast servo controlled pressuring system (Imholz et al., 1998). The front end box is attached to the main unit, which consists of an air pump, electronics and computer (Imholz et al., 1998). If a change is detected in finger artery diameter, counter-pressure is dynamically applied to modulate the arterial diameter through a fast reacting electropneumatic servo-controller system that adjusts the finger cuff pressure (Truijen et al., 2012). For example, during systole the intra-arterial pressure rises causing the arterial diameter to increase, which is detected as a decrease in the plethysmograph signal due to the fact that light absorption by the blood has increased (TNO Finger Pressure Reference Guide, 2001). Consequently the servo-controller system rapidly increases the finger cuff pressure to prevent the change in diameter (Bogert and van Lieshout, 2005). The cuff pressure is measured using an electronic pressure gauge (Langewouters et al., 1998) and continuously reflects intra-arterial pressure waveform. From this SBP and DBP can be indirectly measured in a beat-to-beat mode (Imholz et al., 1998).



**Figure 2.3.** Finometer finger cuff (TNO Finger Pressure Reference Guide, 2001).

### 2.5.5a *Physiocal*

The diameter that the finger artery is clamped at is termed the 'set point' at which the arterial wall is fully 'unloaded' or unstretched at zero transmural pressure (the internal pressure inside the artery equals the external pressure of the surrounding tissue) (TNO Finger Pressure Reference Guide, 2001; Truijen et al., 2012). There is no tension on the arterial wall but it is not collapsed (Truijen et al., 2012). Unstressed arteries retain approximately one third or half of their original maximal arterial volume (Truijen et al., 2012). Thus, the point when the finger artery is at its unloaded diameter the finger cuff pressure equals the intra-arterial pressure (Bogert and van Lieshout, 2005).

The volume-clamp set point for finger arterial diameter is defined and established by the servo-controller system using the criteria developed by Wesseling et al. (1995b) termed 'Physiocal', which is an abbreviation for 'physiological calibration'. The actual value is measured from the infrared light detector

and is compared with the set point value (TNO Finger Pressure Reference Guide, 2001). The difference between the two values, termed the ‘error signal’, is used to control the electropneumatic valve and quickly adjust the cuff pressure as required (TNO Finger Pressure Reference Guide, 2001).

Defining this set point value is not a simple process as the unloaded arterial diameter is affected by changes in haematocrit, stress and smooth muscle tone so it is not constant during measurement (TNO Finger Pressure Reference Guide, 2001; Bogert and van Lieshout, 2005). A dynamic servo setpoint adjuster was developed (Imholz et al., 1998), which periodically verifies the set point at intervals to keep the finger artery fully unloaded during a cardiac cycle. To do this, the measurement of BP is temporarily interrupted by periods of steady cuff pressure at two or more levels. During this time the PhysioCal algorithm analyses the curvature and shape of the plethysmogram to explore the pressure-diameter relationships and can consequently track the finger artery’s unloaded diameter even if there is a change in the smooth muscle tone (TNO Finger Pressure Reference Guide, 2001; Truijen et al., 2012). The set point is checked at intervals of 70 beats (Imholz et al., 1998).

#### *2.5.5b Waveform filtering and level correction*

The Finometer measures finger arterial pressure, however BP is clinically measured at the brachial site (Gizdulich, Prentza and Wesseling, 1997; Truijen et al., 2012). Blood pressure values differ depending on which part of the arterial tree the measurement is being derived from (Pickering et al., 2005) as changes occur to both the shape and level of the pressure waveform due to pulse wave distortion and pressure gradients (Bos et al., 1996; Gizdulich, Prentza and Wesseling, 1997). It is known that the pressure waveform becomes more peaked near the periphery due to the narrower arteries causing a backwards reflection of the pressure waves (Truijen et al., 2012). Furthermore, finger BP is lower than brachial pressure (Bogert and van Lieshout, 2005) due to a pressure gradient created by the smaller peripheral arteries resisting blood flow (Gizdulich, Prentza and Wesseling, 1997; Truijen et al., 2012). To this end the Finometer displays brachial artery pressure that has been reconstructed from finger pressure (Truijen et al., 2012), which is achieved using a combination of two methods: 1) waveform filtering; 2) level correction. Waveform filtering has been developed to derive brachial pressure waveforms from finger arterial pressure (TNO Finger Pressure Reference Guide, 2001). The waveform filter applies an inverse transfer function of the finger arterial pressure (Fourier transformation) to describe the waveform distortion that occurs throughout the arterial system (Gizdulich, Prentza and Wesseling, 1997) and estimates the ‘brachial-alike’ pressure waveform (Imholz et al., 1998; Guelen et al., 2003). Although the reconstructed brachial waveform is similar in shape, the magnitude is still somewhat different (Bos et al., 1996). Further to this, a multiple regression-based level correction equation is then applied. This is a population based formulae (Truijen et al., 2012), which considers the model parameters finger pressure, HR and age (Gizdulich, Prentza and Wesseling, 1997). After applying the level correction, the differences between finger arterial pressure and brachial arterial pressure are almost zero (Guelen et al., 2003).

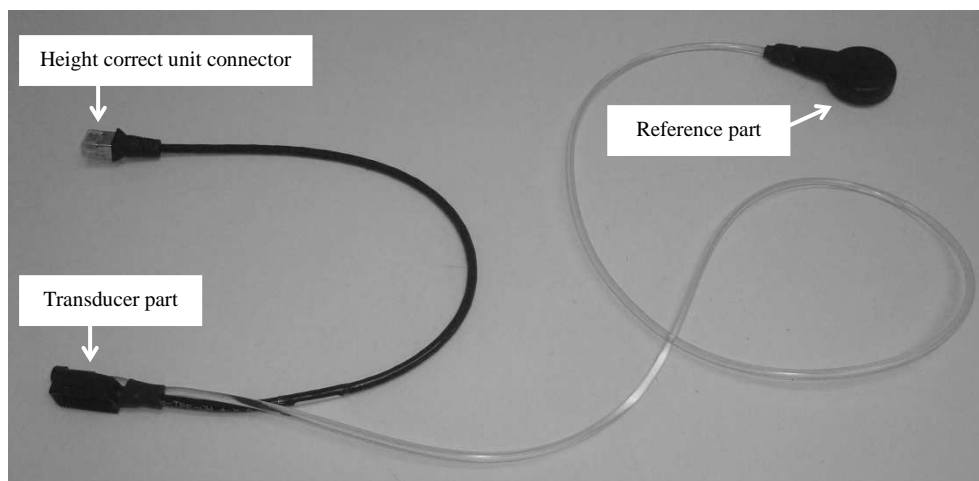
#### *2.5.5c Level calibration – Return-to-flow*

To further reduce the differences between finger and brachial arterial pressure the waveform-filtered and level-corrected pressure is calibrated using return-to-flow systolic BP (Guelen et al., 2003). A standard Riva-Rocci cuff is deflated around the upper arm on the side of the body that finger arterial pressure is

being measured (Guelen et al., 2003). The instant return of pulsations to the distal finger is called return-to-flow and this coincides with auscultatory Korotkoff phase I (Guelen et al., 2003). The upper arm cuff is inflated 30 mmHg above the estimated SBP, which is predicted from the waveform-filtered and level-corrected pressure, and the cuff is then deflated to detect the return-to-flow value (Guelen et al., 2003). This process is repeated twice and the average of the two values is the return-to-flow SBP for the level calibration (Guelen et al., 2003). The level calibration brings the Finometer BP measurements within the AAMI requirements and thus the Finometer provides an accurate measure of BP (Bos et al., 1996).

#### 2.5.5d Height correction unit

The Finometer also has a height correction unit, which is a compensation system to continuously sense changes in height of the measured finger and consists of a liquid filled tube connected to: 1) a pressure transducer part; 2) a reference part (cylindrical housing containing a compliment small plastic bag) (see Figure 2.4) (TNO Finger Pressure Reference Guide, 2001). The transducer part is placed on the finger cuff and the reference part is placed at the level of the right atrium. Before measurement the height correction transducer must be nulled. During measurement the signal from the height sensor is low pass filtered and consequently added to the finger pressure measurement to compensate for hydrostatic effects. Thus the hydrostatic correction unit can adjust the BP value for changes in the hand position with the respect to the level of the heart (Guelen et al., 2003).



**Figure 2.4.** Height correction unit (TNO Finger Pressure Reference Guide, 2001).

#### 2.5.6 Laboratory-based measurement of resting and exercising blood pressure using the Finometer

The non-invasive hemodynamic monitor (Finometer, model 1, Finapres Medical Systems BV, Amsterdam, The Netherlands) was used to measure continuous beat-to-beat BP during rest and exercise in the 'Finometer-research' mode. Prior to testing, in the familiarisation session, the circumference of the upper left arm was measured (greatest circumference whilst relaxed) in centimetres (cm) using an ergonomic circumference measuring tape (Seca 201, Seca GmbH & Co. KG., Hamburg, Germany) to select the ideal arm cuff size. The standard Finometer arm cuff (29-42cm) was appropriate for all participants. Also the circumference of the middle phalanx of the middle finger on the left hand was measured in centimetres (cm) using an ergonomic circumference measuring tape (Seca 201, Seca GmbH

& Co. KG., Hamburg, Germany) to select the finger cuff size from a selection of small (4.5-5.5cm), medium (5.5-6.5cm) and large (6.5-7.5cm).

Before placement of the arm and finger cuffs, the participant was asked to remove any clothing that covered the left arm, wrist and hand. Furthermore, the investigator ensured that a participant's sleeve was not rolled up presenting a tourniquet effect (Pickering et al., 2005). The participant was then seated in a comfortable position with the legs uncrossed and the back supported. The upper arm cuff, which was connected to the main unit via two air hoses, was placed around the ipsilateral left arm where the finger pressure was to be measured. The arm cuff was positioned on the bare upper left arm so that the midline of the cuff bladder, marked with an arrow and the word 'arteria', was aligned the brachial artery (located by palpating the antecubital fossa) and the middle of the cuff was positioned level with the right atrium (Pickering et al., 2005). The left arm was then supported on a side table on the left hand side of the chair.

The frontend box of the Finometer was attached to the participant's left wrist by a Velcro strap and the appropriate sized finger cuff was placed on the middle phalanx of the middle finger on the left hand ensuring the following: 1) the air hose and cuff connector cables were pointed towards the wrist; 2) the light emitting diode and photo diode were centred symmetrically on the soft palmer parts of the finger; 3) the cuff was wrapped tightly following the curvature of the finger to ensure the air bladder was touching with no overlap or hiatus. The air hose and cuff connector cables from the finger cuff were then connected to the frontend box (see Figure 2.5). The frontend unit was then connected via the frontend cable and air hose to the main unit. An additional Velcro strap was also placed around the participant's left forearm to secure the air hose position during wall squat exercise.



**Figure 2.5.** The setup of the Finometer finger cuff, height correction unit, front end box and upper arm cuff.

The participant's descriptive data (age, gender, height and weight) was entered into the Finometer. The height correction unit was then attached; the height correction electrical connector was connected to the front end unit, the transducer part was placed on the finger cuff and the reference part was placed on the arm cuff approximately at the level of the right atrium (see Figure 2.5). The height correction transducer was nulled and the participant was instructed to gently move the hand in height to ensure that the correct

changes in height level could be observed. The Finometer measurement of BP was then started, at which point the displayed BP was uncalibrated. After 2 minutes the return-to-flow calibration was carried out. Once completed the Finometer displayed waveform filtered, level corrected and return-to-flow calibrated finger arterial pressure.

The Finometer BP data were interfaced with a Windows PC using an analog I/O box (Finapres Medical Systems BV, Amsterdam, The Netherlands) and a 16 channel data acquisition system (PowerLab/16SP, ML795, ADInstruments Pty Ltd, Castle Hill, Australia). The 'analog I/O box' was connected to the Finometer at the rear, which allowed analog signals from the Finometer to be recorded using the PowerLab. The Finometer BP data were then continuously displayed on a computer using LabChart Pro software (version 7.1, ADInstruments Pty Ltd, Castle Hill, Australia). Three dedicated LabChart channels were configured to instantaneously display BP (SBP, DBP and MAP) in units of millimetres of mercury (mmHg). All BP data were sampled at a frequency of 400 Hz. Systolic and diastolic BP were displayed in two separate LabChart channels (channels 4 and 5, respectively) using the 'Arithmetic' function of LabChart in which the raw data inputted from the Finometer (analog I/O box outputs 1 and 2) to the PowerLab was multiplied by a calibration factor of 100, as specified in the 'Finometer-research' mode in the 'Configure' tab. Mean arterial pressure was displayed in a third LabChart channel (channel 6) and was instantly calculated with the data from the SBP and DBP channels using the MAP equation (see section 2.5.1, page 51).

Once the data were recorded and saved on to the computer's hard drive, they were then exported to spreadsheet software (Microsoft Excel, Microsoft Corporation, Redmond, Washington, USA) and displayed in 1 second intervals for further analysis. Blood pressure was recorded throughout a 5 minute seated rest and the mean resting BP was calculated for this 5 minute period. Blood pressure was also recorded throughout isometric wall squat exercise and the mean exercising BP for the last 5 seconds of each 30 second period was calculated.

### ***2.5.7 Published data on the validity and reliability of the Finometer measurement of blood pressure***

The Finometer device has been shown to satisfy the validation criteria of the AAMI (Bos et al., 1996; Guelen et al., 2003; Schutte et al., 2004; Guelen et al., 2008) and the BHS guidelines (Schutte et al., 2004). Bos et al. (1996) measured continuous finger arterial pressure using the Finapres whilst simultaneously measuring intra-arterial brachial pressure via a cannula as a reference. Fifty-seven healthy elderly participants and patients with vascular disease and/or hypertension were studied. Before reconstruction, the Finapres pressure measurements underestimate mean and diastolic brachial artery pressure. However, after filtering and correction the Finapres measurements met the AAMI criteria. When reconstructed finger pressure from the Finapres was subtracted from intra-arterial-brachial pressure the differences were SBP:  $3.7 \pm 7.0$  mmHg, DBP:  $1.0 \pm 4.9$  mmHg and MAP:  $0.7 \pm 4.6$  mmHg. Thus it was concluded that brachial artery pressure can be reconstructed from non-invasive Finapres measurements.

Guelen et al. (2003) compared the Finometer's reconstructed brachial pressure in one arm with intra-arterial brachial pressure measured via catheterization simultaneously in the other arm in 37 participants aged between 41 to 83 years. Once the Finometer finger arterial pressure had been waveform filtered,

level corrected and return-to-flow calibrated and compared with intra-arterial pressure, the differences fell within the AAMI criteria. The differences were SBP:  $3.1 \pm 7.6$  mmHg, DBP:  $4.0 \pm 5.6$  mmHg and MAP:  $2.7 \pm 4.7$  mmHg.

Schutte et al. (2004) carried out a study to validate the Finometer against both the AAMI criteria and also the BHS criteria. Finometer measurements of brachial pressure were compared to sphygmomanometer measurements in a group of 102 black women. The results showed that the average differences between the Finometer and sphygmomanometer measured BP were SBP:  $-1.83 \pm -6.8$  mmHg and DBP:  $0.88 \pm -7.5$  mmHg. From these results it was concluded that the Finometer satisfies the criteria for BP measurement set by the AAMI and also achieves an A/B grading according to the BHS protocol.

While the validity of the Finometer device has been established, there is less information existing related to the reproducibility of non-invasive finger BP (Parati et al., 2001). Further to this, there appears to be few studies that have measured the reliability of resting BP using the Finometer. However the reliability of the predecessor device, the Finapres, has been assessed (Parati et al., 2001; Højgaard et al., 2005). Parati et al. (2001) studied the reproducibility of BP values obtained using the Finapres device in 8 women with grade 1 essential hypertension. Blood pressure was recorded in the supine position for 15 minutes on two separate occasions at an interval of one month. The CV for the mean values was 7% for both SBP and DBP. Thus it was concluded that BP recorded in the supine position for 15 minutes produces good reproducibility.

Højgaard et al. (2005) examined the reproducibility of BP using the Finapres in 14 healthy participants during both supine rest and head-up tilt at 60 degrees. Blood pressure was recorded for 1024 seconds during each experimental condition on three different days for comparison; there was a mean of  $14 \pm 3$  days between day 1 and 3. During supine rest the CV was 6% for SBP, 5% for DBP and 6% for MAP. Further to this, during head-up tilt the CV was 5% for SBP, 7% for DBP and 8% for MAP. Thus it was concluded that the day to day reproducibility of BP during both supine rest and head-up tilt was good (Højgaard et al., 2005).

The intratester reliability of the Finometer device for measuring BP (SBP, DBP and MAP) obtained by the one investigator who measured BP during the studies in this thesis was determined. Study 1 in Chapter 3 investigated the short term reliability of the Finometer BP values during both rest and exercise; see the results section 3.3 (page 97). Whereas study 3 in Chapter 5 explored the long term reliability of the resting Finometer BP values; see the results section 5.3 (page 143).

## **2.6 Heart rate (HR) measurement**

### **2.6.1 Background information on heart rate**

Heart rate is simply defined as the number of times the heart beats per minute and is expressed as  $\text{beats} \cdot \text{min}^{-1}$  (Kent, 2006). Heart rate is commonly used to indicate the intensity of exercise due to the linear relationships it establishes with oxygen uptake ( $\dot{V}O_2$ ) during submaximal exercise (Achten and Jeukendrup, 2003). Furthermore, it is also useful to measure HR as it is an indication of physiological adaptations (Laukkanen and Virtanen, 1998). As HR is a determinant of cardiac output ( $\dot{Q} = \text{HR} \times \text{SV}$ ) (Tortora and Derrickson, 2012), its measurement allows some explanation of any chronic changes to  $\dot{Q}$

that may occur, such as those due to exercise training. An adaptation to HR could indicate that changes in the sympathetic and/or parasympathetic nerve activity have occurred (Smith and Fernhall, 2011).

To measure HR, the electrical activity of the heart is often monitored (Cohen, Kessler and Gordon, 1997). The heart is a muscular pump that contracts to circulate blood throughout the blood vessels of the body. These contractions are achieved through the rhythmical electrical activity of specialised self-excitabile cardiac muscle cells called autorhythmic fibres (Tortora and Derrickson, 2012). These cells repeatedly generate cardiac action potentials that cause the heart to contract.

The heart's electrical events are initiated in the cells of the sinoatrial (SA) node, which are located in the upper posterior wall of the right atrium. The SA node spontaneously depolarizes and is often termed the heart's pacemaker as this provides the initial stimulus for the contraction of the heart. The electrical impulse generated from the SA node spreads throughout both atria, causing the right and left atria to contract. The electrical impulse then reaches the atrioventricular (AV) node, located in the wall of the right atrium near the centre of the heart, which conducts the electrical impulse from the atria to the ventricles. The electrical impulse travels to the AV bundle, also known as the bundle of His, which extends through the interventricular septum and then propagates into right and left branches of both ventricles towards the apex of the heart and then outward. Eventually the electrical impulse reaches the distal ends of the bundle branches, called the Purkinje fibres, which conduct the electrical impulse upwards to the remaining right and left ventricular walls. Finally the ventricles contract, causing blood to be pushed upward through the semi-lunar valves into the arteries (Wilmore, Costill and Kenney, 2008; McArdle, Katch and Katch, 2010; Tortora and Derrickson, 2012).

The heart establishes its own fundamental rhythm and the autorhythmic fibres of the SA node inherently initiate an electrical impulse approximately every 0.6 seconds, causing the heart to beat 100 times per minute (McArdle, Katch and Katch, 2010; Tortora and Derrickson, 2012). However, the time and strength of each heart beat can be modified by several extrinsic mechanisms, most importantly by the ANS and the endocrine system (Tortora and Derrickson, 2012). The ANS control of HR originates centrally in the cardiovascular centre in the medulla oblongata and then flows through the parasympathetic and sympathetic pathways to either decrease or increase HR. Parasympathetic nerve impulses reach the heart by vagus (X) nerves, which release acetylcholine and decreases the rate of spontaneous SA node depolarisation, consequently decreasing HR. Sympathetic nerve impulses reach the heart by cardiac accelerator nerves, which trigger the release of noradrenaline and increases the rate of spontaneous SA node depolarisation, consequently increasing HR (Tortora and Derrickson, 2012).

An electrocardiograph (ECG) enables a graphic recording to be made of the electrical activity of the heart (Achten and Jeukendrup, 2003). This is due to the fact that the electrical impulses of the heart can be detected on the surface of the body by attaching electrodes to the skin (McArdle, Katch and Katch, 2010; Tortora and Derrickson, 2012). An ECG is composed of three sections: 1) P wave, which represents the depolarisation of the atria; 2) a QRS wave, which represents the depolarisation of the ventricles; 3) a T wave, which represents the repolarisation of the ventricles (Achten and Jeukendrup, 2003). The QRS complex is often used to calculate HR because it represents the activation of the ventricles, which causes the heart to contract and pump blood around the body (Baltazar, 2009). Furthermore, within the QRS complex, the R wave represents depolarization of the main ventricular mass and thus produces the largest



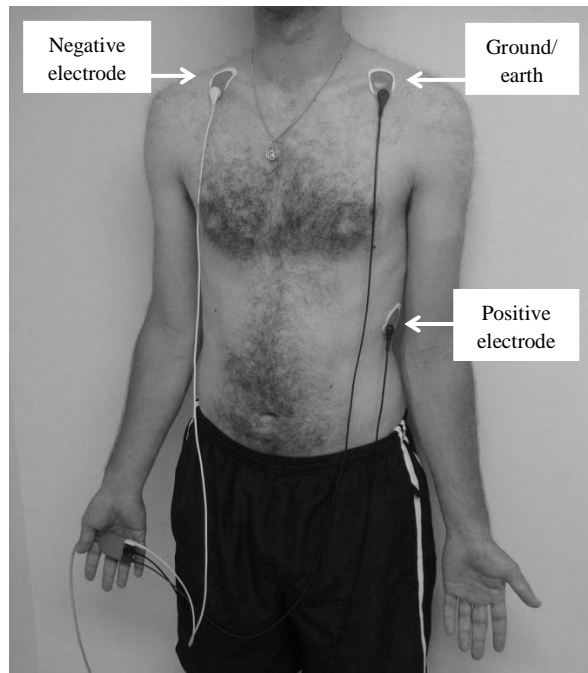
wave (Ashley and Niebauer, 2004). As the R peak is readily distinguishable due its amplitude (Peltola, 2012), it is often used to detect the QRS complex and calculate HR. Consequently, HR is calculated from the average number of ventricular QRS complexes, or R waves, in a given range of time using the following equation;  $HR = 60/R-R$ , where R-R is the average RR interval in seconds (Rautaharju and Rautaharju, 2007).

Although ECG has been shown to accurately detect HR, it is not always a practicable measurement technique due to the expense, size of equipment and the complexity of operation (Laukkanen and Virtanen, 1998). Wireless, light-weight telemetric heart rate monitors (HRM) have been developed for assessment of HR in the field (Laukkanen and Virtanen, 1998) and are relatively cheap (Achten and Jeukendrup, 2003). Heart rate monitors consist of a transmitter, which is attached to an individual using an electrode belt situated on the chest, and a receiver, which is a watch like computer that is worn on the wrist. The HR data is then stored and can be downloaded to a computer for analysis (Achten and Jeukendrup, 2003). In the studies in this thesis, HR was measured by ECG in the laboratory and using a HRM during home-based IET.

### ***2.6.2 Laboratory-based measurement of resting and exercising heart rate using ECG***

In the studies in this thesis, HR was measured and recorded in the laboratory during rest and exercise using an ECG trace. The ECG signal was registered using a 16 channel data acquisition system (PowerLab/16SP, ML795, ADInstruments Pty Ltd, Castle Hill, Australia) and was continuously displayed on a computer using LabChart Pro software (version 7.1, ADInstruments Pty Ltd, Castle Hill, Australia). Before testing, participants were fitted with three single patient use ECG electrodes (Ambu<sup>®</sup> Blue Sensor R, Ambu A/S, Ballerup, Denmark), which were placed in a standard three-lead bipolar ECG arrangement, as recommended by ADInstruments (see Figure 2.6). This modified Lead II configuration was used as it produces a positive deflection (Kowalak, 2009) and a pronounced complex of QRS waves of the ECG (Cohen, Kessler and Gordon, 1997). For the modified lead II configuration, the leads are placed on the torso for convenience (Kowalak, 2009), which is particularly useful when performing exercise such as a wall squat.

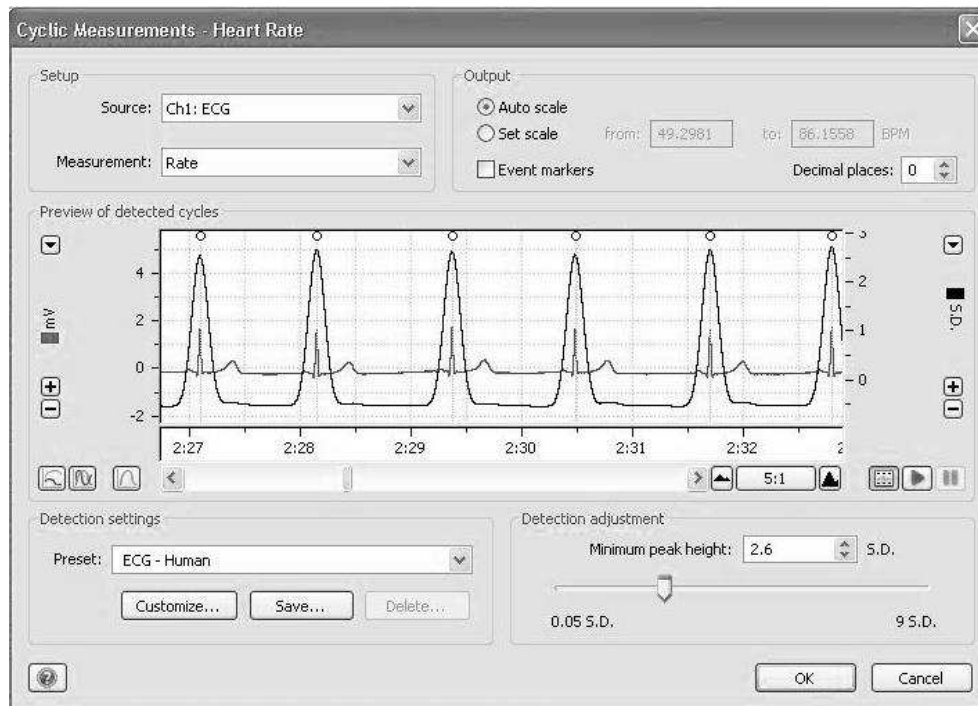
Before the electrode placement, the skin was prepared in three phases to enhance the skin-electrode interface and ensure a good quality ECG signal: 1) First of all, if necessary, the participant's chest hair was shaved with an electric razor. This was only carried out if the chest hair was too dense such that it would compromise electrode adhesion and prevent good electrical contact; 2) The skin was then scrubbed with an alcohol free cleansing wipe (Sterowipe, Steroplast Healthcare, Manchester, United Kingdom) to clean the surface; 3) Finally, the area was dried and abraded using a paper towel to further reduce skin impedance (Bowbrick and Borg, 2006). Two electrodes were then placed on the mid-clavicular point inferior to each clavicle; the negative electrode was placed on the right clavicle and the ground/earth was placed on the left clavicle. A third electrode (positive electrode) was placed on the mid-clavicular line below the lowest palpable rib (Kowalak, 2009).



**Figure 2.6.** The three lead bipolar ECG arrangement. Adapted from Wiles (2008a).

Three Shielded Lead Wires (MLA2503, ADInstruments Pty Ltd, Castle Hill, Australia) were attached to the placed electrodes using three leads; 1) a white lead for the negative electrode; 2) a black lead for the positive electrode; 3) a green lead for the ground/earth. The three leads were then attached to a 3-Lead Shielded Bio Amp cable (MLA2340, ADInstruments Pty Ltd, Castle Hill, Australia), which was then connected to the PowerLab/16SP through a Bio Amp CF (ML132, ADInstruments Pty Ltd, Castle Hill, Australia).

A dedicated LabChart channel (channel 1) was configured to continuously sample the raw ECG waveform received from the Bio Amp CF at a frequency of 400 Hz. Heart rate was instantaneously calculated in another channel (channel 2) using the Cyclic Measurements 'Rate' function of LabChart in which the raw ECG waveform was converted to computed HR data. The cyclic rate detection algorithm identified the R wave peaks in the raw ECG waveform, as indicated by a circular events marker above the peak, and from this R-R intervals were generated (see Figure 2.7). Heart rate was consequently calculated by dividing the time in one minute (60 seconds) by the R-R interval:  $HR = 60 / R-R \text{ interval}$ . As a result the number of beats that occur in one minute was derived and expressed in units of beats per minute ( $\text{beats} \cdot \text{min}^{-1}$ ).



**Figure 2.7.** Cyclic Measurement ‘rate’ function of LabChart. Detected R-waves are indicated by the circular events marker above the signal.

Following data collection, the ECG R wave peaks were visually inspected and manually filtered offline to exclude any undesirable beats and include any missed beats. If it was found that any beats were not detected the sensitivity was increased by adjusting the ‘Minimum Peak Height’ to consequently include all the beats whilst avoiding smaller secondary peaks or noise being detected mistakenly. The data were then exported to spreadsheet software (Microsoft Excel, Microsoft Corporation, Redmond, Washington, USA) and displayed in 1 second intervals for further analysis. Heart rate was recorded throughout a 5 minute seated rest and the mean resting HR was calculated for this period. Heart rate was also recorded throughout isometric wall squat exercise and the mean exercising HR for the last 5 seconds of each 30 second period was calculated.

### **2.6.3 Published data on the validity and reliability of ECG measurement of heart rate**

The ECG is considered to be the ‘gold’ standard for HR measurement (Engström et al., 2012). Accordingly, alternative HR measurement techniques are often compared to ECG readings for validation, such as HRMs (Seaward et al., 1990; Godsen, Carroll and Stone, 1991; Terbizan, Dolezal and Albano, 2002; Gamelin, Berthoin and Bosquet, 2006; Engström et al., 2012), ambulatory BP monitors (Vrijkotte and de Geus, 2001), and pulse oximeters (Iyriboz et al., 1991). Due to this fact, the HR values derived from the ECG using the PowerLab in this thesis were considered to be valid. The reliability of the ECG measurement of HR has been studied during both rest and exercise.

Højgaard et al. (2005) examined the reproducibility of resting HR values using ECG data obtained from three chest electrodes in 14 healthy participants. Heart rate was recorded for 1024 seconds during supine rest on three different days for comparison; there was a mean of  $14 \pm 3$  days between day 1 and 3. It was found that HR produced a CV of 6% and thus it was concluded that the day to day reproducibility of HR during supine rest was good (Højgaard et al., 2005).

Wilmore et al. (1998) studied the reproducibility of the cardiovascular response to submaximal exercise in 390 participants. On two separate occasions, participants completed submaximal cycle ergometer exercise at two power outputs (absolute power of 50W and relative power output equivalent to 60% maximal oxygen uptake ( $\dot{V}O_{2max}$ )) during which time HR was measured via ECG. The exercise was performed for approximately 12-15 minutes at each work rate with 4 minutes of seated rest between the two work rates. It was found that the two 50W trials produced a HR CV of 5.1% and the two 60%  $\dot{V}O_{2max}$  trails produced a HR CV of 4.4%. It was concluded by the authors that HR ECG measurement was highly reproducible (CV < 9%) during submaximal exercise (Wilmore et al., 1998). Further to this Skinner et al. (1999) determined the reproducibility of HR values recorded during maximal cycle ergometer exercise tests performed on two days by 390 participants. Participants began the maximal exercise test at a power output of 50 W for 3 minutes, which was then increased by 25W every 2 minutes until volitional fatigue. Heart rate was calculated manually using ECG tracings, which were recorded during the last 15 seconds of each work stage. The mean HR was calculated for each of the two maximal exercise tests and a CV of 2.9% was produced, which again showed that the HR ECG measurement was highly reproducible (CV < 10%) as suggested by Scott, Randolph and Leier (1989).

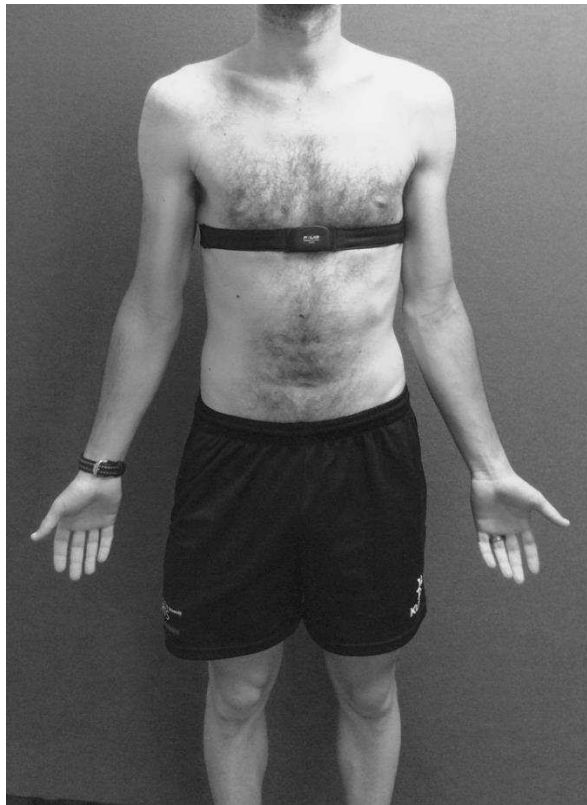
The intratester reliability of the ECG for measuring HR obtained by the one investigator who measured HR during the studies in this thesis was determined. Study 1 in Chapter 3 investigated the short term reliability of ECG HR values during both rest and exercise; see the results section 3.3 (page 97). Whereas study 3 in Chapter 5 explored the long term reliability of the resting ECG HR values; see the results section 5.3 (page 143).

#### ***2.6.4 Home-based measurement of exercising heart rate using a heart rate monitor***

For the continuous measurement of HR during home-based IET, participants were provided with a HRM. The HRM consisted of the following: 1) a Polar RS400 Computer (Polar RS400, Polar Electro Oy, Kempele, Finland), which is a watch like computer that displays and records HR; 2) a Polar WearLink transmitter (Wearlink V2, Polar Electro Oy, Kempele, Finland), which sends the HR signal to the computer and consists of a connector and chest strap.

Before the HRM was distributed, the participant's demographic details (height, weight, date of birth and sex) were entered into the computer for participant identification. The computer was configured to the default 'heart rate view', so that HR and time were on display during a training session. The recording rate was set to 1 second intervals so that HR was recorded continuously throughout an isometric training session. The connector was also attached to the chest strap.

Before commencing the training period, the participants were given instructions regarding the attachment of the HRM. Participants were informed to: 1) ensure the electrodes on the chest strap were well moistened with water before fitting the transmitter; 2) adjust the chest strap length to fit 'snugly' and 'comfortably' just below the chest muscles (see Figure 2.8); 3) ensure the wet electrodes were firmly against the skin; 4) attach the watch like computer to the wrist so that it can be easily read.



**Figure 2.8.** Positioning of the Polar WearLink transmitter.

Once the HRM was setup and participants were ready to begin training, participants were instructed to start the HR recording immediately once they were in the correct exercise position. The Polar WearLink transmitter detected the QRS-complexes and sent this information via an electromagnetic signal to the wrist worn HRM (Engström et al., 2012). The R-R interval was then calculated by the HRM and HR was displayed instantly in beats per minute ( $\text{beats}\cdot\text{min}^{-1}$ ) (Engström et al., 2012). The RS400 has a HR recording range of 15 to 240  $\text{beats}\cdot\text{min}^{-1}$  (Polar Electro Oy, 2010). During the training session participants were instructed to record the HR value displayed at the end of each of the four 2 minute wall squats on the training session 'Data Sheet' (see Appendix 8, Section 1, page 233). Participants were instructed to stop the HRM recording at the end of the session, at which point the data were stored onto the HRM.

After every three exercise training sessions the participants brought the HRM into the laboratory and the data were downloaded from the HRM to a computer via IrDA (an infra-red USB link) and analysed using Polar ProTrainer5 software (Polar ProTrainer 5, Polar Electro Oy, Kempele, Finland). The data were then exported to spreadsheet software (Microsoft Excel, Microsoft Corporation, Redmond, Washington, USA) and displayed in 1 second intervals for further analysis. Heart rate was recorded throughout the isometric wall squat exercise training sessions and the mean exercising HR for the last 5 seconds of each 30 second period was calculated.

#### ***2.6.5 Published data on the validity and reliability of heart rate monitor measurement of heart rate***

The validity and reliability of the wireless HRM has been investigated extensively and has been shown to be accurate during both rest and exercise conditions (Seaward et al., 1990; Godsen, Carroll and Stone, 1991; Terbizan, Dolezal and Albano, 2002; Engström et al., 2012). One particular study of interest by

Engström et al. (2012) compared the validity and reliability of the Polar RS400 HRM, which is the device used in the studies in this thesis, to ECG. This comparison was made during a cycle ergometer test in which participants cycled for 5 minutes at three different workloads (50W, 100W and 150W). The exercise test was repeated after at least one hours rest to measure test-retest repeatability. Results showed a significant coefficient correlation (ranging from 0.97 to 1.00) between the HR values obtained by the Polar RS400 HRM and the ECG values demonstrating good criterion-related validity. When comparing the HR values obtained between repeated cycling tests, the Polar RS400 produced a non-significant difference of 3 beats·min<sup>-1</sup>, thus producing reliable HR values. It was concluded by the authors that the Polar RS400 is suitable for measuring HR during exercise training. Further to this the technical information in Polar RS400 User Manual (Polar Electro Oy, 2010) states that the HRM provides an accurate measurement of HR within  $\pm 1$  beats·min<sup>-1</sup> or 1%.

## **2.7 Cardiac output ( $\dot{Q}$ ) measurement**

### ***2.7.1 Background information on cardiac output***

Cardiac output ( $\dot{Q}$ ) is defined as the volume of blood pumped by the heart (from the left ventricle to the aorta) per minute (Tortora and Derrickson, 2012). Cardiac output is the product of SV, which is the volume of blood ejected during each contraction, and HR, which is the number of contractions per minute (Tortora and Derrickson, 2012) and is usually expressed in litres per minute (L·min<sup>-1</sup>) (Kaijser and Kanstrup, 2000). The measurement of  $\dot{Q}$  is important as it is an indicator of cardiac function (Sugawara et al., 2003). Cardiac output provides an estimate of whole body oxygen delivery and can also help to enhance the understanding of BP (Lavdaniti, 2008), as MAP is calculated using the equation:  $MAP = \dot{Q} \times TPR$  (Sherwood, 2014). An adaptation to  $\dot{Q}$  could suggest that changes have occurred to either SV and/or HR as  $\dot{Q} = HR \times SV$  (Smith and Fernhall, 2011).

The first clinical device to measure  $\dot{Q}$  was thermodilution using a pulmonary artery catheter and is often considered the practical 'gold' standard measurement technique (Pugsley and Lerner, 2010). However, due to the risks associated with the catheterization, less invasive methods have been developed to determine  $\dot{Q}$  (Lee, Cohn and Ranasinghe, 2011). These methods include oesophageal Doppler ultrasound monitoring, transoesophageal echocardiography, lithium indicator dilution, pulse contour and pulse power analysis, the derivative Fick method using partial CO<sub>2</sub> rebreathing or electrical bioimpedance (Lavdaniti, 2008; Mathews and Singh, 2008).

Mathews and Singh (2008) suggest that a  $\dot{Q}$  measurement technique should be non-invasive, easy to use, accurate, reliable and continuous; however currently no single method meets all the proposed criteria as all the techniques have limitations. For example, the  $\dot{Q}$  values produced by thermodilution and inert gas rebreathing represent an average value over several heart beats ( $\leq 20$  beats·min<sup>-1</sup>) (Bogert et al., 2010). Consequently, alterations in  $\dot{Q}$  cannot be measured with high time resolution (Nissen et al., 2009). For alterations in  $\dot{Q}$  to be detected, the changes must remain constant for as long as the measurement technique takes and consequently rapid changes are difficult to detect (Bogert et al., 2010). From all of the available devices, the methods that have the greatest potential to replace pulmonary artery catheter thermodilution are the oesophageal Doppler ultrasound and arterial pulse contour monitors (Funk, Moretti and Gan, 2009). These two devices assess SV on a beat to beat basis and are thus better equipped to

monitor changes in  $\dot{Q}$  (de Wilde et al., 2007). The device used to measure  $\dot{Q}$  in the studies within this thesis was the Finometer, which uses the arterial pulse contour analysis technique.

### ***2.7.2 Finometer measurement of cardiac output***

Cardiac output was measured using the same non-invasive hemodynamic monitor that measured BP (Finometer, model 1, Finapres Medical Systems BV, Amsterdam, The Netherlands). This device estimated the  $\dot{Q}$  values using the Modelflow method developed by Wesseling et al. (1993), which is an arterial pulse contour technique. Using this technique,  $\dot{Q}$  is computed indirectly from an arterial pressure waveform (Jansen and van den Berg, 2005).

#### ***2.7.2a Brief history of pulse contour analysis***

The concept of pulse contour analysis is based on calculating  $\dot{Q}$  from an arterial waveform (Cecconi, Rhodes and Rocca, 2008). The first pulse contour model established was the classic Windkessel model, which was originally put forward by Stephen Hales (1733) and later developed by Otto Frank (1899). Frank (1899) found similarities between the old-fashioned hand-pumps used by fireman (in German this is called a 'windkessel' pump) and the circulatory system (Olufsen and Nadim, 2004; Cecconi, Rhodes and Rocca, 2008). The fireman's pump is a closed circuit in which a pump pushes water from the canal through an air chamber (known as a windkessel) into a spout (Cecconi, Rhodes and Rocca, 2008; Funk, Moretti and Gan, 2009). When water is pumped into the air chamber the air is compressed and the pressure in the chamber increases. When the air chamber is full, the pressure is at its highest and consequently drives water out of the spout in a steady jet (Olufsen and Nadim, 2004).

This Windkessel model was consequently used to describe the blood flow in the heart and systemic arteries (Olufsen and Nadim, 2004). In the analogy, the water and pump simply represent the circulating blood and heart. The compressibility of air in the chamber represents the arterial compliance, which is the elasticity of the arteries, and the resistance that is met by the water leaving the windkessel pump represents the peripheral resistance (Funk, Moretti and Gan, 2009). This analogy led to the development of the original Windkessel model, which comprised of an electrical circuit with two-elements; one capacitor, which represents the compliance of the large arteries, and one resistor, which represents the resistance of the small arteries and arterioles (Olufsen and Nadim, 2004). Over the years, refinements have been made to the original Windkessel model, such as the development of a third and fourth element (Funk, Moretti and Gan, 2009). The three-element windkessel model additionally included the characteristic impedance of the aorta and the large compliance vessels and the fourth-element windkessel model includes an inductor representing the inertia of the blood (Olufsen and Nadim, 2004).

Frank (1899) further elucidated that from the change in pressure that occurs, SV could be subsequently calculated (Cecconi, Rhodes and Rocca, 2008). Erlanger and Hooker (1904) later described that there was a relationship between SV and change in arterial pressure. If it is known how much the aorta complies with a 1 mmHg increment in pressure (change in aortic volume per unit change in pressure) then SV can be subsequently calculated through the measurement of the associated aortic pressure change (Mathews and Singh, 2008). For example, if a 1 mmHg pressure increase leads to a consequent 2 mL compliance, then a 40 mmHg rise in pressure would correspond to a SV of 80 mL (40 x 2) (van Lieshout and Wesseling, 2001). From this it was theorised that  $\dot{Q}$  was proportional to the arterial pressure (Funk,

Moretti and Gan, 2009) and based on this, a variety of algorithms have been developed that estimate beat-to-beat  $\dot{Q}$  from arterial pulse contour (Cecconi, Rhodes and Rocca, 2008).

One important step in being able to clinically apply Frank's concept was the development of the  $C_z$  method by Wesseling (Wesseling et al., 1983; Jansen et al., 1990). Using this method,  $\dot{Q}$  is related to the area under the systolic portion of the arterial pressure wave (Asys) (de Wilde et al., 2007). In brief, left ventricular SV ( $V_z$ ) is calculated by taking the Asys and dividing this by aortic impedance (Zao):  $V_z = \text{Asys} / \text{Zao}$  (de Wilde et al., 2007). The systolic area is defined as the end of diastole to the ejection phase end (Reuter and Goetz, 2005). However, this model was deemed too simplistic for human circulation and was therefore extended (Jansen and van den Berg, 2005). Indeed, mean arterial pressure (Pmean) is used in the model to correct for pressure dependent non-linear changes in the cross sectional aortic area and heart rate (HR) is used to correct for pressure reflections from the periphery. However, these corrections are age dependent (Age). The calculation for Wesseling's pulse contour  $\dot{Q}$  can be written as:

$$V_{cz} = V_z [0.66 + 0.005 \times \text{HR} - 0.01 \times \text{Age} \times (0.014 \times \text{Pmean} - 0.8)]$$

$$\text{CO}_{cz} = \text{cal} \times \text{HR} \times V_{cz}$$

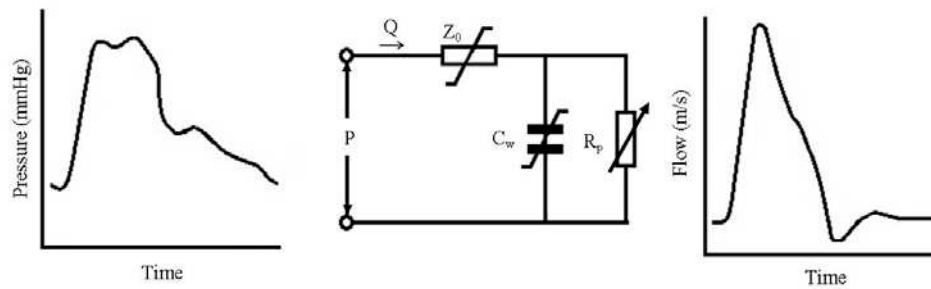
(de Wilde et al., 2007).

However, there are limitations of this method. It requires calibration (cal) at least once for each person (Perel and Settels, 2011), which is completed by comparing the  $\dot{Q}$  value determined by the pulse contour method to an absolute  $\dot{Q}$  estimated from thermodilution (Jansen and van den Berg, 2005). Furthermore, the model does not account for strong vasoconstriction and vasodilation in the peripheral arterioles (Perel and Settels, 2011). To overcome these limitations further refinements were made by Wesseling et al. (1993) to develop the Modelflow method (Perel and Settels, 2011), which is used by the Finometer.

### 2.7.2b Finometer Modelflow method

As previously mentioned, the hemodynamic monitor used to measure  $\dot{Q}$  during the studies in this thesis was the Finometer, which utilises the Modelflow method developed by Wesseling et al. (1993) for arterial pulse contour analysis. The Modelflow technique involves a simple extension of the classical two-element Windkessel model. As the heart (left ventricle) contracts, aortic pressure increases and causes an inflow of blood into the arterial system. This inflow is moderated and opposed by properties of the aorta and peripheral vascular system, such as arterial counter pressure and aortic and peripheral systemic input impedance (Jansen and van den Berg, 2005; de Vaal et al, 2005). The Modelflow method uses a hemodynamic model of arterial input impedance, which relates aortic pressure and inflow by simulating the behaviour of the aorta in opposing the injection of blood from the left ventricle (Jellema et al., 1999); see Figure 2.9. The model has three principle elements; 1) aortic characteristic impedance ( $Z_0$ ); 2) Windkessel (or arterial) compliance ( $C_w$ ); 3) systemic vascular resistance ( $R_p$ ) (Wesseling et al., 1993).





**Figure 2.9.** A diagram of the Modelflow method used to compute flow from pressure displaying the input pressure (left), schematic diagram of the three-element non-linear, self-adapting model of the aortic input impedance (middle), and simulated aortic flow (right). Adapted from the Finapres Medical Systems (FMS) user guide (FMS, 2002) and website (FMS, 2010).  $P$  is the arterial pressure waveform applied to the model;  $Z_0$ , characteristic impedance of the proximal aorta;  $C_w$ , ‘Windkessel’ compliance of the arterial system;  $R_p$ , total systemic peripheral resistance. The result of the model simulation is  $Q$ , which is blood flow. The  $Z_0$  and  $C_w$  elements have non-linear, pressure dependent properties, indicated by the stylized  $f$  symbol.  $R_p$  and  $Q$  vary with time as symbolised by the arrows.

### 2.7.2c Aortic characteristic impedance ( $Z_0$ )

Aortic characteristic impedance is a dynamic property that represents the aortic opposition to pulsatile inflow from the contracting left ventricle (Wesseling et al., 1993). When the left ventricle contracts, the blood that is ejected into the aorta meets opposition from the existing aortic blood and consequent pressure (Jellema et al., 1999). The increase in blood volume subsequently increases aortic pressure further and the magnitude of this rise will depend on instantaneous flow, cross-sectional area of the aorta, and aortic compliance (Jellema et al., 1999). Thus the aortic characteristic impedance is the relationship between the pulsatile flow and pressure and can be derived from the formula:  $Z_0 = \sqrt{\rho/A \cdot C'}$ , where  $\rho$  is the density of blood,  $A$  is the cross-sectional area of the aorta, and  $C'$  is the aortic compliance per unit length (Wesseling et al., 1993).

### 2.7.2d Windkessel compliance ( $C_w$ )

Windkessel compliance, also known as arterial compliance, describes the ability of the aorta and arterial system to elastically store the blood that is expelled from the left ventricle (Wesseling et al., 1993). When blood enters the aorta from the left ventricle, the aorta elastically expands, which in turn increases the aortic pressure and this opposes further inflow into the aorta to the point where the pressure in the left ventricle also rises (Jellema et al., 1999). Thus,  $C_w$  describes the magnitude of the aortic pressure rise for a given volume of blood and is defined as a change in volume ( $dV$ ) divided by a change in pressure ( $dP$ ) (Harms et al., 1999). If the aortic length ( $l$ ) is assumed to be constant then changes in volume ( $V = \pi \cdot r^2 \cdot l$  or  $\pi \cdot A \cdot l$ ) are consequently proportional to changes in aortic cross-sectional area (Jellema et al., 1999). Thus compliance is calculated using the equation  $C' = dA/dP$  (Wesseling et al., 1993). To calculate the arterial compliance ( $C_w$ ) it is assumed that this value is equal to the compliance of one unit length of the thoracic aorta times an aortic length,  $l$ , and is expressed as:  $C_w = l \cdot C'$ . For an adult, the aortic length is assumed to be 80 cm. However, aortic length will depend on an individual’s height and weight

(Wesseling et al., 1993). Furthermore, the arterial compliance will also depend on age, as a young individual will have a compliant aortic wall and thus only produces a small rise in aortic pressure (Jellema et al., 1999), whereas compliance decreases with age (O'Rourke et al., 1968) and is thus likely to produce a greater rise in aortic pressure.

#### 2.7.2e Peripheral vascular resistance ( $R_p$ )

Peripheral vascular resistance signifies the opposition of the vascular beds to blood flow and drainage (Jansen et al., 2001; Jansen and van den Berg, 2005). Wesseling et al. (1993) describes this as the Poiseuille resistance of all the vascular beds together and can be defined as the ratio between mean pressure and mean flow. It has been found that the changes in the peripheral vascular resistance value are slow (Sprangers et al., 1991) with a time constant of approximately 10 seconds (Jansen et al., 2001) and therefore to simulate flow the value of the previous beat is used (Wesseling et al., 1993) using a self-adaptive system (de Vaal et al., 2005). In order to initially calculate the  $R_p$  at the start of model simulation a reasonable initial average population value is assumed for the first beat, which is the ratio of 100 mmHg for pressure and  $3 \text{ L}\cdot\text{min}^{-1}$  for  $\dot{Q}$  (Wesseling et al., 1993). The new  $R_p$  value for the second beat is calculated using the ratio of mean pressure to mean flow from the first beat, and so on. After approximately 5 beats, this converges to the correct value and  $R_p$  stabilises, as the true mean pressure and consequent computed mean flow have been established; thus a more accurate peripheral vascular resistance can be estimated (Wesseling et al., 1993; de Vaal et al., 2005).

The three elements of the model are not constant (Jansen et al., 2001). The aortic characteristic impedance and arterial compliance are the major determinants of systolic inflow (Bogert and van Lieshout, 2005) and depend on pressure itself (Langewouters, Wesseling and Goedhard, 1984). The aortic characteristic impedance increases only moderately when aortic pressure increases whereas, in contrast, the aortic Windkessel compliance decreases substantially when aortic pressure increases (de Vaal et al., 2005). Thus, the first two elements of the model,  $Z_0$  and  $C_w$  depend of the aorta's elastic properties (Jellema et al., 1999). The third element of the model, systemic vascular resistance, is not a major determinant of systolic inflow (Bogert and van Lieshout, 2005) and depends on many factors such as circulatory filling, metabolism, sympathetic tone, and vasoactive drugs (Jansen and van den Berg, 2005; de Vaal et al., 2005).

#### 2.7.2f The elastic properties of the aorta

The elastic behaviour of the aorta (cross-sectional area) varies in a non-linear fashion with pressure changes (Langewouters, Wesseling and Goedhard, 1984). When a volume of blood enters the aorta, at a low aortic pressure the cross-sectional area of the aorta increases quickly, whereas at higher pressures the area increases slowly (Jellema et al., 1999; Funk, Moretti and Gan, 2009). Early pulse contour methods did not take this into account (Bogert and van Lieshout, 2005), which would consequently be a major source of error (de Wilde et al., 2007). However, the cross-sectional area of the aorta included in the Modelflow method does increase non-linearly with increases in aortic pressure (Bogert and van Lieshout, 2005). These non-linear relationships were described by Langewouters et al. (1984) as mathematical functions whose properties regress closely dependent on an individual's age and gender, and slightly dependent on height and weight (de Wilde et al., 2007). Accordingly, the elastic behaviour of the aorta

i.e. the relationship between aortic cross-sectional area (A) and pressure (P) can be calculated using the following arctangent equation:

$$A(P) = A_{\max} \left[ 0.5 + \frac{1}{\pi} \arctan \left( \frac{P - P_0}{P_1} \right) \right]$$

A (P) is the aortic cross-sectional area for any pressure P and is determined by three major components: 1)  $A_{\max}$ , represents the maximal aortic cross-sectional area at very high pressure; 2)  $P_0$ , is the position of the inflection point on the pressure axis at  $0.5 A_{\max}$  (which is 40 mmHg); 3)  $P_1$ , is the steepness of the curve at  $0.75 A_{\max}$  and defines the width between the points at  $0.5$  and  $0.75 A_{\max}$  (which is 50 mmHg) (Jellema et al., 1999; Wesseling et al., 1993). Furthermore, aortic compliance per unit length (C') can also be calculated for any given pressure using the formulae:

$$C'(P) = \frac{A_{\max}/\pi P_1}{1 + \left( \frac{P - P_0}{P_1} \right)^2}$$

### 2.7.2g Arctangent parameters

The three arctangent parameters  $A_{\max}$ ,  $P_0$  and  $P_1$  have been determined by Langewouters et al. (1984) studying 45 human thoracic aortas in vitro.  $P_0$  and  $P_1$  regress tightly with age and differ slightly between females and males, however  $A_{\max}$  does not regress with age but does differ depending on gender; the average  $A_{\max}$  values are larger for men than for women (Wesseling et al., 1993; Jellema et al., 1999). However, an individual's actual  $A_{\max}$  value can differ between 40% from the group average and thus ideally an actual value for maximal area should be obtained another way; however if this is not possible the group average is used as a best estimate (Wesseling et al., 1993). Given an individual's gender and age, the three arctangent parameters can be calculated using Langewouters' regression equations (Langewouters, Wesseling and Goedhard, 1984), which are based on population averages (Jansen et al., 2001). Consequently, a pressure-area relationship for an individual can be computed (Wesseling et al., 1993). In the computer memory of the Finometer there are 'look-up' tables stored for each pressure level, which are created from these regression equations, so that the corresponding  $A_{\max}$ ,  $P_0$  and  $P_1$  values can then be read and entered into the model (Jansen et al., 2001).

### 2.7.2h Modelflow computation

Before the start of measurement, the demographic data of an individual (gender, age, height and weight) is input into the Finometer. This determines the pressure-volume, pressure-compliance, and pressure-characteristic impedance relationships from Langewouters' regression equations (Jansen et al., 2001) and the three arctangent parameters  $A_{\max}$ ,  $P_0$  and  $P_1$  can be calculated for the individual. From this the Modelflow software (BeatScope, version 1.1, Finapres Medical Systems BV, Amsterdam, The Netherlands) calculates the parameters  $Z_0$  and  $C_w$  instantaneously for any given pressure (Wesseling et al., 1993). Due to the fact that the aortic properties behaviour in a non-linear fashion and rely on pressure, the values for these parameters are computed for each new pressure sample taken at 100 Hz (Jellema et al., 1999). The  $Z_0$  and  $C_w$  values are then used to simulate the behaviour of the arterial system and consequently aortic flow waveform can be obtained from arterial pressure.

Each flow waveform per beat is integrated during arterial systole to give SV (de Vaal et al., 2005). Stroke volume is computed by calculating the systolic area, which represents the area under the arterial pressure waveform until the end diastolic pressure level. This signifies the area between the onset of increased BP and the dicrotic notch, i.e. the moment the aortic valve closes (Sugawara et al., 2003). Cardiac output is subsequently calculated beat-to-beat as the product of SV and instantaneous HR (Bogert and van Lieshout, 2005; de Vaal et al., 2005).

#### *2.7.2i Summary*

In summary, the Modelflow method utilised by the Finometer indirectly estimates  $\dot{Q}$  by computing aortic flow from the arterial pressure waveform (Mathews and Singh, 2008; Compton and Schäfer, 2009). Continuous corrections are made for aortic characteristic impedance, arterial compliance and systemic vascular resistance using the three-element, non-linear model (Wesseling et al., 1993), which depends on the participant's gender, age, height and weight (de Wilde et al., 2009). The aortic flow is then integrated per beat to give SV (Mathews and Singh, 2008; Compton and Schäfer, 2009), which is multiplied by HR to give  $\dot{Q}$  (Bogert and van Lieshout, 2005).

#### *2.7.3 Laboratory-based measurement of resting cardiac output using the Finometer*

The non-invasive hemodynamic monitor (Finometer, model 1, Finapres Medical Systems BV, Amsterdam, The Netherlands) was also used to measure continuous beat-to-beat  $\dot{Q}$  during rest in the 'Finometer-research' mode. The measurement preparation for  $\dot{Q}$  followed the same process as the Finometer BP, see section 2.5.6 (page 59), as these variables were measured concurrently.

The Finometer  $\dot{Q}$  data were interfaced with a Windows PC using an analog I/O box (Finapres Medical Systems BV, Amsterdam, The Netherlands) and a 16 channel data acquisition system (PowerLab/16SP, ML795, ADInstruments Pty Ltd, Castle Hill, Australia). The Finometer  $\dot{Q}$  data were then continuously displayed on a computer using LabChart Pro software (version 7.1, ADInstruments Pty Ltd, Castle Hill, Australia). A dedicated LabChart channel (channel 7) was configured to instantaneously display  $\dot{Q}$  in units of litres per minute ( $\text{L}\cdot\text{min}^{-1}$ ). The data were sampled at a frequency of 400 Hz. Cardiac output was displayed using the 'Arithmetic' function of LabChart in which the raw data inputted from the Finometer (analog I/O box output 3) to the PowerLab was multiplied by a calibration factor of 10, as specified in the 'Finometer-research' mode under the 'Configure' tab. Once the data were recorded and saved on to the computer's hard drive, it was then exported to spreadsheet software (Microsoft Excel, Microsoft Corporation, Redmond, Washington, USA) and displayed in 1 second intervals for further analysis. Cardiac output was recorded throughout a 5 minute seated rest and the mean resting  $\dot{Q}$  was calculated for this period.

#### *2.7.4 Published data on the validity and reliability of the Finometer measurement of cardiac output*

The accuracy of the Modelflow method has been previously validated with other  $\dot{Q}$  measurement techniques such as echocardiography (Sugawara et al., 2003), pulse dye-densitometry (Matsukawa et al., 2004), Doppler ultrasound (van Lieshout et al., 2003; Dyson et al., 2010) and thermodilution (Harms et al., 1999; Jansen et al., 2001) during several different experimental conditions such as supine rest (van Lieshout et al., 2003), orthostatic stress (Harms et al., 1999; van Lieshout et al., 2003; Dyson et al., 2010),

aerobic exercise (Sugawara et al., 2003; Matsukawa et al., 2004), isometric exercise (Dyson et al., 2010), vasoactive drugs (Dyson et al., 2010) and clinical evaluations (Jansen et al., 2001). The general consensus from these studies is that the Modelflow method provides a reliable estimation of  $\dot{Q}$  changes (Shibasaki et al., 2011), however for absolute values the Modelflow method must be calibrated against a 'gold' standard technique (Wesseling et al., 1993; Harms et al., 1999), such as thermodilution (Jansen and van den Berg, 2005).

Pivotal research by Jansen et al. (2001) studied the bias, precision and tracking ability of Modelflow method  $\dot{Q}$  ( $CO_{mf}$ ) compared to thermodilution values ( $CO_{td}$ ) in individuals undergoing cardiac surgery. The Modelflow  $\dot{Q}$  values were measured both uncalibrated and calibrated; uncalibrated values were based on the individual's gender, age, height and weight and calibrated values were calculated by multiplying the Modelflow  $\dot{Q}$  by a thermodilution calibration factor;  $K_1 = CO_{td}/CO_{mf}$ . When comparing the  $\dot{Q}$  values obtained from uncalibrated Modelflow and thermodilution, the standard deviation of the difference is approximately 18%, but this error is largely systematic. Therefore when measuring the percentage changes in  $\dot{Q}$  from control, calibration is not needed. Once the Modelflow values are calibrated against thermodilution, the error of the comparison is reduced to 7%. Therefore it was concluded that  $\dot{Q}$  computed by uncalibrated Modelflow is reliable to track changes and once calibrated can replace the thermodilution technique for determining absolute values.

The reason why the validity of the uncalibrated  $\dot{Q}$  value remains uncertain is due to the limitations of the Modelflow method, such as the fact that it is assumed that the participant has a normal human aorta (Compton and Schäfer, 2009) and a proper functioning aortic valve (Bogert and van Lieshout, 2005). Therefore as the Modelflow method is based on mathematical equations, if an individual's physiology reality deviates from the model, then there are negative consequences in the estimation of  $\dot{Q}$  (Geerts, Aarts and Jansen, 2011). Further to this, the Finometer measures arterial pressure from a peripheral finger artery rather than aortic pressure and thus the arterial pressure waveform is somewhat distorted in comparison (Wesseling et al., 1993; Harms et al., 1999). This consequently distorts the calculated flow waveform (Harms et al., 1999), however precise estimates of  $\dot{Q}$  are still produced (Wesseling et al., 1993). The measurement of non-invasive peripheral arterial pressure appears to present a pressure waveform sufficiently close to that of aortic pressure and thus has been found to produce reliable estimates of SV (Wesseling et al., 1993; Jellema et al., 1999).

In conclusion, for absolute  $\dot{Q}$  values of high accuracy and precision the Modelflow method must be calibrated against a standard (Wesseling et al., 1993; Harms et al., 1999), however this is not necessary if the absolute values are not relevant. Without calibration the Modelflow method has been shown to reliably track  $\dot{Q}$  changes (Shibasaki et al., 2011) and  $\dot{Q}$  can be expressed as changes from control (Harms et al., 1999). For the studies included within this thesis, the Modelflow method was not calibrated against a 'gold' standard as only pre to post experimental condition comparisons were required. Thus, the absolute  $\dot{Q}$  values obtained were not necessarily valid, but when used for this purpose it, was not deemed necessary. Nonetheless, the uncalibrated  $\dot{Q}$  values calculated do provide reliable data that can track changes in  $\dot{Q}$  relatively accurately. Further to this, as the Modelflow method was not required to be calibrated the non-invasive and ease of use aspects of this technique were maintained.

The intratester reliability of the Finometer device for measuring  $\dot{Q}$  obtained by the one investigator in the studies in this thesis was determined. Study 3 in Chapter 5 explored the long term reliability of the resting Finometer  $\dot{Q}$  values; see the results section 5.3 (page 143).

## **2.8 Total peripheral resistance (TPR) estimation**

### ***2.8.1 Background information on total peripheral resistance***

Total peripheral resistance (TPR), also known as systemic vascular resistance, represents the vascular resistance presented by all of the systemic blood vessels (Tortora and Derrickson, 2012). As previously discussed, TPR is a determinant of BP ( $MAP = \dot{Q} \times TPR$ ) (Sherwood, 2014) and thus its measurement could provide a valuable insight into the mechanisms that control chronic adaptations to BP. Total peripheral resistance is governed by the size of the lumen, blood viscosity, and total blood vessel length (Tortora and Derrickson, 2012) and thus an adaptation to TPR could suggest a change to any of these parameters.

Total peripheral resistance cannot be measured directly but is instead estimated from BP and  $\dot{Q}$  (Wesseling et al., 1995a). Blood flow ( $F$ ) through the circulatory system is proportional to the pressure gradient ( $\Delta P$ ), which is the driving force of blood flow, and the total resistance ( $R$ ) offered by all the systemic peripheral vessels, which is a hindrance to blood flow (Sherwood, 2014), as discussed in section 2.5.1 (page 52). Consequently blood flow can be calculated using the equation:  $F = \Delta P/R$ , where  $F$  is equal to cardiac output,  $\Delta P$  is the mean arterial pressure and  $R$  is the total peripheral resistance (Sherwood, 2014). Thus, the equation can be expressed as  $\dot{Q} = MAP/TPR$  and subsequently rearranged to estimate TPR using the formulae  $TPR = MAP/\dot{Q}$ .

### ***2.8.2 Laboratory-based estimation of resting total peripheral resistance***

Resting TPR was estimated offline using the calculated resting MAP data and the resting  $\dot{Q}$  data from the Finometer, which were obtained during the 5 minute rest period. Subsequent to this rest period, resting TPR was estimated using the following formulae:

$$TPR = \frac{MAP}{\dot{Q}}$$

(McArdle, Katch and Katch, 2010).

### ***2.8.3 The validity and reliability of the Finometer estimation of total peripheral resistance***

As previously mentioned it is not possible to directly measure TPR (Wesseling et al., 1995a) and thus TPR must be estimated from the non-invasive, indirect measurement of MAP and  $\dot{Q}$ . Whilst the validity of the Finometer BP values has been established, the absolute Finometer  $\dot{Q}$  values are less accurate when left uncalibrated (Jansen et al., 2001), as in the studies within this thesis, and subsequently the estimation of TPR may be less accurate. However, despite these facts both measurements are suggested to be reliable, as previously discussed, and are thus likely to produce a reliable estimation of TPR. This was the main criteria of the TPR estimation in the studies in this thesis as only pre to post experimental condition comparisons were required. The intratester reliability of the TPR values obtained by the one investigator

in the studies in this thesis was determined. Study 3 in Chapter 5 explored the long term reliability of the resting TPR values; see the results section 5.3 (page 143).

## **2.9 Stroke volume (SV) estimation**

### ***2.9.1 Background information on stroke volume***

Stroke volume (SV) is the volume of blood ejected during each contraction (Tortora and Derrickson, 2012). As previously discussed, SV is a determinant of cardiac output ( $\dot{Q} = SV \times HR$ ) (Tortora and Derrickson, 2012) and thus could provide a valuable insight into the mechanisms that govern chronic adaptations of  $\dot{Q}$ . Adaptations to SV could indicate changes in cardiac dimensions, blood volume and/or venous return (Smith and Fernhall, 2011). Calculating SV forms the basis of  $\dot{Q}$  measurement and, as discussed in section 2.7.1 (page 69), the Finometer estimates  $\dot{Q}$  by multiplying the Modelflow SV by the instantaneous HR (Bogert and van Lieshout, 2005; de Vaal et al., 2005). Therefore, SV can be consequently estimated from dividing  $\dot{Q}$  by HR (McArdle, Katch and Katch, 2010).

### ***2.9.2 Laboratory-based estimation of resting stroke volume***

Resting SV was estimated offline using the resting Finometer  $\dot{Q}$  data and the resting HR data from the ECG measurement, which were obtained during the 5 minute rest period. Subsequent to this rest period, using the 5 minute mean of both  $\dot{Q}$  and HR resting SV was estimated using the following formulae:

$$SV = \frac{\dot{Q}}{HR} \times 1000$$

(Headley, 2002).

As  $\dot{Q}$  was expressed in  $L \cdot \text{min}^{-1}$ , the division of  $\dot{Q}$  by HR was multiplied by 1000 to convert the SV units from litres (L) to millilitres (mL).

### ***2.9.3 The validity and reliability of the estimation of stroke volume***

Due to the fact that SV is estimated using the Finometer  $\dot{Q}$  and ECG HR data, the validity and reliability of SV will consequently be affected by any measurement limitations of these variables. This is particularly pertinent in relation to  $\dot{Q}$ , which has been shown to produce less accurate absolute values when measured using the Finometer uncalibrated (Jansen et al., 2001); subsequently the validity of the SV estimation will be affected. However, despite this both Finometer  $\dot{Q}$  and ECG HR have been found to be reliable measures, as previously discussed, and are thus likely to produce a reliable estimation of SV. This was the main criteria of the SV estimation in the studies in this thesis as only pre to post experimental condition comparisons were required. The intratester reliability of the SV values obtained by the one investigator in the studies in this thesis was determined. Study 3 in Chapter 5 explored the long term reliability of the resting SV values; see the results section 5.3 (page 143).

## **2.10 Isometric wall squat knee joint angle measurement**

### ***2.10.1 Background information on joint angle measurement***

Radiographic methods are traditionally used to measure joint angle and are considered to be the gold standard technique (Reese and Bandy, 2010). However, this method is not cost effective, is potentially dangerous to health (Reese and Bandy, 2010) and, additionally, it is not a practical method for the measurement of knee joint angle during the isometric wall squat exercise. Other measurement devices used to assess joint angle include the goniometer, inclinometer, electrogoniometer, as well as photographic and video recording equipment (Reese and Bandy, 2010). From these devices, the more common and easily accessible method widely used to measure joint angle is the goniometer. A universal (standard) goniometer generally consists of a central 360° protractor portion from which two mounted arms join consisting of a stationary arm, which is in a fixed position as it is an extension of the protractor, and a moving arm, which rotates around the protractors axis and is attached by a central rivet (Clarkson, 2005; Reese and Bandy, 2010). Goniometry has been traditionally used to quantify joint range of motion by occupational and physical therapists (Clarkson, 2005). Further to this, the universal goniometer has also been used previously to quantify knee joint angle and exercise position during squatting type exercises, such as the double-leg semisquat (Coqueiro et al., 2005), single leg squat (Youdas et al., 2007) and the wall squat (Nolan, 2011). A clinical goniometer was used to measure knee joint angle during isometric wall squat exercise performed in the laboratory in the studies within this thesis.

### ***2.10.2 Laboratory-based measurement of the isometric wall squat knee joint angle using a Goniometer***

The wall squat knee joint angle was measured using a clinical goniometer (MIE Clinical Goniometer, MIE Medical Research Ltd., Leeds, U.K.). This clear plastic goniometer with a 0 to 360 degree scale in 1 degree increments was selected to attain optimum accuracy in the measurement of knee joint angle (Reese and Bandy, 2010). A spirit level was attached to the stationary arm of the goniometer to ensure that the lower leg was vertical during the wall squat. Furthermore, four 25mm elastic Velcro straps were fitted to the goniometer so that it could be kept in place on the knee joint throughout exercise; two straps were fitted on each arm, which attached to the participant's leg, as shown in Figure 2.10.





**Figure 2.10.** Goniometry of the knee joint.

To position the goniometer, participants were placed in a seated position with their left knee at a 90° angle. The stationary arm is typically aligned with the midline of the stationary segment of the joint (Dutton, 2012), which is the lower portion of the leg during the wall squat. The moving arm is aligned with the midline of the moving segment of the joint (Dutton, 2012), which is the upper portion of the leg during the wall squat. Finally, the fulcrum of the goniometer is aligned with the axis of rotation of the joint. Thus the knee joint angle was measured in the sagittal plane with the fulcrum aligned with the lateral epicondyle of the femur, the moving arm placed on the lateral midline of the femur using the greater trochanter for reference and the stationary arm on the lateral midline of the fibula using the lateral malleolus and fibular head for reference (modified from Dutton, 2012). Any loose clothing was adjusted in order to gain an optimal view for determining the segment midline and the relevant bony landmarks of the knee, hip and ankle joints were palpated to align the goniometer. The goniometer was then attached to the participant's left leg using the four elastic Velcro straps, which were carefully fitted to ensure that compression of the muscle did not occur. The alignment of the goniometer was rechecked throughout the exercise, particularly after movement occurred, as the axis of rotation is not stationary throughout the motion of a joint (Dutton, 2012). The knee joint angle measured was the internal angle between the femur and fibula.

### ***2.10.3 Published data on the validity and reliability of the goniometer measurement of knee joint angle***

The validity of the universal goniometer for measuring knee joint angle was studied by Gogia et al. (1987). Measurements of knee joint angle were made with the goniometer and compared to values derived from the gold standard roentgenograms (now known as a radiograph). High correlation coefficients for validity were reported, which ranged from 0.97 to 0.98 ( $r$  = Pearson product-moment

correlation coefficient) and from 0.98 to 0.99 (ICC = intraclass correlation coefficient). It was concluded that knee joint angle measurements made with the goniometer are valid and reflect the actual position of the knee.

As the measurement of wall squat knee joint angle was such an integral part of the studies in this thesis to set the exercise position, the validity and intratester reliability of knee joint goniometry was assessed in a preliminary study. In this context, the radiographic measurement of joint angle was not a practical method to use as a gold standard and goniometry values were instead compared to the joint angle values attained using video recording equipment with analysis software.

#### ***2.10.4 Preliminary study 1: Validity and reliability of goniometer knee joint angle measurements during isometric wall squat exercise***

##### *2.10.4a Aim*

The aim of the preliminary study was to establish both the validity and intratester reliability of measuring knee joint angle using the goniometer during a range of isometric wall squat exercise positions. The goniometer measures were compared to those recorded using a video camcorder and analysed digitally using video analysis software.

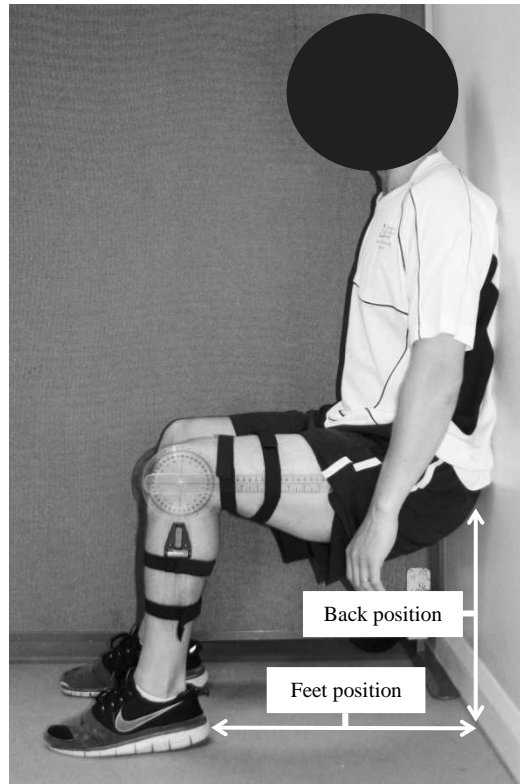
##### *2.10.4b Method*

*Participants:* Ten healthy participants (8 males and 2 females) volunteered to participate in this preliminary study (age  $28.9 \pm 7.0$  years; stature  $1.76 \pm 0.07$  m; body mass  $74.7 \pm 8.0$  kg). All participants completed a familiarisation session as outlined in section 2.3.5 (page 50).

*Equipment:* Knee joint angle was measured using a clinical goniometer (MIE Clinical Goniometer, MIE Medical Research Ltd., Leeds, U.K.). In addition, each wall squat was recorded using a digital video camera recorder (Sony DCR-HC51 MiniDV Handycam Camcorder, Sony Corporation, Tokyo, Japan). The digital camcorder was mounted on a rigid tripod (Hama Star 45 Tripod, Hama (UK) Ltd., Hampshire, UK) at a height of 70cm, and placed perpendicular to the participant's sagittal plane of motion facing their left side, 2.4 meters away from their exercise position. The camcorder's field of view was positioned to allow the ankle, knee and hip to be in full view. Using double-sided adhesive tape, three retro-reflective markers (1.5 cm in diameter) (made in-house, Department of Sport Science, Tourism and Leisure, Canterbury Christ Church University, Canterbury, United Kingdom) were placed on the participant's left side: 1) at the ankle on the lateral malleolus and fibular head; 2) at the knee on the lateral epicondyle of the femur; 3) at the hip on the greater trochanter. After the recording was processed, video analysis software (Quintic Biomechanics 9.03 v9a, Quintic Consultancy Ltd., Coventry, United Kingdom) was then used to calculate the knee joint angle using the 'Freehand' angles feature.

*Protocol:* Each participant performed five wall squats at five different knee joint angles ( $130^\circ$ ,  $120^\circ$ ,  $110^\circ$ ,  $100^\circ$  and  $90^\circ$ ) in a randomised order. The knee joint angle was determined by the goniometer. Each wall squat was held for a maximum period of 10 seconds with a 30 second rest period between each exercise. During the 10 second period, the position of the participant's feet and back positions were recorded to the nearest centimetre using a standard metre rule. The feet position was measured as the direct distance from

the back of the left heel to the wall (see Figure 2.11). The back position was measured as the direct distance from the ground to the lower back, which was defined as the last point of contact that the participant's back had with the wall (see Figure 2.11). These measurements were taken to observe the consistency of the feet and back positions between repeated wall squats. Each wall squat was recorded using a digital camcorder and later analysed to calculate knee joint angle using the Quintic Biomechanics software. After all five joint angles were completed; this process was repeated for a second and third time to obtain reliability data.



**Figure 2.11.** Measurement of the isometric wall squat exercise feet and back positions.

*Data analysis:* Differences between the joint angle measurement techniques were calculated using the 95% ratio limits of agreement (Bland and Altman, 1986).

#### 2.10.4c Results

The mean Quintic values calculated for each wall squat knee joint performed can be seen in Table 2.1.

**Table 2.1.** Mean values calculated digitally for each knee joint angle performed.

	Knee Joint Angle (Degrees)				
Goniometer	130°	120°	110°	100°	90°
Quintic	131 ± 1°	121 ± 1°	111 ± 1°	101 ± 2°	91 ± 1°

The ratio limits of agreement were 0.99 x/÷ 1.04. Therefore these findings suggest that when the wall squat knee joint angle was set at 110° using the goniometer the actual wall squat position was 109.20° with the true value lying between 105.44° and 113.11°.

#### 2.10.4d Discussion

From the results of this preliminary study it is suggested that the goniometer provides a valid measure of knee joint angle during isometric wall squat exercise. Due to this important finding it was proposed that the goniometer could be used as a measurement tool to accurately manipulate the knee joint angle to set and adjust the wall squat position in the studies within this thesis.

#### 2.10.5 Home-based measurement of the isometric wall squat knee joint angle using a Bend and Squat device

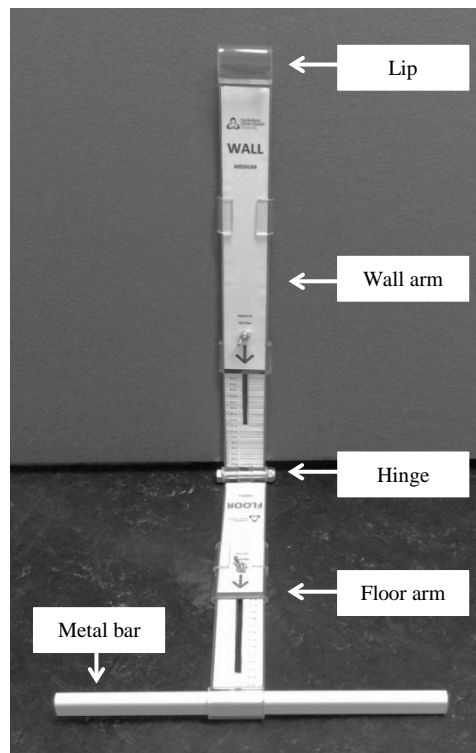
Although the goniometer is suitable for the measurement of knee joint angle in a laboratory-based setting, it is not a practical method to measure and set the isometric wall squat knee joint angle during home-based training as the goniometer could easily be misaligned by the participant. This would lead to training being completed at an incorrect knee joint angle and could cause the participant to either over or under train. Thus a method for setting knee joint angle in a simple manner was devised.

An isometric wall squat is performed by a participant moving their back down the wall and their feet forward into the required exercise position, which is determined by the knee joint angle. Generally speaking, the lower the wall squat knee joint angle the further the participant's back moves down the wall and the further their feet move forward; this was observed to be true during preliminary study 1. Therefore it was proposed that for a given wall squat exercise position, the participant's feet and back could be positioned to attain the correct knee joint angle. The required feet and back positions would be governed by the wall squat knee joint angle and the participant's stature. Based on this theory, a prototype device was designed and created called the 'Bend and Squat' to place a participant's back and feet into the correct wall squat exercise position (Figure 2.12).



**Figure 2.12.** The Bend and Squat device for setting knee joint angle during isometric wall squat exercise.

This simple device consists of two adjustable plastic arms labelled 'floor' and 'wall', which are connected by a hinge; Figure 2.13 displays the components of the Bend and Squat device. The adjustable arms contain a measurement scale marked in centimetres. The arm adjustment range for the Bend and Squat prototype device was based on the feet and back positions recorded in preliminary study 1; the floor arm could be set from 34 to 54cm and the wall arm could be set from 50 to 83cm. Before positioning the Bend and Squat device for exercise, the two arms were adjusted to the desired lengths for the wall squat angle to be performed and fixed into position. The Bend and Squat device was then placed at a right angle to the floor and wall; the first arm labelled 'floor' was placed on the ground for the participant's feet to rest against, and the second arm labelled 'wall' was rested against a wall to align the participant's lower back. A metal bar was attached to the end of the floor arm for the participant's feet to rest against shoulder width apart and the end of the wall arm had a small rounded lip for the participant's lower back to rest on (see Figure 2.13). This lip was too small to support any of the participant's weight and therefore did not aid the wall squat exercise but rather provided a physical reference point to inform the correct position.



**Figure 2.13.** The main components of the Bend and Squat device.

A second preliminary study was carried out to 1) ascertain the relationships between the isometric wall squat knee joint angle and both the feet and back positions, and 2) determine the validity and reliability of using a prototype Bend and Squat device to accurately set the wall squat exercise position to attain a specific knee joint angle.

### ***2.10.6 Preliminary study 2: Validity and reliability of the Bend and Squat device for setting knee joint angle during isometric wall squat exercise***

#### ***2.10.6a Aim***

The aim of the second preliminary study was twofold. The first aim was to establish the relationships between the isometric wall squat knee joint angle and both the feet and back positions. The second and main aim was to determine both the validity and reliability of the prototype Bend and Squat device for setting the wall squat exercise position at a range of knee joint angles. The wall squat knee joint angle positions set using the Bend and Squat device were compared to those recorded using a video camcorder and analysed digitally using video analysis software.

#### ***2.10.6b Method***

*Participants:* Ten healthy participants (8 males and 2 females) volunteered to participate in this second preliminary study (age  $28.9 \pm 7.0$  years; stature  $1.76 \pm 0.07$  m; body mass  $74.7 \pm 8.0$  kg). All participants completed a familiarisation session as outlined in section 2.3.5 (page 50).

*Equipment:* Knee joint angle was measured using a clinical goniometer (MIE Clinical Goniometer, MIE Medical Research Ltd., Leeds, U.K.) and the participant's back and feet position were measured using a standard metre rule; measurements were recorded in centimetres. The wall squat exercise position was then set using the Bend and Squat device (made in-house, Department of Sport Science, Tourism and Leisure, Canterbury Christ Church University, Canterbury, United Kingdom). In addition, each wall squat was recorded using a digital video camera recorder (Sony DCR-HC51 MiniDV Handycam Camcorder, Sony Corporation, Tokyo, Japan). The digital camcorder was mounted on a rigid tripod (Hama Star 45 Tripod, Hama (UK) Ltd., Hampshire, UK) at a height of 70cm, and placed perpendicular to the participant's sagittal plane of motion facing their left side, 2.4 meters away from their exercise position. The camcorder's field of view was positioned to allow the ankle, knee and hip to be in full view. Using double-sided adhesive tape, three retro-reflective markers (1.5 cm in diameter) (made in-house, Department of Sport Science, Tourism and Leisure, Canterbury Christ Church University, Canterbury, United Kingdom) were placed on the participant's left side: 1) at the ankle on the lateral malleolus and fibular head; 2) at the knee on the lateral epicondyle of the femur; 3) at the hip on the greater trochanter. After the recording was processed, video analysis software (Quintic Biomechanics 9.03 v9a, Quintic Consultancy Ltd., Coventry, United Kingdom) was then used to calculate the knee joint angle using the 'Freehand' angles feature.

*Protocol:* Each participant performed twelve wall squats in total. Four different knee joint angles ( $130^\circ$ ,  $120^\circ$ ,  $110^\circ$  and  $100^\circ$ ) were completed in a randomised order three times. The knee joint angle was determined by the goniometer. Each wall squat was held for a maximum period of 10 seconds with a 30 second rest period between each exercise. During the 10 second period, the position of the participant's feet and back positions were recorded using a standard metre rule to the nearest centimetre. The feet position was measured as the direct distance from the back of the left heel to the wall (see Figure 2.11, page 82). The back position was measured as the direct distance from the ground to the lower back, which was defined as the last point of contact that the participant's back had with the wall (see Figure 2.11, page

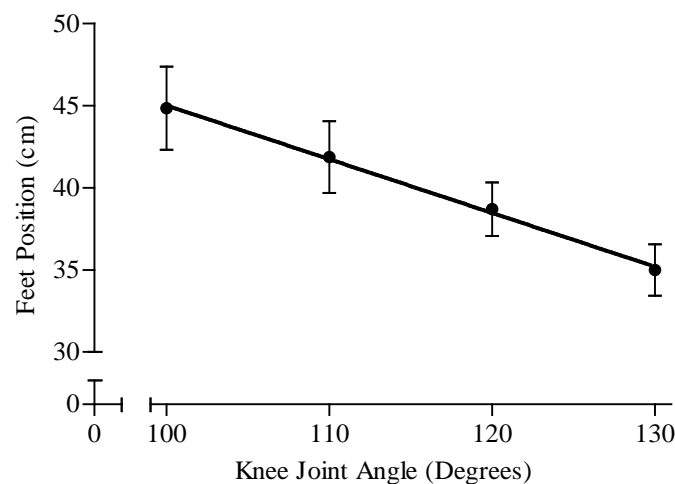
82). After all twelve wall squats were completed the mean of the three feet and back positions for each knee joint angle were calculated.

Participants then performed three wall squats at each knee joint angle (130°, 120°, 110° and 100°) in a randomised order using the Bend and Squat device. The Bend and Squat device's 'floor' and 'wall' arms were adjusted accordingly for each participant using their recorded mean feet and back position data for each wall squat knee joint angle. The range of wall squat knee joint angles was selected based on the prototype Bend and Squat device's available arm adjustment range. Each wall squat was held for a maximum period of 10 seconds with a 30 second rest period between each exercise. All wall squats performed with the Bend and Squat device were recorded using a digital camcorder and later analysed to calculate knee joint angle using Quintic Biomechanics software.

*Data analysis:* Pearson's product-moment correlation was used to explore the relationships between isometric wall squat knee joint angle and the feet and back positions. Differences between the Bend and Squat device and Quintic knee joint angle values were calculated using the 95% ratio limits of agreement (Bland and Altman, 1986).

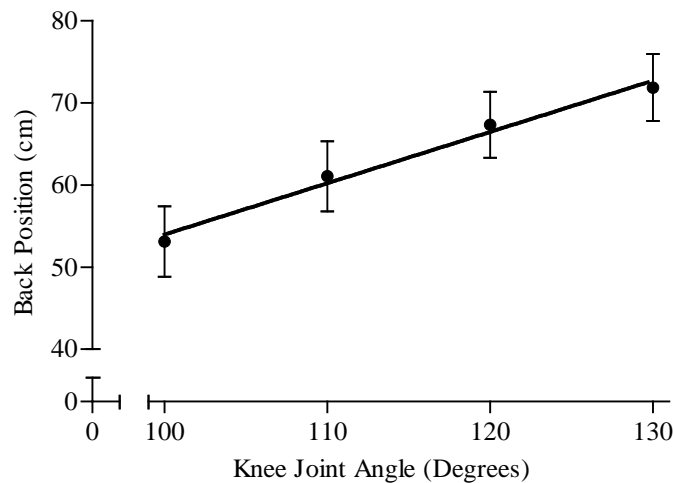
#### 2.10.6c Results

It can be seen in Figure 2.14 that isometric wall squat knee joint angle and the mean feet position data produced a significant inverse linear relationship ( $r = -1.00$ ;  $P < 0.05$ ). When each participant's individual inverse linear relationship between wall squat knee joint angle and feet position was examined it was found that  $r$  ranged from -0.98 to -1.00 ( $P < 0.05$ ).



**Figure 2.14.** The relationship between isometric wall squat knee joint angle and the mean feet position data.

Further to this, it can be seen in Figure 2.15 that isometric wall squat knee joint angle and the mean back position data produced a significant linear relationship ( $r = 0.99$ ;  $P < 0.05$ ). When each participant's individual linear relationship between wall squat knee joint angle and back position was examined it was found that  $r$  ranged from 0.98 to 1.00 ( $P < 0.05$ ).



**Figure 2.15.** The relationship between isometric wall squat knee joint angle and the mean back position data.

The mean Quintic values for each wall squat knee joint angle performed with the Bend and Squat device can be seen in Table 2.2.

**Table 2.2.** Mean values calculated digitally for each wall knee joint angle set using the Bend and Squat device.

	Knee Joint Angle (Degrees)			
Bend and Squat	130°	120°	110°	100°
Quintic	128 ± 3°	121 ± 2°	112 ± 2°	102 ± 2°

The ratio limits of agreement were 0.99 x/÷ 1.05. Therefore these findings suggest that when the wall squat knee joint angle was set at 110° using the Bend and Squat device the actual wall squat position was 109.17° with the true value lying between 103.86° and 114.76°.

#### 2.10.6d Discussion

From the results of the second preliminary study it was confirmed that there are indeed significant relationships between wall squat knee joint angle and the participant’s feet and back positions. The wall squat knee joint angle and participant’s feet position produced a significant inverse linear relationship suggesting that lower wall squat knee joint angles require the feet to be positioned further away from the wall, as hypothesised. Also, the wall squat knee joint angle and back position produced a significant linear relationship suggesting lower wall squat knee joint angles require the back to be positioned lower down the wall, as hypothesised. From this data it can be concluded that the participant’s feet and back positions can be utilised to set knee joint angle and consequently the wall squat exercise position.

Also, the results from the preliminary study suggest that the Bend and Squat device provides a valid method to set the knee joint angle during an isometric wall squat exercise. Due to this outcome it was



proposed that the Bend and Squat could be used as a device to accurately set and adjust the knee joint angle during home-based isometric wall squat exercise training in the studies within this thesis. Based on this finding, the Bend and Squat prototype was developed and 15 Bend and Squat devices were made in five different sizes to account for the differences in participant stature and prescribed wall squat knee joint angle; Small/Large (small wall range: 37-57 cm; large floor range: 35-54 cm), Medium/Small (medium wall range: 47-77 cm; small floor range: 27-41 cm), Medium/Large (medium wall range: 47-77 cm; large floor range: 35-54 cm), Large/Small (large wall range: 57-97 cm; small floor range: 27-41 cm) and Large/Large (large wall range: 57-97 cm; large floor range: 35-54 cm) (made in-house, Department of Sport Science, Tourism and Leisure, Canterbury Christ Church University, Canterbury, United Kingdom). These simple Bend and Squat devices were used in study 3 (see Chapter 5, page 131) to set the prescribed wall squat knee joint angle during home-based isometric exercise training.

## **2.11 Rate of perceived discomfort (RPD) measurement**

### ***2.11.1 Background information on rate of perceived discomfort***

The measurement of subjective somatic symptoms is a tool used to gauge a participant's level of effort, exertion, fatigue and pain (Borg, 1998). A common scale used is rate of perceived exertion (RPE), which is a measure used to indicate the degree of physical strain (Borg, 1982). Rate of perceived exertion integrates cues received from the organ systems of the body such as the musculoskeletal, cardiovascular, respiratory and central nervous systems (Borg, 1990) and this information is used to quantify subjective symptoms (Borg, 1982). This subjective rating of exercise intensity by an individual is a good indication of the relative fatigue experienced (Fletcher et al., 2001). Rate of perceived exertion can be measured using several different scales with the two most predominant being the 'Borg RPE scale' and the 'Borg CR10 scale' (Borg, 1998).

The Borg RPE scale is a 15-point, graded scale ranging from 6 to 20 with descriptive verbal anchors from 'no exertion at all' at scale point 6 to 'maximal exertion' at scale point 20. This RPE scale was constructed to increase in a linear fashion with steady-state aerobic exercise (bicycle ergometer), with parameters such as power output, oxygen consumption and HR (Noble et al., 1983; Borg, 1990; 1998). Consequently HR can be estimated by multiplying the RPE value by 10 (O'Sullivan, 1984) and thus the RPE range from 6 to 20 represents HR values from 60 to 200 beats·min<sup>-1</sup>, respectively (Borg, 1982). This RPE scale is commonly used during aerobic exercise testing and training and rehabilitation.

The Borg category ratio (CR10) scale was later developed for scaling perceived exertion and also pain. The principles of the CR10 scale are different to RPE scale in that pain is scaled in a nonlinear fashion with a positively accelerating growth function (Borg, 1998). The scale ranges from 0 to 10, again with descriptive verbal anchors where 0 is 'nothing at all' and 10 is 'extremely strong'. As the CR10 scale is nonlinear the 'moderate' verbal anchor is not in the middle of the scale, it is instead lower down the scale at 3. The number 10 represents the individual's strongest effort and the highest amount of exertion that they have ever experienced (Borg, 1990). However, this scale does not have a fixed end point to allow an individual to choose a higher number than 10 (11 or above) as a person may experience a pain stronger than they have experienced previously (Borg, 1998). The scale also has an open ended anchor without a fixed number, represented by a bold dot at the end of the scale, and is termed 'absolute maximum' as the

individual may imagine an effort of a magnitude that is even stronger than what they have experienced (Borg, 1990). The numbers in the CR10 scale are not fixed (Eston and Reilly, 2001) and individuals are encouraged to use whatever numbers they wish such as half values (1.5 or 2.5) or decimals (0.3 or 5.6) (Borg, 1998). As the scale has non-linear characteristics it may be more suitable to reflect perceived exertion and identify fatigue in those variables that produce a non-linear relationship with exercise intensity, such as lactate production (Noble et al., 1983; Eston and Reilly, 2001). The CR10 scale is commonly used to estimate pain, such as musculoskeletal pain (Borg, 1998), and is best utilised when there is a dominant sensation in one particular area of the body, such as fatigue in the quadriceps (Buckley and Eston, 2007).

Whilst Borg's RPE scale (6-20) has been used to measure perceived exertion during strength training (Buckley and Borg, 2011) and is recommended by the American Heart Association and the American College of Sports Medicine (ACSM) for use during resistance training (Pollock et al., 2000; Williams et al., 2007) the use of the RPE scale in this context is somewhat surprising. This is due to the fact that the RPE scale was designed to measure whole body sensations during aerobic activity, not localised muscle sensations (Buckley and Borg, 2011), such as those found during strength and resistance training. Thus, a more appropriate scale to use during strength training is a scale with ratio properties that more appropriately reflects the curvilinear responses to incremental muscular work, such as Borg's CR10 scale (Buckley and Borg, 2011). Indeed, Buckley and Borg (2011) found that CR10 perceived exertion ratings increased in a curvilinear manner with each weight increment (intensity) when performing both elbow (triceps) extension and knee extension exercise for 2 repetitions. From this research it was suggested that the CR10 scale should be used in preference to the original RPE scale for strength training.

During isometric exercise the CR10 scale has been used to rate perceived exertion (Pincivero, Coelho and Erikson, 2000), pain (Koltyn et al., 2001) and discomfort (Wiles et al., 2005). During isometric exercise an individual will generally experience a level of discomfort or pain in the contracting muscle, particularly during fatiguing contractions (Lind, 2011). This is due to the fact that that high intensity isometric contractions occlude muscle blood flow causing an accumulation of metabolic byproducts, such as lactate, which is associated with fatigue as well as pain and discomfort (Folland et al., 2002). The cellular acidosis which subsequently occurs may be indirectly involved in muscular fatigue as group III-IV nerve afferents may be activated and could produce an acidosis induced discomfort (Westerblad, Allen and Lännergren, 2002). Such discomfort experienced may limit an individual's ability to continue exercising and thus exercise must be terminated (Gandevia, Taylor and Butler, 2000; Sgherza et al., 2002; Noakes, St Clair Gibson and Lambert, 2005). Thus in study 3 of this thesis the CR10 scale was used to rate a participant's perceived discomfort. This variable was used as an alternative indication of exercise intensity to HR. This is an important measure in the validation of a home-based exercise training protocol (Wiles et al., 2005).

### ***2.11.2 Laboratory- and home-based measurement of the rate of perceived discomfort using the Borg CR10 Scale***

The perceived exertion scale used in this thesis was the Borg CR10 scale. The CR10 scale was used to measure and rate discomfort specifically felt in the participant's legs. Discomfort in the front of the upper legs was selected specifically as the quadriceps are the main active muscle utilised during the wall squat.

Before its use, the CR10 scale was explained to the participants using standardised instructions and verbal examples, as suggested by Borg (1998) to confirm the participant's understanding. Due to the fact that the CR10 scale was used to rate discomfort rather than pain, the participants were instructed that the number 10 on the scale, 'Max P', represents their previously worst local muscular discomfort experienced (Wiles et al., 2005).

During laboratory-based isometric wall squat exercise the CR10 scale was placed in a suitable position for the participants to view at all times. At the end of a 2 minute wall squat exercise the participant was asked by the investigator to rate their perceived discomfort. Participants were instructed to think about 'how much discomfort they feel there is in their legs' and rate this feeling on the CR10 scale. Participants were advised that they could select a number higher than 10 if they desired; this number was recorded by the investigator. These data were then entered into spreadsheet software (Microsoft Excel, Microsoft Corporation, Redmond, Washington, USA) for analysis. During home-based training the participants were instructed to place the CR10 scale where it could be viewed at all times. At the end of a 2 minute wall squat participants were instructed to decide what their RPD was and then record this number on the training session 'Data Sheet' (see Appendix 8, Section 1, page 233). After all training was completed, these data were then entered into spreadsheet software (Microsoft Excel, Microsoft Corporation, Redmond, Washington, USA) for analysis.

### ***2.11.3 Published data on the validity and reliability of the Borg CR10 Scale measurement of rate of perceived discomfort***

There is little research investigating the validity and reliability of the CR10 scale for measuring RPD during isometric wall squat exercise, however the CR10 scale has been validated against objective markers of exercise intensity. Noble et al. (1983) investigated the relationship between three perceptual perceived ratings from the CR10 scale (leg effort, cardiorespiratory effort and leg pain) and selected physiological variables (blood and muscle lactate and HR) during a cycle ergometer progressive, maximal exercise test. The results found that both the perceived exertion ratings and lactate measures produced a positively accelerating increase with exercise intensity, whereas HR produced a linear relationship. Thus this scale can be used to identify fatigue related to non-linear physiological variables, such as lactate, which is accumulated during isometric work.

Day et al. (2004) studied the reliability of using the CR10 scale to rate perceived exertion of low-, moderate- and high-intensity resistance training sessions. The resistance training sessions consisted of five exercises including back squat, bench press, overhead press, biceps curl, and triceps push down. Each training session was completed twice and the recorded perceived exertion across the two different trials was compared producing a CV of 14.5%. It was concluded that the CR10 scale appears to be a reliable method for quantifying exercise intensity during various forms of resistance training.

## **CHAPTER 3: STUDY 1**

### **THE ACUTE EFFECTS OF ISOMETRIC WALL SQUAT EXERCISE ON HEART RATE AND BLOOD PRESSURE**

The work in this chapter was presented at the British Association of Sport and Exercise Sciences Annual Conference (Goldring, Wiles and Coleman, 2010) and was published in the Journal of Sports Sciences (Goldring, Wiles and Coleman, 2014); see Appendix 9 (page 245).

#### **3.1 Introduction**

In order to investigate whether simple isometric wall squat exercise training can effectively reduce resting BP as part of a home-based training programme, a method for prescribing and adjusting exercise intensity must first be established to ensure a scientifically sound training prescription. As discussed in Chapter 1, section 1.6.2a (page 37), neither constant force nor constant EMG isometric contraction styles are suitable for inclusion within a home-based IET protocol, due to the necessary use of expensive and/or laboratory-based equipment. Therefore it was suggested that isometric wall squat exercise could be prescribed at a constant position (knee joint angle), which may provide a viable more accessible home-based solution, as joint angle measurement is simple and inexpensive (Reese and Bandy, 2010).

It was further proposed in Chapter 1, section 1.6.2b (page 39), that the intensity of wall squat exercise could be adjusted by manipulating the knee joint angle as previous research of squat based exercise has demonstrated that greater knee flexion increases the quadriceps EMG activity (Escamilla, 2001; Kvist and Gillquist, 2001; Bevilacqua-Grossi et al., 2005), which is a recognised indicator of isometric exercise intensity when using this muscle group (Devereux, Wiles and Swaine, 2011). However, measuring EMG activity is not suitable for home-based training due to the associated expense. As HR and BP have been found to increase with greater EMG activity during isometric double-leg extension exercise (Wiles et al., 2008b), it was proposed that HR, which is cheap and simple to measure (Achten and Jeukendrup, 2003), could be used as an indication of isometric exercise intensity. It was hypothesised that a greater cardiovascular response will be produced when wall squats are performed with an increased degree of knee flexion, which would consequently reflect an increase in intensity. It was therefore important to study the HR response at a wide range of suitable wall squat knee joint angles to explore the relationship between these two variables and evaluate the potential for their use as determinants of wall squat training intensity.

If a relationship does exist between HR and knee joint angle then wall squat training intensity has the potential to be prescribed using the results of an isometric incremental test, as outlined in Chapter 1, section 1.6.2c (page 39). However, previous isometric incremental tests have utilised constant EMG isometric contractions in order to achieve an attenuated 'steady-state' HR response at each incremental stage (Wiles et al., 2008b). It has been proposed that a 'steady-state' HR response is necessary to be able to use this parameter to prescribe intensity (Kraemer, Fleck and Deschenes, 2012). The cardiovascular response of a constant position isometric wall squat exercise has not previously been studied and as such the HR response pattern is currently unknown. Previous single-joint constant position work found that HR continually increased throughout the exercise duration (Hunter et al., 2002; Rudroff et al., 2005, 2007; Hunter et al., 2008). However as outlined in Chapter 1, section 1.6.2d (page 40), several factors

suggest that an attenuated cardiovascular response may be produced during short duration, multi-joint wall squat exercise. Therefore the pattern of HR and BP response during constant position wall squat exercise will be studied to evaluate whether this exercise mode is suitable for use within an incremental test aimed at prescribing training intensity.

Furthermore, if isometric wall squat exercise is to be prescribed in the home, then it is of the utmost importance to ensure that the training method is safe. As isometric exercise is known to produce a distinct pressor response (Mitchell and Wildenthal, 1974), it is necessary to study the magnitude of the BP values throughout a range of wall squat positions. To determine the relative safety of the wall squat, the BP values recorded were compared with the ACSM guidelines, which recommend that exercise should be terminated if the participant has a hypertensive response of SBP > 250 mmHg and/or DBP > 115 mmHg (Whaley, Brubaker and Otto, 2006). Finally, the cardiovascular responses to isometric wall squat exercise must also be reliable to ensure consistent safe cardiovascular responses are produced when participants exercise at home. To this end, a range of wall squat knee joint angles were repeated and the cardiovascular responses produced between repeated exercise positions were compared.

Finally, it is prudent to establish the safety and consistency of the cardiovascular response to wall squat exercise in a normotensive population first before studying hypertensive individuals, as outlined in Chapter 1, section 1.5.7a (page 33). This is primarily due to the fact that the isometric exercise could be potentially harmful for hypertensive individuals as their initial resting BP values are already high and thus the pressor response may be further exaggerated (Mitchell and Wildenthal, 1974). Further to this, it is postulated that the pharmacological therapies of medicated hypertensives may influence the mechanisms that mediate the IET response (Millar et al., 2013b). Indeed, Badrov et al. (2013a) advocate that normotensive participants must be studied first when establishing an IET protocol.

Therefore the purpose of this study was threefold; to explore the HR and BP responses at a variety of wall squat knee joint angles in a normotensive population in order to: 1) establish a method for prescribing and adjusting isometric exercise intensity, 2) explore the pattern of cardiovascular response to evaluate the suitability for inclusion within an incremental test, and 3) determine the magnitude and consistency of the cardiovascular response to assess the relative safety of this exercise mode.

## **3.2 Methods**

### ***3.2.1 Participants***

Twenty-three healthy males (age  $27.3 \pm 6.2$  years; stature  $1.80 \pm 0.05$  m; body mass  $77.3 \pm 9.4$  kg; SBP  $125 \pm 7$  mmHg; DBP  $75 \pm 4$  mmHg; MAP  $91 \pm 4$  mmHg; mean  $\pm$  standard deviation) volunteered to participate in the study. All twenty-three participants completed the study. Participants self-reported that they were physically active, being involved in exercise on average for approximately  $9.8 \pm 6.9$  hours per week. Typically their habitual exercise included walking, running, cycling, swimming, football, hockey, volleyball, golf, table tennis, squash, badminton, rowing, mixed martial arts, resistance training and flexibility training. All participants met the studies participant inclusion criteria as outlined in section 2.3.1 (page 48).

### 3.2.2 Sample size estimation

The participant sample size for study 1 was estimated using the equation,  $n = 16 (s^2/d^2)$  outlined by Hopkins (2001), as described in section 2.3.3 (page 49). In order to estimate the sample size ( $n$ ), data was needed regarding the reliability (coefficient of variation (CV)) of HR values measured via ECG and BP values obtained using the Finometer in order to calculate the values for  $s$ , which is the within-subject standard deviation expressed as a CV (Hopkins, 2001). Also data concerning the likely HR and BP changes that occur due to adjustment of the wall squat knee joint angle were required in order to calculate the value for  $d$ , which is the smallest worthwhile difference that is required to be detected (Hopkins, 2001). However, there was limited data available on the reliability (CV) of the Finometer for BP measurement and there was no data available for the smallest detectable changes that occur to HR and BP through adjustments in wall squat position. Thus the data of unpublished work previously conducted within the Department was utilised to obtain these required values. In this pilot study seven healthy, male participants (age  $24.8 \pm 9.4$  years; stature  $1.65 \pm 0.47$  m; body mass  $76.5 \pm 8.0$  kg; SBP  $135 \pm 9$  mmHg; DBP  $81 \pm 5$  mmHg; MAP  $91 \pm 4$  mmHg) completed a seated rest period of 15 minutes and then performed two isometric wall squat exercises randomly at either  $105^\circ$  or  $90^\circ$  during two separate visits to the laboratory; a third seated rest period was completed during a further visit. The isometric contraction was held for an infinite amount of time until the point of volitional fatigue. During rest and exercise BP was measured using the Finometer device (as outlined in section 2.5.6, page 59) and HR was measured via ECG (as outlined in section 2.6.2, page 64). The wall squat knee joint angle was set using a goniometer (as described in section 2.10.2, page 79). The mean duration that the  $105^\circ$  wall squat position was held for was  $307 \pm 58$  seconds and  $90^\circ$  was held for  $179 \pm 46$  seconds. The HR and BP at 2 minutes were calculated from the mean data between 1 minute 50 seconds and 2 minutes 10 seconds. From this, the mean difference between  $105^\circ$  and  $90^\circ$  at 2 minutes was calculated for the whole group and expressed as a percentage of the mean score ( $d$ ). The resting reliability (CV) was calculated for each participant (standard deviation divided by the mean multiplied by 100; Williams, James and Wilson, 2008) from which the mean CV was calculated for the whole group ( $s$ ). This data can be seen in Table 3.1 along with the estimated number of participants required to be recruited for study 1 ( $n$ ).

**Table 3.1.** The pilot data used for study 1’s sample size calculation and smallest detectable change based upon the methods of Hopkins (2001).

	<b>HR</b> <b>(beats·min<sup>-1</sup>)</b>	<b>SBP</b> <b>(mmHg)</b>	<b>DBP</b> <b>(mmHg)</b>	<b>MAP</b> <b>(mmHg)</b>
90° mean at 2 mins	136	193	122	150
105° mean at 2 mins	115	187	117	145
90° & 105° mean at 2 mins	125	190	120	148
90° - 105° mean difference	21	7	5	4
<i>d</i> expressed as a % of mean score	16.9%	3.5%	4.3%	2.9%
<i>s</i> = resting CV	11.2%	3.4%	5.1%	3.8%
<i>n</i> = no. of participants = 16 ( $s^2/d^2$ )	7	15	22	27

From Table 3.1 it can be seen that HR and BP at 2 minutes was lower during the 105° wall squat. Upon closer inspection of the data there appeared to be a clear outlier, in which one participant’s SBP, DBP and MAP data increased rather than decreased at 2 minutes during the 105° wall squat position. If this outlying data were to be removed then the consequent estimated sample size would have been much lower (SBP:  $n = 3$ ; DBP:  $n = 7$ ; MAP:  $n = 4$ ). However, it was decided to still include this data point due to the fact that there is little previous data available regarding the effects of adjusting wall squat knee joint angle on HR and BP to be fully confident in excluding this participant’s data. Thus the estimated sample size was based on SBP and DBP as these parameters are the main focus of current BP guidelines (Chobanian et al., 2003; Williams et al., 2004; Mancia et al., 2007). Consequently, twenty-three participants were recruited, which covers both the SBP and DBP estimated sample size numbers. It is also important to note that no participants dropped out of this study and therefore twenty-three participants completed study 1 in total.

### 3.2.3 Equipment

*Blood pressure:* All BP parameters (SBP, DBP and MAP) were measured during rest and exercise. Systolic and diastolic BPs were measured using a non-invasive hemodynamic monitor (Finometer, model 1, Finapres Medical Systems BV, Amsterdam, The Netherlands). The Finometer SBP and DBP data were interfaced with a Windows PC using an analog I/O box (Finapres Medical Systems BV, Amsterdam, The Netherlands) and a 16 channel data acquisition system (PowerLab/16SP, ML795, ADInstruments Pty Ltd, Castle Hill, Australia). The Finometer SBP and DBP data were then continuously displayed on a computer using LabChart Pro software (version 7.1, ADInstruments Pty Ltd, Castle Hill, Australia). Mean arterial pressure was also displayed on LabChart and was calculated instantaneously using the Finometer SBP and DBP data, which were input into the MAP equation. For further details see section 2.5.6 (page 59).

*Heart rate:* Heart rate was recorded during rest and exercise via ECG using a 16 channel data acquisition system (PowerLab/16SP, ML795, ADInstruments Pty Ltd, Castle Hill, Australia) and was continuously displayed on a computer using LabChart Pro software (version 7.1, ADInstruments Pty Ltd, Castle Hill, Australia). Participants were fitted with three single patient use ECG electrodes (Ambu® Blue Sensor R, Ambu A/S, Ballerup, Denmark), which were placed in a standard three-lead bipolar ECG arrangement. For further details see section 2.6.2 (page 64).

*Wall squat knee joint angle:* Knee joint angle was measured during exercise using a clinical goniometer (MIE Clinical Goniometer, MIE Medical Research Ltd., Leeds, U.K.). For further details see section 2.10.2 (page 79).

### **3.2.4 Procedures**

#### *Familiarisation*

Prior to all data collection, participants were familiarised with the isometric wall squat exercise protocol and the measurement procedures, as outlined in section 2.3.5 (page 50). All participants adhered to the testing requirements, presented in section 2.3.4 (page 50), and this was verbally confirmed by the participants prior to the start of each testing session.

#### *Resting measures*

At the start of each visit to the laboratory, participants rested in a seated position for 15 minutes. After an initial 10 minute period (Pickering et al., 2005), BP was measured continuously for 5 minutes using the Finometer (Iellamo et al., 1994) with HR measured simultaneously via ECG. After this time, the mean HR, SBP, DBP and MAP were calculated offline for the 5 minute period.

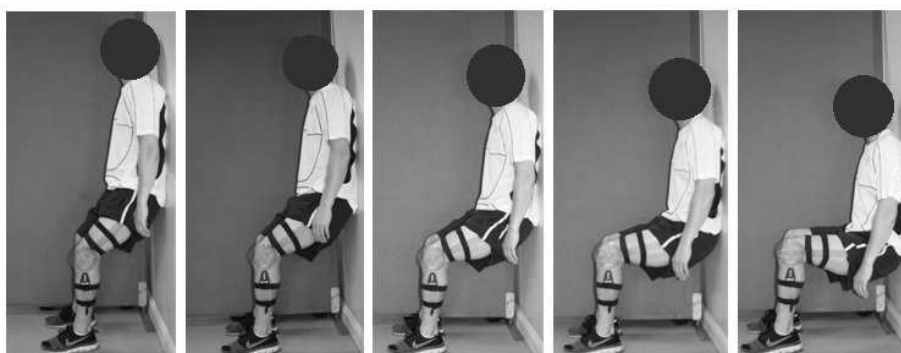
#### *The isometric wall squat exercise protocol*

After resting HR and BP had been measured, participants performed one isometric wall squat exercise starting from an initial upright stance. The participants rested their back against a wall with their feet positioned parallel and shoulder width apart and hands placed by their side. When instructed, participants lowered their back down the wall and moved their feet forward to the required position (see Figure 3.1, page 96) during which time the investigator ensured that the participant's lower legs were kept vertical by means of the spirit level attached to the stationary arm of the goniometer (see Figure 2.10, page 80). The investigator verbally signalled to the participant when they were in the correct wall squat exercise position, determined by the knee joint angle. This exercise position was then held for two minutes or until the point of volitional fatigue. Fatigue was also defined as failure to maintain the target wall squat knee joint angle for 5 consecutive seconds. Participants were instructed to keep their trunk erect and back flat against the wall at all times. Verbal encouragement was given throughout the exercise duration and participants were informed of the elapsed time. Participants were encouraged to keep a normal steady breathing pattern to avoid the Valsalva manoeuvre, which has been associated with extreme elevations in BP during some forms of resistance training (MacDougall et al., 1985). Heart rate and BP were continuously recorded throughout the 2 minute exercise. For analysis, the mean for last 5 seconds of each 30 second period was calculated offline.



### Overall study design

Each participant completed fifteen separate laboratory visits and performed one two minute wall squat exercise per visit. On each occasion the knee joint angle was manipulated to alter the wall squat exercise position. During the first ten visits to the laboratory, participants completed a range of ten different knee joint angles in a counterbalanced design to control for order effects; 135°, 130°, 125°, 120°, 115°, 110°, 105°, 100°, 95° and 90° (see Figure 3.1). It has been subjectively observed that performing wall squats below 90° may change the application of the backs support force, which has been shown to alter the relative contribution of the contracting muscles (Blanpied, 1999). As this would alter the nature of the exercise, wall squats were not performed at knee joint angles lower than 90°. The extent to which manipulating the wall squat knee joint angle would affect HR and BP was unknown and therefore a 5° resolution was chosen in an attempt to explore a full range of wall squat positions. During the final five visits, five of these knee joint angles were randomly assigned and repeated to provide a measure of reliability. The participant's feet were placed in the same position between repeated angles. For analysis, the mean HR and BP for the last 30 seconds were calculated offline for the five repeated knee joint angles and for the five corresponding original angles.



**Figure 3.1** Different wall squat knee joint angles displayed in order of increasing knee flexion: 135°, 125°, 115°, 105°, 95° (left to right).

Between visits there were at least four hours to allow for cardiovascular and muscular recovery. This is important as the incomplete recovery of muscle function can shorten the duration of the subsequent contraction and also HR and BP could change at an increased rate (Lind and McNicol, 1967). Several studies have shown that the cardiovascular recovery is rapid after sustained isometric contractions; HR and BP return to control values within a few minutes (Humphreys and Lind, 1963; Lind et al., 1964). Whereas, the recovery time of muscle function is longer and is measured as the ability to repeat a muscle contraction for the same duration (Lind and McNicol, 1967). After completing a sustained IHG contraction at 33% MVC the muscle function is 70-75% recovered after 40 minutes (Lind, 1959) and at 50% MVC it is recovered by 87% in 42 minutes and 40 seconds (Stull and Kearney, 1978). Also, when performing sustained isometric knee extensions at 66% MVC the endurance capacity of the muscle is 96% recovered after 40 minutes (extrapolated data from Sahlin and Ren, 1989). It is estimated from the theoretical curve that complete muscular recovery from sustained isometric contractions performed to fatigue would occur between 90 minutes (Lind, 1959) and just over 4 hours (Stull and Kearney, 1978).

The contraction duration utilised in this study is a finite time of two minutes and therefore it is likely that recovery will be significantly less than 4 hours.

### **3.2.5 Data analysis**

Before analysis, all data were checked for conformity with the parametric assumptions (Field, 2009). Where the parametric assumptions were met, a factorial repeated measures analysis of variance (ANOVA) was carried out to explore the possible differences in the HR and BP values at a range wall squat knee joint angles. If the ANOVA was statistically significant, a least significant difference (LSD) *post-hoc* test was used to explore any differences detected. This test was selected to maintain statistical power and reduce the probability of a type II error. Where data were not normally distributed, log transformation was attempted in order to achieve a normal distribution pattern. If normal distribution was still not achieved the non-parametric Friedman test was carried out and the Wilcoxon signed ranks test was used for *post-hoc* comparison; this was the case for DBP and MAP. Data analysis was performed with IBM SPSS (BM SPSS Statistics for Windows, version 19.0, Armonk, NY: IBM Corporation). For all tests, an alpha level of  $< 0.05$  was set as the threshold for statistical significance.

The relationships between knee joint angle and HR and BP were explored using Pearson's product-moment correlation coefficient using Microsoft Excel software (Microsoft Excel 10, Microsoft Corporation, Redmond, WA). If the relationship between any parameter and knee joint angle was non-linear, the relationship was then explored through a one-phase exponential decay model using GraphPad Prism (GraphPad Prism version 5.01 for Windows, GraphPad Software, San Diego, CA); this was the case for HR.

Within-participant variation, expressed as a coefficient of variation (CV), was calculated for all cardiovascular variables (HR, SBP, DBP and MAP) at rest and during exercise. The CV was derived by log-transformed two-way ANOVA as described by Atkinson and Nevill (2001), together with the 95% confidence intervals (CI) for a normal distribution (Tate and Klett, 1959).

All data are expressed as mean  $\pm$  standard deviation.

## **3.3 Results**

### **3.3.1 Resting data**

On each of the 15 visits to the laboratory, resting measures of HR and BP were recorded for each participant prior to completion of wall squat exercise. The mean resting values were  $63 \pm 10$  beats $\cdot$ min<sup>-1</sup> for HR,  $125 \pm 7$  mmHg for SBP,  $75 \pm 4$  mmHg for DBP and  $91 \pm 4$  mmHg for MAP. The reliability of resting measures (CV with 95% CI) were 7.1% (6.6-7.7%) for HR, 4.9% (4.6-5.3%) for SBP, 5.7% (5.2-6.1%) for DBP and 5.0% (4.6-5.4%) for MAP.

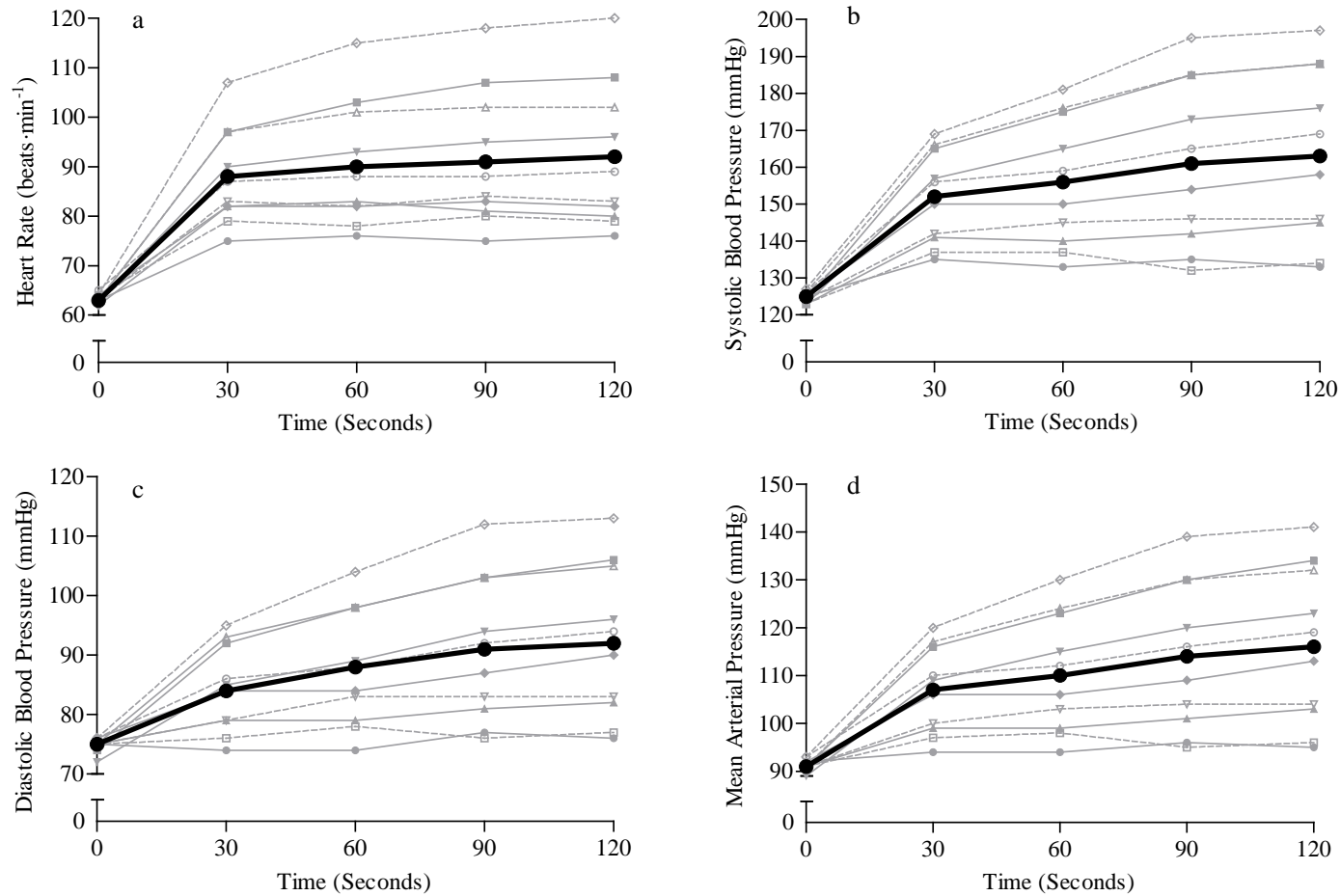
### **3.3.2 Isometric wall squat exercise data**

All participants completed every wall squat exercise for the full 2 minute duration, regardless of the knee joint angle being performed. For each wall squat performed, the mean HR and BP values were calculated for the last 5 seconds of each 30 second period (30, 60, 90 and 120 seconds). The differences in HR

between each successive 30 second time period for the overall mean knee joint angle were:  $2 \pm 3$  beats·min<sup>-1</sup> between 30 and 60 seconds (88 vs. 90 beats·min<sup>-1</sup>:  $P = 0.02$ ),  $1 \pm 2$  beats·min<sup>-1</sup> between 60 and 90 seconds (90 vs. 91 beats·min<sup>-1</sup>:  $P = 0.041$ ), and  $0 \pm 1$  beats·min<sup>-1</sup> between 90 and 120 seconds (91 vs. 92 beats·min<sup>-1</sup>:  $P = 0.954$ ). The relationship between HR and time for each individual wall squat knee joint angle and the overall mean wall squat knee joint angle is shown in Figure 3.2a.

All BP parameters (SBP, DBP and MAP) produced statistically significant ( $P < 0.05$ ) differences between all successive time periods. The differences in the BP values between 90 and 120 seconds were  $2 \pm 2$  mmHg for SBP,  $1 \pm 1$  mmHg for DBP and  $2 \pm 2$  mmHg for MAP, however these differences are considered to be small when compared with previous research (Wiles et al., 2008a). The relationships between the BP parameters and time for each individual wall squat knee joint angle and the overall mean wall squat knee joint angle are shown in Figure 3.2b, c, and d.

Previous work by Wiles et al. (2008b), which explored the relationships between isometric exercise intensity and HR and SBP during incremental isometric exercise, utilised the mean data of the last 30 seconds of each incremental stage (mean of the 90 seconds and 120 seconds values). Thus, for comparison all further data analysis on all parameters were assessed in this manner.



**Figure 3.2.** The relationships between heart rate (a), systolic blood pressure (b), diastolic blood pressure (c) and mean arterial pressure (d), and time at each wall squat knee joint angle; ●—135°, —□—130°, —▲—125°, —▽—120°, —◆—115°, —○—110°, —▼—105°, —△—100°, —■—95°, —◇—90° and —●— mean data for all ten knee joint angles.

### Reliability of exercise data

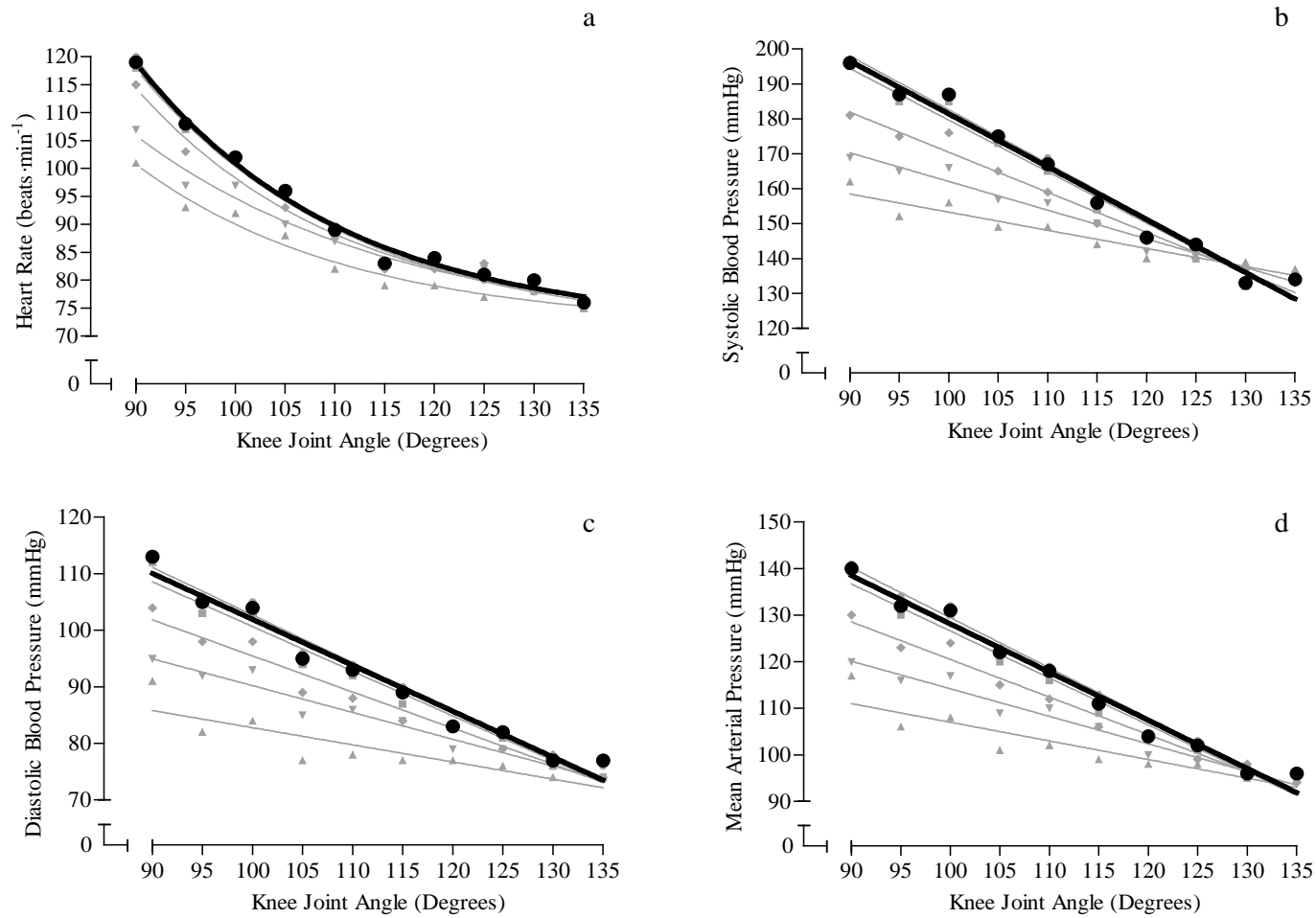
The mean HR and BP values attained during the last 30 seconds of each wall squat knee joint angle are presented in Table 3.2. To calculate the reliability of exercise HR, SBP, DBP and MAP (CV with 95% CI) the mean data for the last 30 seconds of the five repeated knee joint angles and the five corresponding original angles were compared. The reliability of exercise data were 3.6 % (2.8-5.2%) for HR, 3.1% (2.4-4.5%) for SBP, 4.0% (3.1-5.8%) for DBP and 3.4% (2.7-5.0%) for MAP. There were no significant differences between the mean data for five original angles compared to the five repeated angles:  $2 \pm 5$  beats $\cdot$ min $^{-1}$  for HR (91 vs. 89 beats $\cdot$ min $^{-1}$ :  $P = 0.07$ );  $1 \pm 7$  mmHg for SBP (161 vs. 160 mmHg:  $P = 0.50$ ),  $0 \pm 5$  mmHg for DBP (91 vs. 91 mmHg:  $P = 0.83$ ) and  $0 \pm 6$  mmHg for MAP (114 vs. 114 mmHg:  $P = 0.71$ ).

**Table 3.2.** Mean heart rate and blood pressure values for each wall squat knee joint angle during the last 30 seconds of wall squat exercise.

Knee Joint Angle	HR (beats $\cdot$ min $^{-1}$ )	SBP (mmHg)	DBP (mmHg)	MAP (mmHg)
135°	76 $\pm$ 10	134 $\pm$ 14	76 $\pm$ 6	95 $\pm$ 8
130°	79 $\pm$ 9	133 $\pm$ 12	77 $\pm$ 5	95 $\pm$ 7
125°	80 $\pm$ 11	143 $\pm$ 14	82 $\pm$ 7	102 $\pm$ 9
120°	83 $\pm$ 13	146 $\pm$ 14	83 $\pm$ 7	104 $\pm$ 9
115°	82 $\pm$ 11	156 $\pm$ 14	88 $\pm$ 6	111 $\pm$ 8
110°	89 $\pm$ 11	167 $\pm$ 18	93 $\pm$ 9	118 $\pm$ 12
105°	96 $\pm$ 14	174 $\pm$ 11	95 $\pm$ 8	122 $\pm$ 8
100°	102 $\pm$ 15	186 $\pm$ 16	104 $\pm$ 10	131 $\pm$ 11
95°	107 $\pm$ 18	186 $\pm$ 17	105 $\pm$ 6	132 $\pm$ 9
90°	119 $\pm$ 20	196 $\pm$ 18	112 $\pm$ 13	140 $\pm$ 14

### The relationships between heart rate, blood pressure and wall squat knee joint angle

The mean HR data produced a significant inverse curvilinear relationship with wall squat knee joint angle ( $r = -1.00$ ;  $P < 0.05$ ), as seen in Figure 3.3a. When each participant's HR and knee joint angle relationship was analysed individually it was found that the  $r$  values ranged from -0.84 to -0.99 ( $P < 0.05$ ). The mean BP parameters revealed significant ( $P < 0.05$ ) linear relationships with wall squat knee joint angle (SBP:  $r = -0.99$ ; DBP:  $r = -0.99$ ; MAP:  $r = -0.99$ ). Upon analysing each participant's individual data, linear relationships were found between each of the BP parameters and knee joint angle for all participants ( $r$  ranged from -0.80 to -0.98;  $P < 0.05$ , see Figure 3.3b, c, d). Furthermore, the *post hoc* analysis found that the HR and BP responses were significantly different when wall squats with a 10° knee joint angle resolution were compared ( $P < 0.05$ ) but the responses were not significant with a 5° resolution ( $P > 0.05$ ).



**Figure 3.3.** The relationships between heart rate (a), systolic blood pressure (b), diastolic blood pressure (c) and mean arterial pressure (d), and wall squat knee joint angle for each time period;  $\nabla$ —30 seconds,  $\diamond$ —60 seconds,  $\square$ —90 seconds,  $\triangle$ —120 seconds and  $\bullet$ —last 30 seconds mean.

The mean maximum values attained by the participants during the isometric wall squat exercise across all knee joint angles were  $129 \pm 20$  beats·min<sup>-1</sup> for HR,  $219 \pm 14$  mmHg for SBP,  $128 \pm 13$  mmHg for DBP and  $157 \pm 11$  mmHg for MAP. The mean maximum data were analysed for each individual wall squat knee joint angle and this data can be found in Table 3.3.

**Table 3.3.** Maximum heart rate and blood pressure data for each wall squat knee joint angle.

<b>Knee Joint Angle</b>	<b>Maximum HR (beats·min<sup>-1</sup>)</b>	<b>Maximum SBP (mmHg)</b>	<b>Maximum DBP (mmHg)</b>	<b>Maximum MAP (mmHg)</b>
<b>135°</b>	88 ± 12	153 ± 14	87 ± 7	108 ± 9
<b>130°</b>	93 ± 10	154 ± 13	88 ± 7	109 ± 7
<b>125°</b>	93 ± 11	160 ± 16	93 ± 10	114 ± 10
<b>120°</b>	95 ± 12	162 ± 13	94 ± 6	116 ± 8
<b>115°</b>	94 ± 11	168 ± 15	96 ± 7	120 ± 10
<b>110°</b>	99 ± 10	180 ± 19	102 ± 10	128 ± 12
<b>105°</b>	104 ± 12	187 ± 13	105 ± 6	132 ± 8
<b>100°</b>	110 ± 14	199 ± 18	114 ± 14	142 ± 14
<b>95°</b>	116 ± 15	201 ± 18	115 ± 8	143 ± 10
<b>90°</b>	127 ± 20	214 ± 17	124 ± 12	153 ± 13

None of the participants reported any adverse symptoms, such as shortness of breath, dizziness, chest pain, light-headedness, etc., during any of the isometric wall squats performed.

### **3.4 Discussion**

One of the main aims of this study was to establish a method by which constant position isometric wall squat exercise intensity could be measured and adjusted. The results showed that both HR and all the BP parameters produced significant inverse relationships with wall squat knee joint angle; HR specifically producing an inverse curvilinear relationship and the BP parameters produced an inverse linear relationship. Wiles et al. (2008b) established similar relationships during an incremental isometric test that utilised double-leg extension exercise performed at a constant EMG. Indeed isometric exercise intensity, determined by the percentage of EMG<sub>peak</sub>, produced significant linear relationships with both HR and SBP ( $r$  at least 0.91;  $P < 0.05$ ). From the findings of the current study it is proposed that the isometric intensity of a wall squat exercise can be altered by manipulating the knee joint angle, which will consequently also reliably alter the HR and BP values.

#### ***3.4.1 Possible explanations for the inverse linear relationships produced between wall squat knee joint angle and the blood pressure parameters***

It is plausible to suggest that the BP parameters and wall squat knee joint angle produced inverse linear relationships due to the isometrically contracting muscles compressing the blood vessels at higher intensities, as is suggested to have occurred during static handgrip exercise (Humphreys and Lind, 1963; Lind et al., 1964). Such mechanical interference is thought to affect the ability of the blood supply to meet

the muscle's metabolic requirements (Lind and McNicol, 1967), which may consequently cause an increase in BP (Lind et al., 1964). This phenomenon may have occurred in the present study as previous research has found that quadriceps EMG activity increases with greater levels of wall squat knee flexion (Bevilaqua-Grossi et al., 2005), as previously outlined in Chapter 1, section 1.6.2b (page 39).

At low wall squat intensities ( $135^{\circ}$  to  $115^{\circ}$ ), it is likely that the quadriceps activity would be relatively low as minimal knee flexion is required (Bevilaqua-Grossi et al., 2005). It is proposed that blood flow may be minimally restricted and consequently the metabolic requirements of the muscle would be sufficiently met by the blood supply (Lind and McNicol, 1967) so that BP values are similar to that of resting, as seen in Figure 3.3 (b, c, d). As the wall squat intensity increases ( $< 115^{\circ}$ ), greater levels of knee flexion are required, which would consequently increase the quadriceps activity (Bevilaqua-Grossi et al., 2005). The greater muscle activation required may begin to restrict blood flow. If a disparity develops between the muscle blood flow and metabolism, then a flow error occurs causing an imbalance between the oxygen supplied to the muscle and the demand (Sinoway et al., 1989). Consequently there is a greater need for ATP (adenosine triphosphate) to be anaerobically resynthesized (Sinoway et al., 1989), which leads to an accumulation of metabolites and consequent activation of the metaboreceptors (Mostoufi-Moab et al., 1998). The increased sympathetic activation will lead to an increase in BP to deliver more oxygen to the skeletal muscle and clear metabolites (Sinoway et al., 1989). At the highest wall squat exercise intensity used in this investigation ( $90^{\circ}$ ), the greatest amount of knee flexion occurs and therefore the largest quadriceps activity may be produced. This would theoretically compromise the blood flow the greatest causing the largest increase in BP (Hietanen, 1984).

Further to this, the increased BP that occurs with greater wall squat knee flexion, and consequent linear relationship, could be due to the greater quadriceps EMG activity (Bevilaqua-Grossi et al., 2005) increasing the activation of central command and the exercise pressor reflex. Indeed, Gálvez et al. (2000) postulate that an increase in the number of motor units required to complete an isometric contraction would necessitate a greater contribution from the higher brain centres, which would irradiate signals to the cardiovascular control centres and thus contribute to enhanced cardiovascular changes. Gálvez et al. (2000) also suggested that an isometric exercise that requires greater motor unit recruitment will activate the afferent nerve endings to a greater extent (metabolic and mechanical), thus causing a greater exercise pressor reflex subsequently leading to greater cardiovascular response. As such, it seems plausible that both increased mechanical disruption to blood flow and greater motor unit recruitment could explain the increase in BP with greater wall squat knee flexion. Further research is required to establish the exact contributions of these proposed mechanisms.

### ***3.4.2 Potential reasons for the differential inverse curvilinear relationship between wall squat knee joint angle and heart rate***

A significant inverse relationship was also produced between HR and wall squat knee joint angle; however this relationship was curvilinear due an exaggerated HR response when performing wall squats with a greater degree of knee flexion. It is suggested that while the HR responses were compared between equal increments of wall squat knee flexion ( $5^{\circ}$ ), these increments may not produce subsequent equal increases in quadriceps activity. If increases in motor unit recruitment were disproportionate between wall squat knee joint angles then this could lead to disparate increases in HR due to the simultaneous unequal



activation of the cardiovascular control centres through central command (Franke, Boettger and McLean, 2000), and/or the exercise pressor reflex (Gálvez et al., 2000). Indeed, the HR results may suggest that increases in quadriceps activity may have been greater between higher intensity wall squats ( $\leq 115^\circ$ ). Conversely, Wiles et al. (2008b) found a linear relationship between HR and isometric double-leg extension intensity during an incremental test. It might be suggested that the increases in HR were more uniform in the study completed by Wiles et al. (2008b) due to the fact that exercise was performed at a constant EMG and intensity was increased in equal increments of EMG (10, 15, 20, 25, and 30%  $EMG_{peak}$ ). This would likely produce more equal increases in the activation of central command and the exercise pressor reflex between stages.

Further to this, it is also of interest to note that muscle tremors were subjectively reported by the researcher for all participants during wall squats completed with a higher degree of knee flexion ( $\leq 105^\circ$ ). It is therefore proposed that the curvilinear relationship between HR and knee joint angle may also have been produced due to these involuntary muscular tremors. Humphreys and Lind (1963) described similar involuntary movements occurring during IHG exercise at 70% MVC. It is theorised that some of the pressure on the intramuscular blood vessels may have been relieved due to the momentary relaxation of the muscles during tremor consequently allowing a metabolic efflux. If the peripheral chemoreceptors are subsequently activated this may induce vasoconstriction of the active skeletal muscle (O'Regan and Majcherczyk, 1982), which may lead to a flow error causing greater anaerobic ATP generation (Sinoway et al., 1989). This could consequently result in an increased metabolite accumulation due to a paradoxical increase in local metaboreceptor stimulation (Mostoufi-Moab et al., 1998) leading to a disproportionate HR increase. Alternatively, due to the onset of the muscle tremor, the muscle mechanoreflex may be re-stimulated (O'Leary, 1996) and further serve as a feedback to the cardiovascular control areas (Mitchell, 1990), which could possibly explain the HR results obtained in this study. Theoretically, either of these proposed mechanisms may produce a dose-response relationship between involuntary muscle tremor and HR, such that a greater degree of muscle tremor could cause a larger increase in HR, due to either greater chemoreceptor or mechanoreceptor stimulation. If this is the case, it is possible that the wall squats performed with a higher degree of knee flexion may have produced a greater degree of tremors, due to the fact that significantly higher HR values were reported. However, this is just conjecture and future research needs to quantify this concept objectively. Furthermore, it is proposed that the BP parameters and knee joint angle did not produce a similar curvilinear relationship due to the fact that any expected concomitant BP increase may have been masked by a temporary decrease in TPR resulting from the muscles relaxing intermittently during tremor.

When both the HR and BP relationships with wall squat knee joint angle were analysed further it was discovered that the  $10^\circ$  increment generated significant differences in the HR and BP values produced, however this was not always the case with a  $5^\circ$  increment. It is suggested that although a  $5^\circ$  change in the wall squat exercise position was relatively small, it is likely that some additional quadriceps muscle fibre recruitment would still be required that should theoretically have altered HR and BP to some extent. However, any changes remained undetected as it is probable that the magnitude of change was too small to identify because it fell within the measurement error and/or daily variability. Based on this data, a  $10^\circ$  resolution appears to be a more appropriate increment to alter isometric wall squat exercise intensity as it brings about a more pronounced and measurable cardiovascular response.

### ***3.4.3 Assessing the potential for constant position isometric wall squat exercise to be utilised within an incremental test for the prescription of intensity***

Whilst this study has established that manipulating knee joint angle will consequently alter the wall squat intensity, a method for prescribing the appropriate intensity for home-based training must still be explored before it can be effectively used for IET in the home. If the relationship between HR and wall squat knee joint angle found in the present study can be reproduced during an incremental test, then the methods of Wiles et al. (2008b) can be adapted to prescribe wall squat intensity at an individualised knee joint angle to elicit a target HR, as outline in Chapter 1, section 1.6.2c (page 39). A key feature of the incremental test designed by Wiles et al. (2008b) was that constant EMG isometric exercise was utilised to produce a steady-state HR response at each work stage, which is required in order to prescribe intensity (Kraemer, Fleck and Deschenes, 2012). This condition was achieved in the present study during constant position wall squat exercise, in which HR produced a 'steady-state' response during the last 30 seconds of all knee joint angles performed, as presented in section 3.3.2 (page 97). However, this is contrary to the finding of previous constant position research that found HR to continuously increase throughout the contraction duration (Hunter et al., 2002; Rudroff et al., 2005; 2007; Hunter et al., 2008).

However, as proposed in Chapter 1, section 1.6.2d (page 40) there may be several factors that enable constant position isometric wall squat exercise to produce such an attenuated response in comparison. For example, these constant position tasks were carried out to fatigue ( $\geq 5$  minutes), whereas contractions in this study were completed for a finite time of 2 minutes. Furthermore, the wall squat is a multi-joint exercise that utilises several joints and muscles, which may enable different patterns of muscular recruitment (McBride, Deane and Nimphius, 2007; Boyas, Maïsetti and Guével, 2009). Finally, the wall squat imposes no physical restraints on the body that may allow slight changes in the exercise position to occur, which could alter the relative contribution of the muscles involved (Blanpied, 1999). Such factors may have reduced localised fatigue, which could decrease the associated metabolite accumulation (Enoka and Duchateau, 2008) and modify feedback to the cardiovascular control centre from the group III and IV muscle afferents (Mitchell, 1990) to produce an attenuated the HR response.

### ***3.4.4 The suitability of isometric wall squat exercise to be used within a home-based training protocol in normotensive participants***

Another important aim of this study was to explore the cardiovascular responses produced during constant position wall squat exercise to elucidate its potential suitability as an alternative exercise method that could be utilised within home-based isometric training aimed at reducing resting BP. The mean HR and BP values produced during wall squat exercise in this study are comparable to other isometric contraction styles and exercise modes that have been shown to successfully lower resting BP, such as constant force handgrip contractions (Lind et al., 1964; Mitchell et al., 1980; Boutcher and Stocker, 1999), constant force knee extensions (Mitchell et al., 1980; Friedman, Peel and Mitchell, 1992) and constant EMG knee extensions (Schibye et al., 1981; Franke, Boettger and McLean, 2000). This finding suggests that the wall squat presents a sufficient cardiovascular stimulus to induce BP adaptations with training similar to other isometric contraction styles and exercise modes utilised within training protocols. Therefore it is proposed that the constant position wall squat could provide a viable alternative exercise

method that has the potential to be utilised within a home-based isometric training regime aimed at lowering resting BP.

The current study also explored the magnitude of the cardiovascular responses to indicate the safety of the wall squat. Despite the fact that many forms of IET have successfully been shown to lower resting BP, isometric exercise continues to be approached with some caution due to the fact that static contractions can result in a more pronounced pressor response than dynamic contractions (Mitchell and Wildenthal, 1974). Indeed, this is clear to see when comparing the mean BP values recorded in the present study during the wall squat to aerobic exercise recommended for reducing BP, such as walking (Navalta, Sedlock and Park, 2004; Dolbow et al., 2008; Thijssen et al., 2009) and cycling (Åstrand et al., 1965; Boutcher and Stocker, 1999). However, whilst the isometric wall squat exercise did produce an exaggerated pressor response, the increases recorded (except for maximum DBP at 90°) were within the ASCM's guidelines for exercise termination (SBP < 250 mmHg, DBP < 115 mmHg) (Whaley, Brubaker and Otto, 2006). It should be noted that these guidelines are specific to aerobic exercise (Whaley, Brubaker and Otto, 2006) and unfortunately there appear to be no current guidelines available for isometric exercise despite the fact that this exercise mode is known to produce a distinctly different pattern of cardiovascular response. However, in the absence of specific guidelines these findings suggest that, apart from the 90° wall squat position that should be used with some caution, all the other knee joint angles produced cardiovascular responses that fall within safe limits. However, it is suggested that due to the relatively short exercise duration, and the fact that both SBP and DBP return to resting values within a few minutes (Humphreys and Lind, 1963), even a wall squat performed at 90° is unlikely to cause any significant cardiovascular risk as the time that the body would be subjected to such an exaggerated response would be minimal.

While this study has demonstrated that the isometric wall squat exercise produces a cardiovascular response that is both suitable and safe for inclusion within a home-based IET protocol, the participants investigated were young normotensive healthy males. Although it is important to establish a new IET protocol in such a population (Badrov et al., 2013a), as previously discussed in sections 1.5.7a and 1.5.7b (pages 33 and 35, respectively), it is acknowledged that hypertensive individuals may produce a differential cardiovascular response. Indeed, while the percentage change in BP experienced during isometric exercise is no greater for hypertensives, it is possible that the magnitude of the pressor response may be greater particularly as these individuals have higher initial resting BP levels (Ewing et al., 1973). Therefore future research should investigate the HR and BP responses to isometric wall squat exercise with a hypertensive population to further explore the suitability and safety of this exercise mode for home-based training, as discussed in section 6.7 (page 172).

### ***3.4.5 The reliability of the acute heart rate and blood pressure responses at rest and during isometric wall squat exercise***

A final aim of this study was to also explore the reliability of the HR and BP responses, which were examined during both rest and exercise. The reliability of the resting data compared favourably with that found in other studies that have good levels of reliability measuring intra-arterial BP (Mancia et al., 1983), Finapres BP (Parati et al., 2001; Højgaard et al., 2005) and other BP measurement devices (Scott, Randolph and Leier, 1989; Stanforth et al., 2000). Indeed, according to Scott, Randolph and Leier (1989)

a CV of 10% is considered to be good for most biological data, such as HR and BP. Accordingly the resting reliability data in the current study would be classified as good (CV < 10 %) suggesting a sound level of short term intratester reliability for both the ECG HR and Finometer BP resting values. Any transient changes in resting HR and BP can be explained by the well-documented variable nature of both parameters (Armitage and Rose, 1966; Mancia et al., 1983).

Further to this the reliability of the cardiovascular responses to isometric wall squat exercise compared favourably to that found in submaximal aerobic exercise (Wilmore et al., 1998), maximal aerobic exercise (Skinner et al., 1999) and isometric exercise (Costa et al., 1987; Wiles et al., 2008b). Indeed the variability of the exercising data yielded reliability CV's that were under the lower 95% CI for the resting data for all parameters suggesting more consistent exercise responses compared to resting values. When the wall squats were repeated at the same knee joint angle, small (but not statistically significant) differences in HR and BP were produced, thereby suggesting that the cardiovascular responses to wall squat exercise are highly reproducible. Therefore, when evaluating the suitability of wall squat for home-based training these results suggest that each participant will demonstrate a consistent response to this form of exercise.

### **3.5 Conclusion**

The data presented in this chapter highlights a valuable method for adjusting constant position isometric wall squat exercise intensity and provides an insight into the magnitude and consistency of the acute HR and BP responses. This is a necessary first step in developing a new isometric training regime that has the potential to lower resting BP in a home-based environment. The extent to which the wall squat exercise can be utilised within a home-based protocol aimed at reducing BP remains to be established. The next important step to achieving this is to determine a method of prescribing constant position wall squat training intensity. If the curvilinear relationship between knee joint angle and HR during isolated acute bouts of wall squat exercise can be reproduced during an incremental test, then the methods of Wiles, Coleman and Swaine (2010) could be used to set isometric wall squat intensity and an individualised knee joint angle could be prescribed for each participant to elicit a target HR.



## **CHAPTER 4: STUDY 2**

### **THE RELATIONSHIP BETWEEN EXERCISE INTENSITY, HEART RATE, AND BLOOD PRESSURE DURING AN INCREMENTAL ISOMETRIC WALL SQUAT EXERCISE TEST**

#### **4.1 Introduction**

In study 1, Chapter 3 (page 91), it was found that constant position isometric wall squat exercise intensity could be adjusted by manipulating the knee joint angle, as this was shown to result in reliable changes in HR and BP. However, a method to prescribe isometric wall squat intensity for home-based training remains to be established. Previous studies have utilised the linear relationship that exists between EMG activity and HR (Wiles et al., 2008b) to prescribe IET intensity at an individualised constant EMG value that corresponded to a precise target HR (Devereux, Wiles and Swaine, 2010b; Wiles, Coleman and Swaine, 2010; Baross, Wiles and Swaine, 2012); as discussed in Chapter 1, section 1.5.1 (page 20). Due to the fact that study 1 found a curvilinear relationship between wall squat knee joint angle and HR (see section 3.3.2, page 97), it is proposed that constant position isometric wall squat exercise intensity might be set at a participant-specific knee joint angle to also elicit a target HR. It is suggested that the incremental test protocol devised by Wiles et al. (2008b) could be adapted for isometric wall squat exercise in order to establish the participant's individual relationship between knee joint angle and HR; however this has not previously been investigated.

It is proposed that the incremental test could consist of five incremental stages aimed at eliciting volitional fatigue, as per the methods of Wiles et al. (2008b), with five fixed knee joint angles in 10° increments; 135°, 125°, 115°, 105° and 95°. Each stage would be performed for 2 minutes and participants would continue the incremental test until: 1) the end of 95° stage is completed to maximum; 2) the participant fails to maintain the knee joint angle within 5° of the target value; or 3) the point of volitional fatigue. A 10° resolution is suggested as the appropriate increment, as study 1 did not consistently find significant changes in HR and BP with a 5° resolution (see section 3.3.2, page 97). Further to this, the 95° knee joint angle was selected as the final increment as maximum DBP exceeded the ACSM's exercise termination guidelines during the 90° wall squat in study 1 (DBP > 115 mmHg) (Whaley, Brubaker and Otto, 2006). Thus 95° was selected in an attempt to ensure a lower pressor response and ensure optimal participant safety. While this appears to be a viable protocol, intensity can only be prescribed from an incremental test if a 'steady-state' response is attained at each incremental stage (Kraemer, Fleck and Deschenes, 2012), as achieved in the constant EMG isometric test designed by Wiles et al. (2008b). It is unknown whether this will be the case for constant position isometric wall squat exercise, however study 1 did find that HR remained unchanged during the last 30 seconds of each isolated bout of isometric wall squat exercise performed (see section 3.3.2, page 97).

If the curvilinear relationship between HR and wall squat knee joint angle can be reproduced during the incremental test outlined above, then it would be possible to calculate the individualised wall squat position (knee joint angle) that a participant would be required to work at during training in order to elicit a precise target HR value. Previous research that has prescribed IET intensity to a precise HR value used targets ranging from 70% to 95% of the HR<sub>peak</sub> attained during the pre-training incremental test (Devereux, Wiles and Swaine, 2010b; Wiles, Coleman and Swaine, 2010; Baross, Wiles and Swaine,

2012). However, it would appear beneficial to prescribe isometric wall squat exercise at a high intensity (95%  $HR_{peak}$ ) as this has been found to produce reductions in resting BP at enhanced rate of 4 weeks (Devereux, Wiles and Swaine, 2010b), as discussed in Chapter 1, section 1.5.3b (page 29). It is important to note that  $HR_{peak}$  was utilised in these studies rather than  $HR_{max}$ , which is traditionally utilised for aerobic training (Tanaka, Monahan and Seals, 2001). This is primarily due to the fact that isometric exercise produces submaximal, modest increases in HR values in comparison to aerobic exercise (Lind, 2011). Thus, it was suggested that it would be more suitable to use the  $HR_{peak}$  values actually attained during the incremental test when prescribing isometric intensity (Wiles, 2008a). The  $HR_{peak}$  has been defined as the highest HR value attained during the initial pre-training incremental test (Devereux, Wiles and Swaine, 2010b). However, it may be more appropriate to prescribe target HR from the mean HR value of the last 30 seconds of the incremental test as during this time HR has been shown to reach a relative 'steady-state' (Wiles et al., 2008b; Devereux, 2010a) and thus may produce a target that is more representative of the likely HR training values. In study 1, the maximum singular HR values attained during isometric wall squat exercise were  $11 \pm 2$  beats·min<sup>-1</sup> higher than the last 30 seconds mean (mean knee joint angle data from in study 1, section 3.3.2), which if used to prescribe IET intensity may present a target HR value that is not achievable or sustainable during training. The efficacy of calculating target HR from a percentage of the mean HR value of the last 30 seconds of an initial incremental test remains to be established.

During training the calculated target HR has typically been required to be within  $\pm 5\%$  of the expected value (Devereux, Wiles and Swaine, 2010b; Wiles, Coleman and Swaine, 2010). However, as discussed in Chapter 1, section 1.6.2e (page 43), this 5% value appears to be somewhat arbitrary and presents a rather small range. To determine a more precise THRR for isometric training, it is proposed that the reliability of a variable should be considered, such as within-subject variation, which is the random variation that occurs when the same participant is retested (Hopkins, 2000). One type of within-subject variation that could be utilised is the limits of agreement method (bias  $\pm 1.96$  x standard deviation) (Altman and Bland, 1983; Bland and Altman, 1986), which represents the 95% likely difference in a participant's measured values between repeated tests (Hopkins, 2000). Using a clinically relevant range to express measurement error enables a true change in the value to be identified (Harding et al., 1988). Thus any changes in the values that occur can be consequently interpreted as either a 'real' change, or simply as natural variability (Eliaszewicz et al., 1994). It is proposed that the limits of agreement method could be applied around the target HR (95%  $HR_{peak}$ ) determined from the pre-training incremental test to create a THRR. Consequently, if the HR values change between training sessions and fall outside the THRR, then it is likely that a 'real' change has occurred possibly due to an adaptation from training and therefore training intensity must be adjusted to ensure an adequate cardiovascular stimulus is still reached. However, if HR has altered but is still within the THRR then no modification to the training prescription needs to occur, as this likely signifies that HR has merely fluctuated due to natural variability or measurement error. Furthermore, if similar inverse linear relationships between knee joint angle and the BP parameters (SBP, DBP and MAP) can be reproduced, as found in study 1 (see section 3.3.2, page 97), then a target blood pressure range (TBPR) could also be calculated for the prescribed knee joint angle using the limits of agreement method. Consequently, the likely pressor response to training can be

predicted to maximise participant safety during training. The efficacy and reliability of prescribing a THRR and a TBPR for IET using the limits of agreement method remains to be established.

To this end, the aims of the study in this chapter were to determine whether inverse curvilinear and linear relationships can be established between knee joint angle and both HR and BP respectively during an incremental isometric wall squat exercise test and to compare these relationships between repeated tests. A further aim was to evaluate the efficacy and reliability of prescribing target HR and BP ranges for an isometric wall squat training session.

## **4.2 Methods**

### **4.2.1 Participants**

Twenty healthy males (age  $28.7 \pm 7.4$  years; stature  $1.80 \pm 0.06$  m; body mass  $78.8 \pm 9.8$  kg; SBP  $124 \pm 8$  mmHg; DBP  $77 \pm 4$  mmHg; mean  $\pm$  standard deviation) volunteered to participate in the study. All twenty-three participants completed the study. Participants self-reported that they were physically active, being involved in exercise on average for approximately  $8.6 \pm 5.6$  hours per week. Typically their habitual exercise included walking, running, cycling, swimming, football, hockey, golf, table tennis, squash, badminton, rowing, kick boxing, mixed martial arts, and resistance training. All participants met the studies participant inclusion criteria as outlined in section 2.3.1 (page 48).

### **4.2.2 Sample size estimation**

To estimate the number of participants required for study 1 (Chapter 3), pilot data using a small cohort of only seven participants was utilised as this was the only available data. The pilot study data was entered into the Hopkins (2001) equation,  $n = 16 (s^2/d^2)$  (see section 3.2.2, page 93), which had the potential to produce a lack of precision in the sample size estimation due to the small cohort used in the pilot work. However, from this sample size estimate twenty-three participants were recruited for study 1. Large statistically significant changes in the HR and BP were found when comparing the responses produced during different wall squat knee joint angles; thus producing an indication of the reliability required. Based on this twenty participants were recruited for study 2, which was above the numbers normally recruited for this type of investigation. Previous work by Wiles et al. (2008b) and Devereux (2010a) that looked to establish an incremental isometric exercise protocol used fifteen and seventeen participants, respectively. Recruiting a greater number of participants would only reduce the confidence intervals around the derived CVs. It is also important to note that no participants dropped out of the current study and therefore twenty participants completed study 2 in total.

### **4.2.3 Equipment**

*Blood pressure:* All BP parameters (SBP, DBP and MAP) were measured during rest and exercise. Systolic and diastolic BPs were measured using a non-invasive hemodynamic monitor (Finometer, model 1, Finapres Medical Systems BV, Amsterdam, The Netherlands). The Finometer SBP and DBP data were interfaced with a Windows PC using an analog I/O box (Finapres Medical Systems BV, Amsterdam, The Netherlands) and a 16 channel data acquisition system (PowerLab/16SP, ML795, ADInstruments Pty Ltd, Castle Hill, Australia). The Finometer SBP and DBP data were then continuously displayed on a



computer using LabChart Pro software (version 7.1, ADInstruments Pty Ltd, Castle Hill, Australia). Mean arterial pressure was also displayed on LabChart and was calculated instantaneously using the Finometer SBP and DBP data, which was input into the MAP equation. For further details see section 2.5.6 (page 59).

*Heart rate:* Heart rate was recorded during rest and exercise via ECG using a 16 channel data acquisition system (PowerLab/16SP, ML795, ADInstruments Pty Ltd, Castle Hill, Australia) and was continuously displayed on a computer using LabChart Pro software (version 7.1, ADInstruments Pty Ltd, Castle Hill, Australia). Participants were fitted with three single patient use ECG electrodes (Ambu® Blue Sensor R, Ambu A/S, Ballerup, Denmark), which were placed in a standard three-lead bipolar ECG arrangement. For further details see section 2.6.2 (page 64).

*Wall squat knee joint angle:* Knee joint angle was measured during exercise using a clinical goniometer (MIE Clinical Goniometer, MIE Medical Research Ltd., Leeds, U.K.). For further details see section 2.10.2 (page 79).

#### **4.2.4 Procedures**

##### *Familiarisation*

Prior to all data collection participants were familiarised with the isometric wall squat exercise, the testing protocols and the measurement procedures, as outlined in section 2.3.5 (page 50). All participants adhered to the testing requirements, presented in section 2.3.4 (page 50), and this was verbally confirmed by the participants prior to the start of each testing session.

##### *Resting measures*

At the start of each visit to the laboratory, participants rested in a seated position for 15 minutes. After an initial 10 minute period (Pickering et al., 2005), BP was measured continuously for 5 minutes using the Finometer (Iellamo et al., 1994) with HR measured simultaneously via ECG. After this time, the mean HR, SBP, DBP and MAP were calculated offline for the 5 minute period.

##### *Incremental isometric wall squat exercise test protocol*

The incremental protocol used in this study was based upon the work of Wiles et al. (2008b) in which an incremental isometric test was designed to determine training intensity for isometric double-leg extension exercise training. For the incremental isometric wall squat test in this study, participants were required to perform several isometric wall squat exercises in stages of increasing intensity, which was adjusted by manipulating the knee joint angle. The first stage began at 135° of knee flexion and participants were instructed to hold this position for 2 minutes. Once each stage was complete the knee joint angle was decreased by 10° as follows; 135°, 125°, 115°, 105°, to 95°. The exercise intensity was increased every 2 minutes until the participant reached the end of 95° stage, until the participant could no longer maintain the knee joint angle within 5° of the target value or until the point of volitional fatigue. The test was continuous so there was no rest between the incremental stages. Participants were given verbal instructions to ensure that each wall squat was held at the correct exercise position and also to ensure the proper timing of each incremental stage. Participants were also encouraged to keep a normal steady

breathing pattern to avoid the Valsalva manoeuvre, which has been associated with extreme elevations in BP during some forms of resistance training (MacDougall et al., 1985). Upon cessation, participants were verbally questioned to confirm that a further incremental stage could not have been completed, which provided subjective evidence that the test had been completed to maximum.

#### *The isometric wall squat exercise training protocol*

The training protocol used in this study was based upon the procedure utilised by Wiles, Coleman and Swaine (2010) for isometric double-leg extension training. Using the participant's data from the first initial incremental test completed (INC1), knee joint angle was plotted against the mean HR for the last 30 seconds of each incremental stage. This was only possible if a 'steady-state' response was achieved during each work period, as previously achieved in study 1 during isolated wall squat exercise bouts (see section 3.3.2, page 97). The inverse curvilinear relationship produced was then used to calculate the participant-specific knee joint angle required to elicit a target HR. It is important to note that each participant's individual relationship was used to calculate target HR as this has been found to be more appropriate than using a group's mean relationship (Swain et al., 1994). The target HR selected for training was 95%  $HR_{peak}$  as utilised by Devereux, Wiles and Swaine (2010b) and Wiles, Coleman and Swaine (2010). In the current study  $HR_{peak}$  was defined as the mean HR of the last 30 seconds achieved during the incremental test. Knee joint angle was also plotted against the mean SBP, DBP and MAP for the last 30 seconds of each incremental stage. Based on these linear relationships produced, the target SBP, DBP and MAP values were calculated for the prescribed target knee joint angle.

Further to this each participant's individual THRR was calculated using the limits of agreement method (bias  $\pm$  1.96 x standard deviation) (Altman and Bland, 1983; Bland and Altman, 1986), however this equation was modified so that the CV of a variable could be used within the formula rather than the standard deviation. If the CV is calculated utilising the methods of Hopkins (2000) then the limits of agreement equation can be expressed as: bias  $\pm$  2.77 x CV (Coleman et al., 2005). Consequently, the THRR was calculated as: target HR + bias  $\pm$  2.77 x CV. The group's mean reliability data (CV) of the  $HR_{peak}$  attained for repeated incremental tests (INC1 vs. INC2) was calculated and expressed in beats per minute related to each participant's individual target HR (CV[individual target HR/100]) to input into the THRR equation. The bias value entered was the mean difference in the  $HR_{peak}$  values attained between repeated tests (INC1 vs. INC2). The  $HR_{peak}$  data was utilised for the CV and bias values as the target HR was derived from this parameter. The TBPRs (SBP, DBP and MAP) were also calculated using this method, however the target BP data attained from repeated incremental tests (INC1 vs. INC2) was used for the CV and bias value calculations. This is due to the fact that the BP targets were not based on the peak BP data.

Each training session was composed of four 2 minute bouts of isometric wall squat exercise with 2 minutes rest between bouts. Participants were given verbal instructions to ensure the proper timing of the isometric wall squat exercise and rest periods. Participants were again encouraged to keep a normal steady breathing pattern to avoid the Valsalva manoeuvre. All training sessions were completed at the same participant-specific knee joint angle, which was prescribed from the first initial incremental test (INC1) for comparison.

### *Overall study design*

Each participant completed a total of four separate laboratory visits over a two week period. In week 1, participants completed two incremental tests (INC1 and INC2, respectively). Following this, in week 2, participants completed two exercise sessions following the proposed isometric wall squat training protocol in order to evaluate the intensity prescription method (T1 and T2, respectively). The isometric wall squat exercises during these intensity verification training sessions were all performed at a participant-specific knee joint angle prescribed from INC1.

All isometric wall squat exercises were performed using the same technique as outlined in section 3.2.4 (page 95). Heart rate and BP were recorded continuously throughout all incremental tests and training sessions. For analysis, the mean for last 5 seconds of each 30 second period were calculated offline, as well as the mean for the last 30 seconds of each incremental stage/training exercise bout.

#### **4.2.5 Data analysis**

Before analysis, all data were checked for conformity with the parametric assumptions (Field, 2009). Where the parametric assumptions were met, a factorial repeated measures ANOVA was carried out for: 1) incremental test data to explore possible differences in HR and BP between different time periods, 2) training session data to explore the differences in HR and BP between exercise bouts and time periods, and 3) individual exercise bouts to detect any differences in the percentage of time spent below, in and above the target ranges. The LSD *post-hoc* test was used to explore any significant differences detected. Where data were not normally distributed, it was transformed and analysed in the same manner as study 1 (section 3.2.5, page 97). Data analysis was performed with IBM SPSS (BM SPSS Statistics for Windows, version 19.0, Armonk, NY: IBM Corporation).

The relationships between knee joint angle and HR and BP for the incremental tests were explored using Pearson's product-moment correlation coefficient using Microsoft Excel software (Microsoft Excel 10, Microsoft Corporation, Redmond, WA). If the relationship between any parameter and knee joint angle was non-linear, the relationship was then explored through a one-phase exponential decay model using GraphPad Prism (GraphPad Prism version 5.01 for Windows, GraphPad Software, San Diego, CA); this was the case for HR.

For all data compared between 1) incremental tests (INC1 vs. INC2), 2) training sessions (T1 vs. T2), and 3) prescribed targets and actual values, a paired T-Test was carried out using Microsoft Excel software (Microsoft Excel 10, Microsoft Corporation, Redmond, WA). If a normal distribution was not achieved, the non-parametric Wilcoxon signed ranks test was utilised. Within-participant variation, expressed as a coefficient of variation (CV), was calculated for all cardiovascular variables (HR, SBP, DBP and MAP) at rest, for the incremental test and training session values, and also for the calculated training targets. The CV was derived by log-transformed two-way ANOVA as described by Atkinson and Nevill (2001), together with the 95% confidence intervals (CI) for a normal distribution (Tate and Klett, 1959).

For all tests, an alpha level of  $< 0.05$  was set as the threshold for statistical significance. All data are expressed as mean  $\pm$  standard deviation.

## 4.3 Results

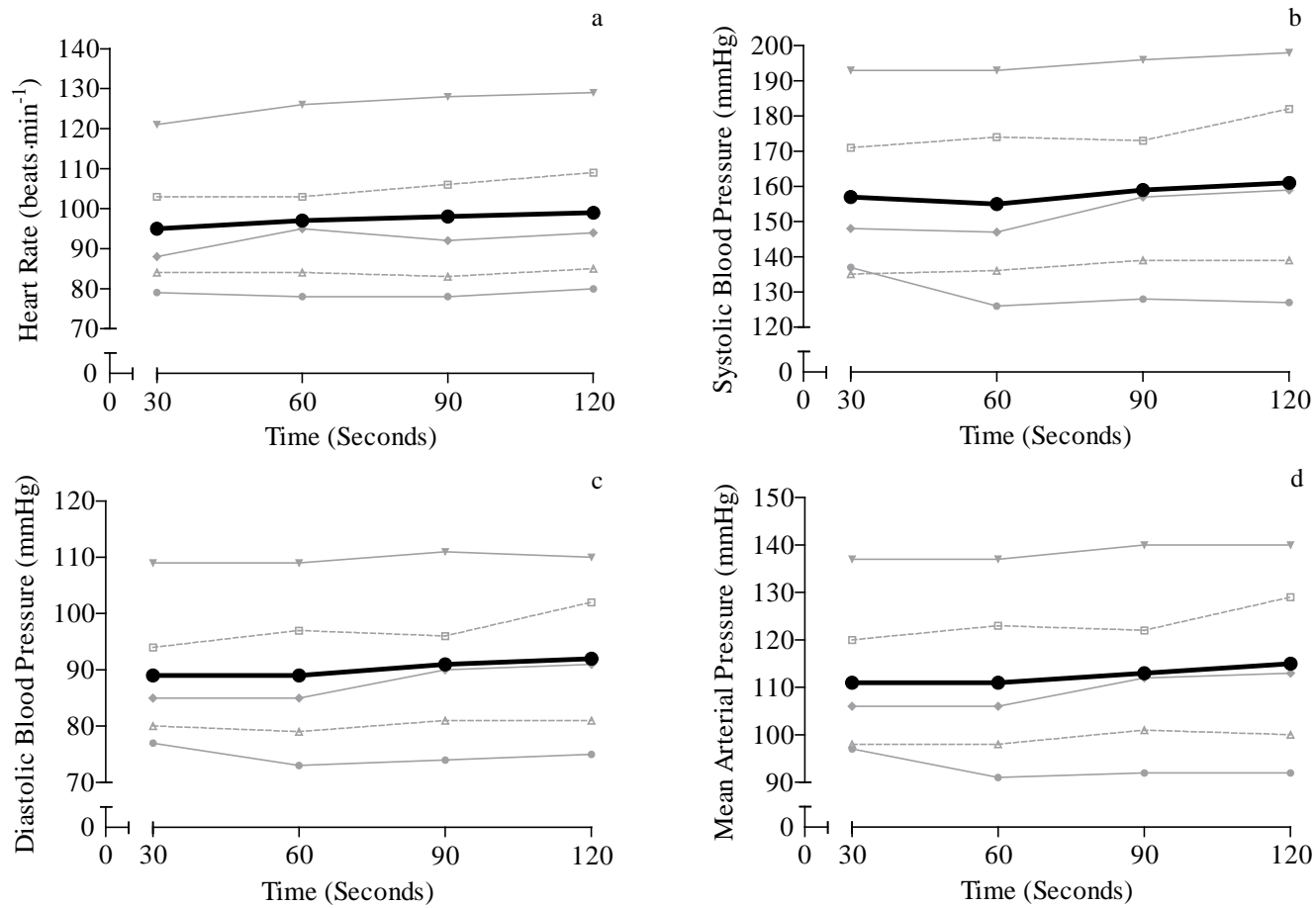
### 4.3.1 Resting data

On each of the 4 visits to the laboratory, resting measures of HR and BP were recorded for each participant prior to completion of either an incremental test or training session. The mean resting values were  $69 \pm 8$  beats·min<sup>-1</sup> for HR,  $124 \pm 8$  mmHg for SBP,  $77 \pm 4$  mmHg for DBP and  $93 \pm 5$  mmHg for MAP. The reliability of the resting measures was 6.3% (5.3-7.7%) for HR, 4.7% (4.0-5.8%) for SBP, 5.5% (4.7-6.8%) for DBP and 5.0% (4.2-6.1%) for MAP.

### 4.3.2 Incremental test data

Of the initial forty incremental tests completed (twenty participants completed two incremental tests each [INC1 and INC2]), ten were fully completed (six from INC1 and four from INC2). Through verbal questioning, it was ascertained that these participants could not have completed a further incremental stage. The mean final incremental stage reached but not completed was stage 5, the mean stage fully completed was 4 and the mean duration of the test was 8 minutes 40 seconds  $\pm$  66 seconds. There was no significant difference ( $P > 0.05$ ) between the INC1 and INC2 data.

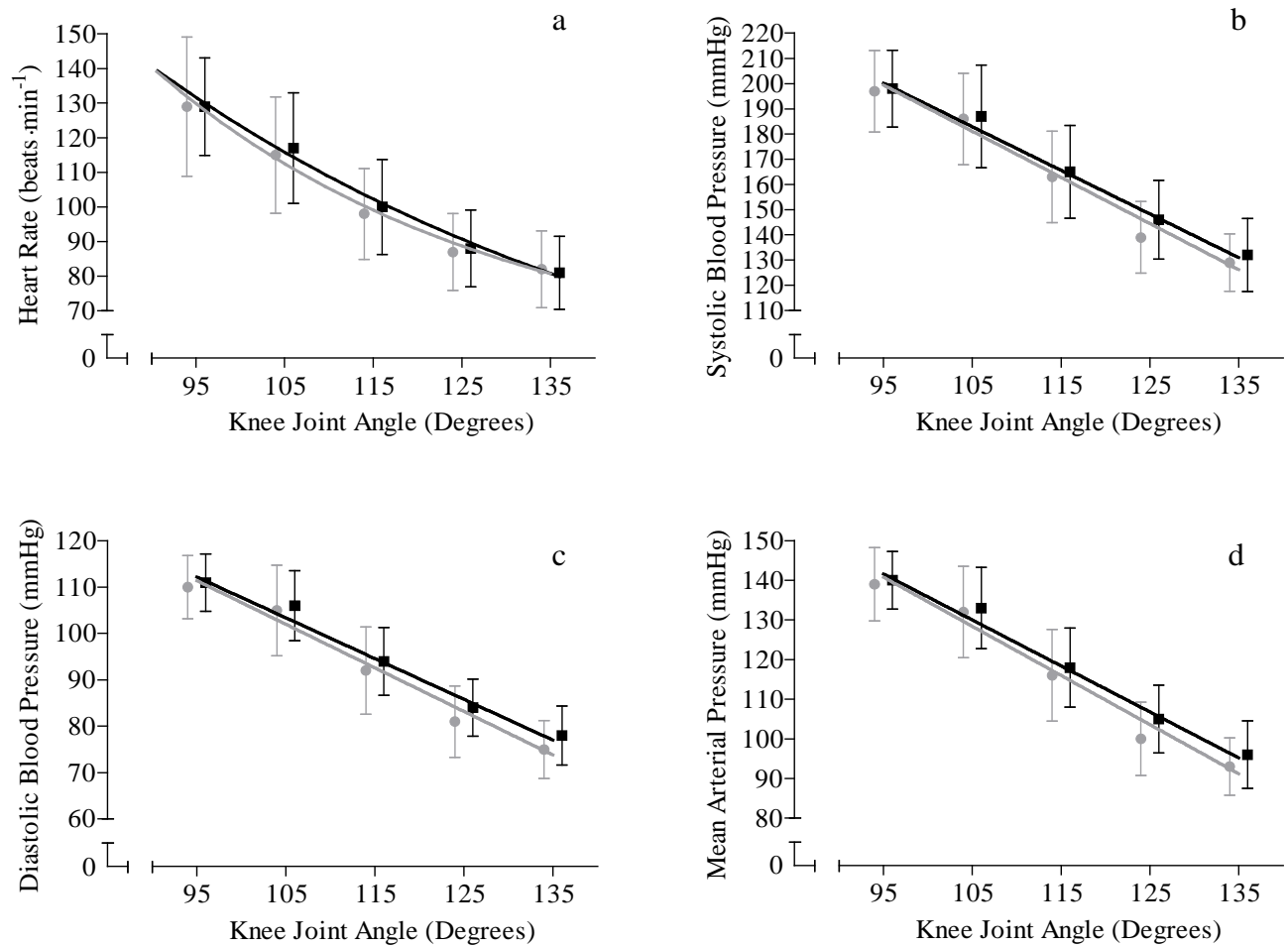
It was important that HR reached a 'steady-state' during each stage of the incremental test and previous research has reported that this occurs during the last 30 seconds (Wiles et al. 2008b). Thus, the mean HR and BP parameter data collected during the incremental tests for each 30 second time period were examined. These data were analysed only for those participants who fully completed the incremental test (INC1 and/or INC2). There were significant differences ( $P < 0.05$ ) in the mean HR and BP parameter data when compared over time during the incremental test; data analysed was the mean of all 5 incremental stages. The differences between 90 and 120 seconds for the mean incremental data were:  $1 \pm 2$  beats·min<sup>-1</sup> for HR (98 vs. 99 beats·min<sup>-1</sup>;  $P = 0.066$ );  $2 \pm 2$  mmHg for SBP (159 vs. 161 mmHg;  $P = 0.049$ ),  $1 \pm 1$  mmHg for DBP (91 vs. 92 mmHg;  $P = 0.089$ ) and  $1 \pm 1$  mmHg for MAP (113 vs. 114 mmHg;  $P = 0.004$ ). Even though SBP and MAP produced significant differences, these differences are considered to be small when compared with previous research (Wiles, 2008a). Therefore all further data analysis on the incremental data for all parameters (HR and BP) was assessed utilising the mean of the last 30 seconds as it appears that a 'steady-state' had been reached. The mean HR and BP data for each incremental stage and time period are shown in Figure 4.1 for those participants that fully completed the incremental test.



**Figure 4.1.** The mean heart rate (a), systolic blood pressure (b), diastolic blood pressure (c) and mean arterial pressure (d), for each incremental stage and time period for those participants that fully completed the incremental test; —●— 135°, - -△- - 125°, —◆— 115°, - -□- - 105°, —▼— 95°, and —●— mean data of all five incremental stages.

The mean HR data produced a significant inverse curvilinear relationship with wall squat knee joint angle for both incremental tests (INC1 and INC2);  $r$  values  $\leq -0.99$ ; ( $P < 0.05$ ). Figure 4.2a illustrates the mean inverse curvilinear relationship between knee joint angle and HR for both incremental tests (INC1 and INC2). When each participant's individual HR and knee joint angle relationship was analysed it was found that the  $r$  values ranged from -0.89 to -1.00 ( $P < 0.05$ ). Of the forty incremental tests completed, six produced curvilinear relationships that were termed 'ambiguous' by GraphPad and one produced an 'interrupted' analysis, in which case a linear relationship was a better fit and thus used for analysis.

The mean BP parameter data revealed significant inverse linear relationships with wall squat knee joint angle for all incremental tests (INC1 and INC2);  $r$  values  $\leq -0.99$  ( $P < 0.05$ ), see Figure 4.2b, c, d. Upon analysing each participant's individual data, inverse linear relationships were found between each of the BP parameters and knee joint angle for all participants (SBP, DBP and MAP  $r$  values ranged from -0.88 to -1.00;  $P < 0.05$ ).



**Figure 4.2.** The relationships between heart rate (a), systolic blood pressure (b), diastolic blood pressure (c) and mean arterial pressure (d), and wall squat knee joint angle for the incremental tests; ■ INC1 and ● INC2.

There was no significant difference in the  $HR_{peak}$  values attained during the last 30 seconds of the two incremental tests (INC1:  $127 \pm 16$  beats·min<sup>-1</sup> vs. INC2:  $126 \pm 20$  beats·min<sup>-1</sup>;  $P = 0.52$ ). The reliability of the  $HR_{peak}$  value was 6.3% (4.8-9.2%) and the bias was  $-1.55$  beats·min<sup>-1</sup>; these values were input into the modified limits of agreement equation to calculate the participants THRR, as outlined in section 4.2.4 (page 112).

From the HR and BP values attained and the relationships produced with knee joint angle during the incremental tests, the target values for training were calculated as well as the ranges around these targets. The mean training targets (HR, knee joint angle, SBP, DBP, and MAP) and ranges calculated from the two incremental tests (INC1 and INC2) are shown in Table 4.1 along with the reliability data for each variable. Further to this, the bias values are displayed for the target BPs as these data were entered into the modified limits of agreement equation to calculate the TBPRs. The HR and BP training targets and ranges displayed for INC2 have been normalised to the knee joint angle predicted for INC1 for comparison. It can be seen that all calculated targets for INC1 and INC2 were not significantly different ( $P > 0.05$ ).

**Table 4.1.** The mean values and coefficient of variation for the training targets and ranges calculated for repeated incremental tests.

	Incremental Test		Sig.	CV (95% CI)	Bias
	INC1	INC2			
Target HR (beats·min <sup>-1</sup> )	$121 \pm 14$	$116 \pm 16$	$P = 0.08$	6.6% (5.0-9.6%)	-
HR range (beats·min <sup>-1</sup> )	98-140	94-135			
Target Knee Joint Angle (degrees)	$104 \pm 7$	$103 \pm 6$	$P = 0.58$	2.8% (2.1-4.1%)	-
Target SBP (mmHg)	$188 \pm 19$	$186 \pm 15$	$P = 0.50$	4.9% (3.7-7.2%)	-1.9
SBP range (mmHg)	161-121	159-210			
Target DBP (mmHg)	$107 \pm 5$	$105 \pm 7$	$P = 0.14$	4.0% (3.0-5.8%)	-2.05
DBP range (mmHg)	93-117	91-115			
Target MAP (mmHg)	$134 \pm 9$	$131 \pm 9$	$P = 0.11$	4.9% (4.0-6.3%)	-3.3
MAP range (mmHg)	113-149	110-145			

The mean maximum values attained during the incremental tests (INC1 and INC2) were  $134 \pm 16$  beats·min<sup>-1</sup> for HR,  $214 \pm 14$  mmHg for SBP,  $126 \pm 8$  mmHg for DBP and  $154 \pm 8$  mmHg for MAP.

#### 4.3.3 Training data

All participants fully completed all of the isometric wall squat exercise training sessions. All training sessions were performed at the knee joint angle prescribed from the first incremental test (INC1). The mean target training wall squat knee joint angle was  $104 \pm 7^\circ$ .

The mean HR and BP data for the whole training session and the last 30 seconds of each training session (T1 and T2) is shown in Table 4.2 along with the reliability data for each variable. It can be seen that there was not a significant difference ( $P > 0.05$ ) in the mean HR and BP values produced between

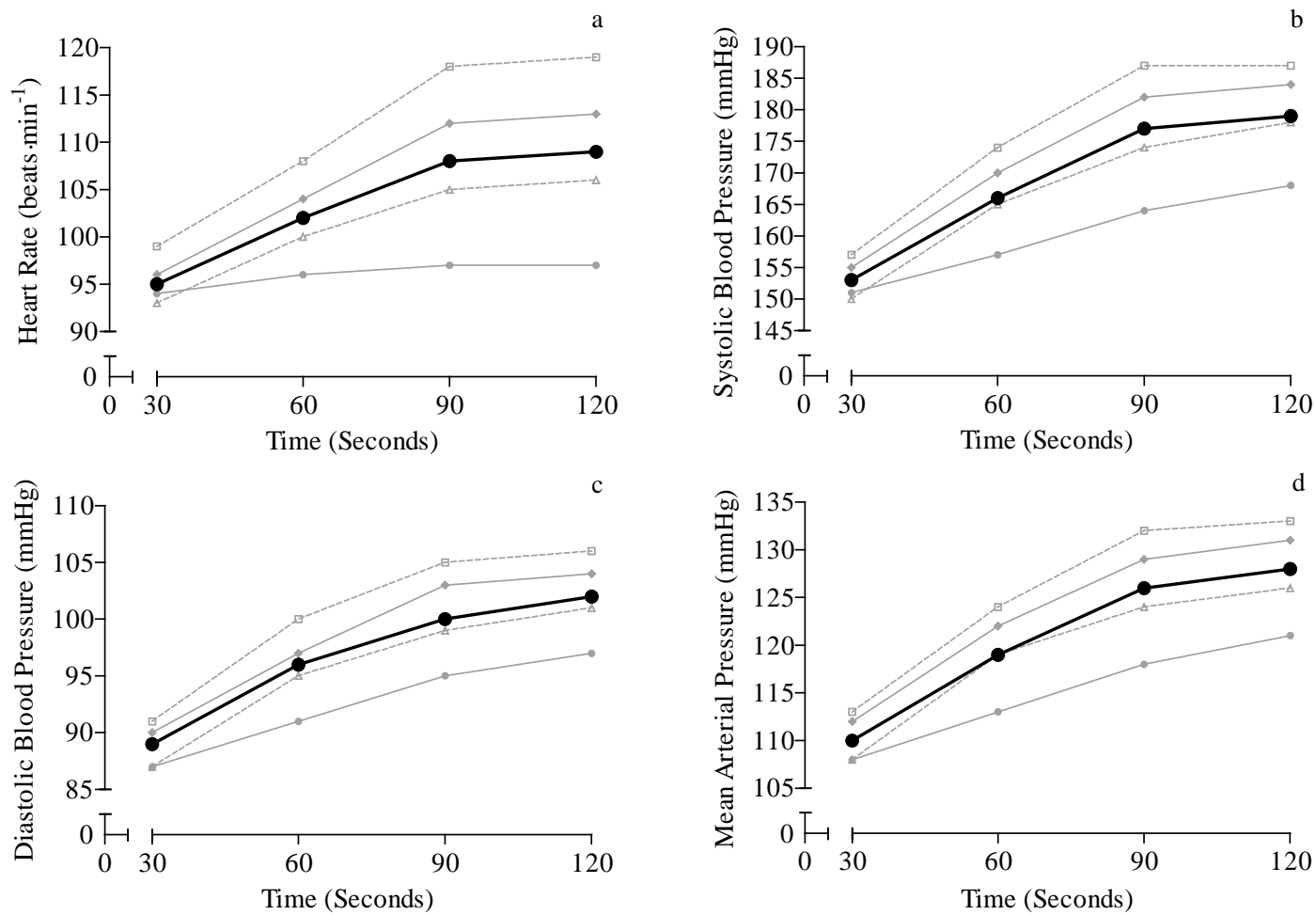


repeated training sessions. Therefore, all further analysis was performed using the mean data of the two training sessions (T1 and T2).

**Table 4.2.** The mean values and coefficient of variation for repeated training sessions.

	Training Session		Significance	CV (95% CI)
	T1	T2		
<b>Whole Session</b>				
HR (beats·min <sup>-1</sup> )	101 ± 10	103 ± 10	<i>P</i> = 0.40	5.0% (3.8-7.3%)
SBP (mmHg)	169 ± 16	169 ± 18	<i>P</i> = 0.83	3.9% (3.0-5.8%)
DBP (mmHg)	96 ± 7	96 ± 6	<i>P</i> = 0.83	4.8% (3.7-7.0%)
MAP (mmHg)	120 ± 10	121 ± 10	<i>P</i> = 0.97	4.3% (3.2-6.2%)
<b>Last 30 seconds</b>				
HR (beats·min <sup>-1</sup> )	110 ± 12	110 ± 13	<i>P</i> = 0.82	5.7% (4.3-8.3%)
SBP (mmHg)	183 ± 20	182 ± 21	<i>P</i> = 0.61	4.1% (3.1-6.0%)
DBP (mmHg)	103 ± 8	103 ± 8	<i>P</i> = 0.94	5.0% (3.8-7.3%)
MAP (mmHg)	130 ± 11	129 ± 11	<i>P</i> = 0.80	4.5% (3.4-6.5%)

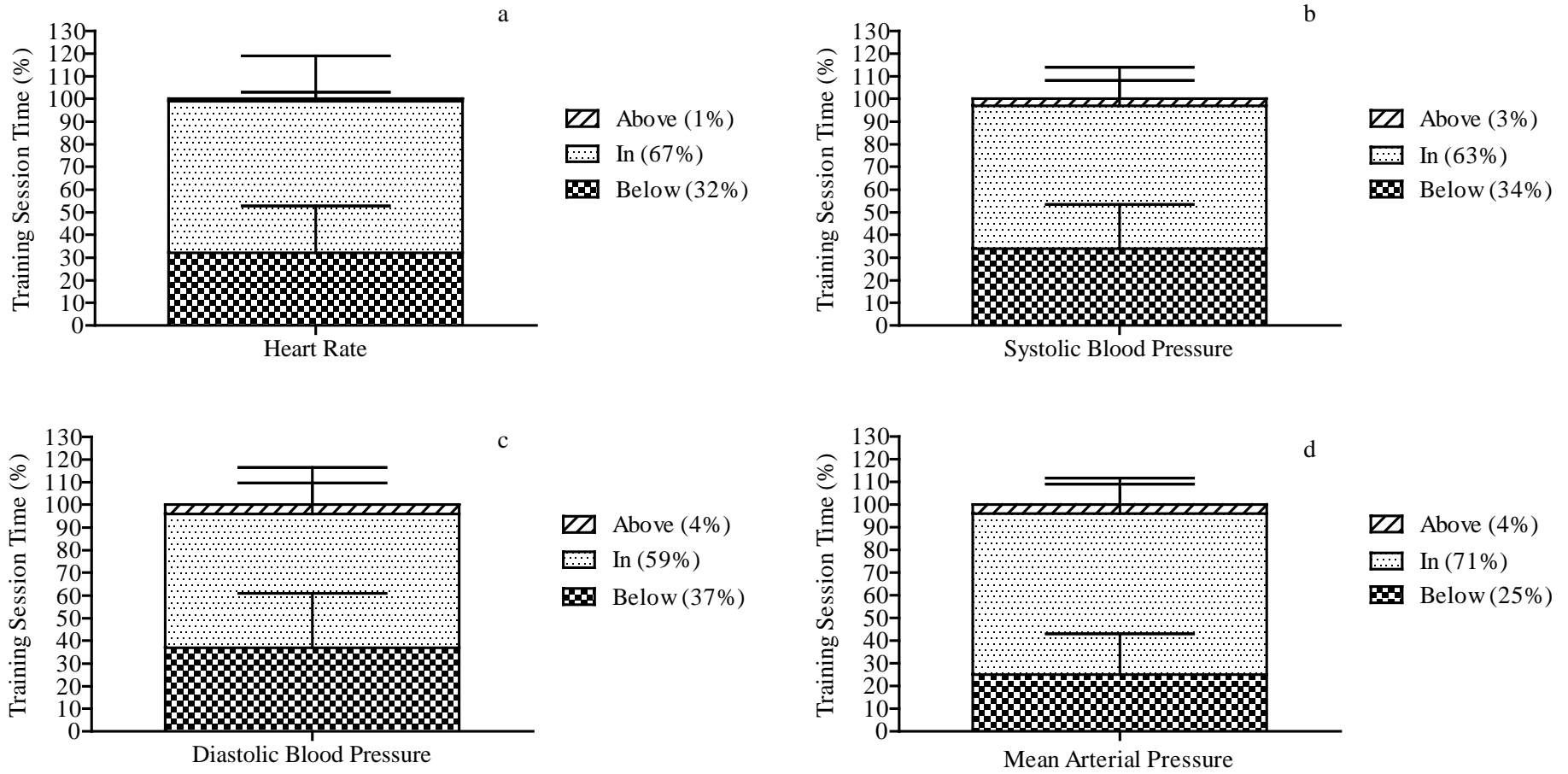
When the mean HR and BP parameter values were compared between all 4 exercise bouts, it was found that there were significant differences (*P* < 0.05) for all bout comparisons. Further to this, there were also significant differences (*P* < 0.05) in the mean HR and BP parameter data when compared over time during a training session; data analysed was the mean of all 4 bouts. However, it was found that there were no significant differences in HR between 90 seconds and 120 seconds: 1 ± 3 beats·min<sup>-1</sup> for HR (109 vs. 110 beats·min<sup>-1</sup>; *P* = 0.059). The mean HR and BP parameter values for each exercise bout and time period during isometric wall squat training are shown in Figure 4.3.



**Figure 4.3.** The mean heart rate (a), systolic blood pressure (b), diastolic blood pressure (c) and mean arterial pressure (d), for each exercise bout and time period during isometric wall squat training (mean data displayed of T1 and T2); —●— bout 1, - -△- - bout 2, —◆— bout 3, - -□- - bout 4 and —●— mean data for all four exercise bouts.

After comparing the actual HR values achieved during training and the expected target HR, it was found that there were significant differences ( $P < 0.001$ ) for both the whole training session data ( $-16 \pm 9$  beats·min<sup>-1</sup>) and for the last 30 seconds of training data ( $-8 \pm 9$  beats·min<sup>-1</sup>). A similar pattern of significant difference ( $P < 0.001$ ) was also present for the BP parameter data when the actual values attained during the whole training session were compared to the targets (SBP:  $-19 \pm 11$  mmHg; DBP:  $-10 \pm 7$  mmHg; MAP:  $-12 \pm 8$  mmHg). However, there was no significant ( $P > 0.05$ ) difference between the actual values attained during the last 30 seconds of training and the prescribed BP targets: SBP:  $-5 \pm 12$  mmHg ( $P = 0.09$ ); DBP:  $-3 \pm 7$  mmHg ( $P = 0.10$ ); MAP:  $-3 \pm 9$  mmHg ( $P = 0.17$ ).

The mean target HR and BP ranges calculated from both the incremental tests (mean data for INC1 and INC2) were compared to the actual values attained during the training sessions (mean T1 and T2). Figure 4.4 illustrates the mean percentage of time spent below, in and above the target HR and BP ranges during the whole training session (exercise bouts 1, 2, 3, and 4). Also, the mean percentage of time SBP and DBP were above the ACSM's exercise termination guidelines (Whaley, Brubaker and Otto, 2006) during the whole training session (mean T1 and T2) was  $0 \pm 0\%$  for SBP ( $> 250$  mmHg) and  $4 \pm 7\%$  for DBP ( $> 115$ mmHg).



**Figure 4.4.** The mean percentage of time below, in and above the heart rate (a), systolic blood pressure (b), diastolic blood pressure (c) and mean arterial pressure (d) target ranges (mean data displayed of INC1 and INC2) during training (mean of T1 and T2).

Further to this, the percentage of time spent below, in and above the target HR and BP ranges were also calculated for each of the four individual exercise bouts. This data is displayed below in Table 4.3 and any significant differences in the percentage of time between successive exercise bouts are highlighted. The percentage of time SBP and DBP were above the ACSM's exercise termination guidelines (Whaley, Brubaker and Otto, 2006) for each of the individual exercise bouts are also displayed in Table 4.3.

**Table 4.3.** The mean percentage of time spent below, in and above the target ranges for each individual exercise bout.

		<b>Exercise Bout</b>			
		<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>
<b>HR</b>	Below	52 ± 34%	37 ± 25%*	22 ± 20%*	16 ± 14%*†
	In	48 ± 34%	63 ± 25%*	77 ± 20%*	81 ± 14%†
	Above	0 ± 0%	0 ± 0%	1 ± 2%	3 ± 10%
<b>SBP</b>	Below	47 ± 27%	35 ± 19%*	29 ± 18%*	23 ± 21%*†
	In	53 ± 27%	63 ± 17%	68 ± 17%*	69 ± 22%†
	Above	0 ± 0%	2 ± 8%	3 ± 11%	8 ± 16%*†
	Above ACSM (> 250 mmHg)	0 ± 0%	0 ± 0%	0 ± 0%	0 ± 0%
<b>DBP</b>	Below	52 ± 30%	38 ± 26%*	32 ± 24%*	25 ± 22%*†
	In	47 ± 30%	59 ± 24%*	63 ± 22%	65 ± 21%†
	Above	1 ± 3%	2 ± 8%	5 ± 13%*	10 ± 17%†
	Above ACSM (> 115 mmHg)	0 ± 1%	1 ± 5%	4 ± 9%*	10 ± 14%*†
<b>MAP</b>	Below	37 ± 27%	26 ± 17%*	21 ± 18%*	17 ± 18%*†
	In	62 ± 26%	72 ± 16%*	75 ± 18%	74 ± 19%
	Above	0 ± 1%	2 ± 9%	4 ± 12%*	9 ± 17%*†

\* = significant ( $P < 0.05$ ) difference in percentage between successive bouts.

† = significant ( $P < 0.05$ ) difference in percentage between bout 1 and 4.

The mean maximum values attained during the isometric wall squat exercise training sessions (T1 and T2) were  $127 \pm 16$  beats·min<sup>-1</sup> for HR,  $211 \pm 23$  mmHg for SBP,  $120 \pm 10$  mmHg for DBP and  $149 \pm 14$  mmHg for MAP.

None of the participants reported any adverse symptoms, such as shortness of breath, dizziness, chest pain, light-headedness, etc., during any of the incremental tests or training sessions.

#### 4.4 Discussion

##### 4.4.1 Establishing the relationships between wall squat knee joint angle and both heart rate and blood pressure from an incremental exercise test

One of the main findings of this study was that an incremental isometric wall squat test produced strong significant inverse relationships between knee joint angle and both HR and BP. Heart rate specifically produced a curvilinear relationship and all BP parameters (SBP, DBP and MAP) produced linear

relationships, as previously found during isolated bouts of wall squat exercise in study 1 (section 3.3.2, page 97). Exploration of these relationships was possible due to the fact that these cardiovascular variables appeared to produce a relatively 'steady-state' response during the last 30 seconds of each incremental stage (Wiles et al., 2008b). Conversely, previous constant position research would suggest HR and BP should increase throughout the contraction duration (Hunter et al., 2002; 2008; Rudroff et al., 2007, 2005), however as outlined in Chapter 1, section 1.6.2d (page 40), there are several factors that may help explain why constant position isometric wall squat exercise produced an attenuated cardiovascular response.

The relationships produced in this study compare favourably to those previously reported from constant EMG incremental tests in which double-leg extension exercise was performed (Wiles et al., 2008; Devereux, Wiles and Swaine, 2010b). Indeed, Wiles et al. (2008b) found significant linear relationships between  $EMG_{peak}$  and both HR and SBP for a continuous incremental protocol ( $r$  at least 0.91;  $P < 0.05$ ) and Devereux, Wiles and Swaine (2010b) established significant linear relationships between  $EMG_{peak}$  and HR for a discontinuous incremental protocol ( $r$  at least 0.93;  $P < 0.05$ ). However, it is important to note that these past studies produced linear relationships between isometric exercise intensity and HR, whereas the relationships produced in the current study were curvilinear. Such differences in the type of relationship produced may be due to variations in the incremental protocols implemented, such as the isometric contractions style utilised (constant EMG vs. constant position), which consequently affects the increments selected for each work stage (5%  $EMG_{peak}$  vs. 10°, respectively). The latter would likely create disparate increases in EMG between increments, which may have simultaneously caused varied activation of central and/or peripheral drive leading to unequal increases in HR at each work stage, as previously discussed in Chapter 3, section 3.4.2 (page 103).

From the assessment of repeated incremental tests, it was found that there was no significant difference in the incremental stage completed and also no significant difference in the target HR and BP values calculated from the relationships produced between knee joint angle and both HR and BP. Further to this, the reliability of the mean HR and BP values attained during whole training sessions were found to be good (CV < 10%) (Scott, Randolph and Leier, 1989), thereby suggesting that the cardiovascular responses are reproducible. This finding is important to ensure a consistent, safe training prescription due to the fact that isometric intensity is calculated from these incremental test responses. The reliability values produced in the present study (CV [95% CI]) compare favourably to those established by Wiles et al. (2008b) for both HR (5.2% [4.0-8.1%]) and SBP (5.3% [3.8-9.1%]) during a continuous incremental test performing isometric double-leg extensions.

As isometric exercise is known to produce an extreme pressor response (Mitchell and Wildenthal, 1974), it was also worth examining the maximum BP values attained during the incremental wall squat test (section 4.3.2, page 115). It can be seen that SBP stayed within the ACSM exercise termination guidelines (< 250 mmHg), but DBP exceeded the upper limit (> 115 mmHg) (Whaley, Brubaker and Otto, 2006). However, it was noteworthy that the mean DBP during the last 30 seconds of the incremental tests (mean INC1 and INC2) was 16 mmHg lower than the mean maximum DBP value ( $110 \pm 7$  mmHg vs.  $126 \pm 8$  mmHg, respectively). Therefore, it would seem that the maximum DBP represents a one-off value that does not represent the overall pressor response experienced during the incremental test due to

the fact that the mean stayed much lower than the recorded maximum. Thus, as it appears that the maximum DBP value was sustained for an extremely short duration, it is suggested that this would be very unlikely to cause any significant cardiovascular risk due to the time that the body is subjected to such an extreme pressor response is minimal.

#### ***4.4.2 Prescribing isometric wall squat exercise intensity using the curvilinear relationship established between knee joint angle and heart rate during an incremental test***

From the reliable HR values produced during the incremental wall squat test, the target HR (95% HR<sub>peak</sub>) for training was calculated for each participant. On comparing this data to previous research, it was found that the mean target HR calculated from the incremental tests in the current study (mean INC1 and INC2:  $118 \pm 14$  beats·min<sup>-1</sup>) was 17 beats·min<sup>-1</sup> higher than the 95% HR<sub>peak</sub> target prescribed by Wiles, Coleman and Swaine (2010) ( $101 \pm 16$  beats·min<sup>-1</sup>). The difference in these target values was likely due to the fact that the HR values during the final incremental stage of the present study, from which the target HR was prescribed, were approximately 10 beats·min<sup>-1</sup> higher than those attained in the incremental test of Wiles, Coleman and Swaine (2010). This may be attributable to isometric wall squat exercise potentially utilising a larger muscle mass than the double-leg extension exercise used in the protocol of Wiles, Coleman and Swaine (2010). Indeed, leg extension is a single-joint exercise that isolates the quadriceps (Delavier, 2010), whereas isometric wall squat exercise is a multijoint exercise that utilises additional muscle groups to stabilise the exercise position (Contreras, 2014). This being the case, isometric wall squat exercise would require a greater level of motor unit recruitment, which may simultaneously stimulate the cardiovascular control centres to a greater extent through central command (Franke, Boettger and McLean, 2000) and/or the exercise pressor reflex (Gálvez et al., 2000) generating the higher HR response.

Based on the curvilinear relationship established between wall squat knee joint angle and HR, it was then possible to interpolate the wall squat position (knee joint angle) at which a participant would have to train at in order to achieve the target HR. The mean knee joint angle prescribed for training was  $104 \pm 7^\circ$ ; see section 4.3.2 (page 115). It appears that the isometric training intensity prescribed for each participant was realistic and manageable as all four exercise bouts of each training session were completed. Further to this, the mean HR and BP values attained between repeated training sessions were not significantly different and a good level of reliability was produced as both the HR and BP parameters produced CVs less than 10% (Scott, Randolph and Leier, 1989). It is also worth noting that data from the first incremental test was utilised to calculate the training wall squat knee joint angle, however there was no significant difference in the knee joint angle prescribed from repeated incremental tests and the reliability was found to be excellent.

When the training data was compared to the targets prescribed from the incremental test, it was found that the actual HR values attained during the training session were significantly lower than the prescribed target HR. The mean HR for the whole training session was 16 beats·min<sup>-1</sup> lower, whereas the last 30 second data was only 8 beats·min<sup>-1</sup> lower. This is likely due to the fact that the target HR was prescribed from the mean of the last 30 seconds of the incremental test and thus the last 30 seconds of each exercise bout may better reflect the prescribed target. This data would suggest that overall the participants were working at a slightly lower intensity than that prescribed. However, despite the discrepancy between the target and actual values, the mean HR achieved during training in the present study was very similar to

that achieved by Wiles, Coleman and Swaine (2010) in which BP was successfully lowered by setting the isometric training intensity at a participant-specific EMG to achieve a HR target of 95%  $HR_{peak}$ . Thus it is proposed that isometric wall squat training may provide a sufficient cardiovascular stimulus that could potentially produce training reductions in resting BP similar to those achieved by Wiles, Coleman and Swaine (2010).

Furthermore, it is probably more appropriate to compare the actual training values attained to a target range rather than a single value due to the variable nature of HR (Scott, Randolph and Leier, 1989; Stanforth et al., 2000; Højgaard et al., 2005). Indeed, a training session should aim to achieve a steady-state HR response with the mean HR value lying within the THRR and close to the target HR (Whaley, Brubaker and Otto, 2006). Monitoring HR in this manner can be used to detect and prevent large errors in training intensity (Jeukendrup and VanDiemen, 1998), which is important when prescribing an effective but safe training programme; the use of THRR in this study will be discussed in the proceeding section.

#### ***4.4.3 Using the modified limits of agreement equation to determine target ranges for training***

Prescribing isometric training through a THRR provides a more stringent control of the training intensity in which both under and, more importantly, the risk of too much overload can be monitored. To this end, a further aim of this study was to devise a method to more precisely determine the THRR for training, rather than using the  $\pm 5\%$  range previously applied within IET studies (Devereux, Wiles and Swaine, 2010b; Wiles, Coleman and Swaine, 2010). To this end, the modified limits of agreement equation was utilised (Hopkins, 2000; Coleman et al., 2005), which takes into account the variability of a measure such as HR. The size of the mean THRR in the present study (mean of INC1 and INC2: 96-138  $beats \cdot min^{-1}$ ) was much wider than the HR ranges utilised in the isometric training study of Wiles, Coleman and Swaine (2010), which produced a THRR of 96-106  $beats \cdot min^{-1}$  (target 95%  $HR_{peak} \pm 5\%$ ) (values extrapolated from graph). It was possible to use a narrower THRR in the study of Wiles, Coleman and Swaine (2010) as training was completed at a constant EMG value, which has been shown to produce an attenuated cardiovascular response (Schibye et al., 1981; Franke, Boettger and McLean, 2000). However, when the THRR calculated from the current study is compared to the THRR used to determine the intensity of vigorous aerobic exercise (77-95%  $HR_{max}$ ), the size is similar and therefore more representative of THRRs commonly prescribed. For example, the vigorous aerobic exercise THRR was 147-181  $beats \cdot min^{-1}$  when calculated using the present study's group mean age (29 years, see page 111) and the well-known target HR equation:  $HR_{max} \times \text{desired intensity percentage}$ , where  $HR_{max}$  is 220 - age (Thompson, 2010).

When the actual HR values attained during the isometric wall squat training sessions were compared to the calculated THRR it was found that participants spent 67% of the time (~5 minutes 22 seconds) within the calculated target range during the whole training session (8 minutes in total: 4 x 2 minute wall squats). Thus the time in the THRR per training session was found to be high and therefore the training intensity prescribed was sufficient for each participant to reach their target range despite the fact that the mean training HR was lower than the prescribed target. However, it is important to note that there was a statistically significant increase in the mean HR of each exercise bout throughout a training session, which suggests that the 2 minute rest period was not sufficient to achieve a full cardiovascular recovery. This had an impact on the time spent in the THRR per exercise bout, such that the percentage of time



spent in the target range significantly increased throughout the training session from bout 1 (48%) to bout 4 (81%). Therefore it was the cumulative effect of these 4 exercise bouts that lead to the target HR being attained for a large duration (67%) of the whole training session. As isometric exercise is known to produce significant cardiovascular stress (Fisher et al., 1973), this form of exercise has previously been approached with some caution, particularly in special populations (Millar, Paashuis and McCartney, 2009b), such as those with hypertension or heart disease (Araújo et al., 2011). However, the current study demonstrates that isometric wall squat exercise may produce a gradational increase in intensity towards the target throughout a training session. Therefore this might provide an important beneficial feature for home-based isometric exercise to ensure an effective but importantly safe training prescription.

Whilst a large majority of the actual HR values attained during training were within the THRR, it is likely that in reality the HR values will vary and sometimes be below or above the prescribed range (Whaley, Brubaker and Otto, 2006). Indeed participants spent some time below the THRR throughout the whole training session (32%: ~2 minutes and 34 seconds), which is inevitable as HR gradually increases at the beginning of exercise (Boutcher and Stocker, 1999) due to the withdrawal of vagal tone (Martin et al., 1974). However, the percentage of time spent below the target range significantly decreased throughout the training session from bout 1 (52%) to bout 4 (16%), presumably due to incomplete cardiovascular recovery from the previous exercise bout. If a longer rest period had been utilised between exercise bouts then this may have allowed a greater cardiovascular recovery, however, this would likely reduce the mean HR and therefore participants would have spent more time below the THRR. Furthermore, participants also spent a short amount of time above the THRR (1%: ~5 seconds); this did not significantly increase throughout the training session (bout 1: 0% vs. bout 4: 3%). If a shorter rest period was used between bouts this would likely result in less cardiovascular recovery, which could cause an increase in mean HR leading to the THRR being exceeded to a greater extent.

Taken together, this data suggests that the THRR range calculated in this study appears to represent a realistic target to be achieved and maintained during isometric wall squat training and it is therefore proposed that this method can be utilised to monitor the intensity of an isometric wall squat training programme. Indeed, using the modified limits of agreement equation (Hopkins, 2000; Coleman et al., 2005), any variation in HR between training sessions can be discerned as either a natural fluctuation, which will fall within the THRR, or a 'real' change, which will fall outside the THRR and therefore the training intensity will have to be consequently modified in order to achieve the target HR and maintain an adequate training stimulus. However, this method is yet to be applied within an IET programme.

The target HR (95%  $HR_{peak}$ ) in the current study was prescribed from the mean HR value of the last 30 seconds of the incremental test, rather than the highest HR value attained as used previously (Wiles et al., 2008b; Devereux, 2010a). If the singular maximum value had been used instead, the target HR would have been approximately 9  $beats \cdot min^{-1}$  higher and therefore the percentage of time spent in the THRR may have been less. Further to this, if the THRR was simply  $\pm 5\%$  of the target HR value (Devereux, Wiles and Swaine, 2010b; Wiles, Coleman and Swaine, 2010), then size of the THRR would have been much narrower and the percentage of time in the target range would have been further reduced. Thus, it is concluded that the methods to calculate the HR target and range in the present study strongly reflect the

HR values attained during the training session and thereby present an accurate means of prescribing isometric wall squat training intensity.

Further to this, a TBPR was also calculated to estimate the likely BP response for the prescribed target knee joint angle (see section 4.3.2, page 115); this was deemed necessary due to the pronounced pressor response associated with isometric exercise (Mitchell and Wildenthal, 1974). It was found that the upper range calculated for both SBP and DBP were below the ASCM's guidelines for exercise termination (SBP < 250 mmHg, DBP < 115 mmHg) (Whaley, Brubaker and Otto, 2006). When the actual BP values attained during training were compared to the TBPRs it was found that the percentage of time spent in the prescribed TBPR was high at 63% (~5 minutes and 2 seconds) for SBP and 59% (~4 minutes and 43 seconds) for DBP, with 34% (~2 minutes and 43 seconds) and 37% (~2 minutes and 58 seconds) of the time for SBP and DBP respectively spent below the prescribed range. For both SBP and DBP the time spent in the BP target range increased from bout 1 to 4, with the time below the target decreasing. However, most importantly, the time spent above the TBPR throughout the whole training session was very limited at 3% for SBP (~14 seconds) and 4% for DBP (~19 seconds), although this did increase from exercise bouts 1 to 4. When the actual training BP values were also compared to the ACSM guidelines for exercise termination (Whaley, Brubaker and Otto, 2006), it can be seen that the mean maximum DBP value exceeded the recommendations. Indeed, 0% (0 seconds) of the time was spent above the SBP guideline (> 250 mmHg), and this remained unchanged from exercise bouts 1 to 4, however 4% (~ 19 seconds) of the time was spent above the DBP guideline (> 115 mmHg) (Whaley, Brubaker and Otto, 2006). It is important to note that in most cases the time spent above the DBP guidelines did not occur during one constant time period and was instead spread across a training session. Indeed, typically the DBP guidelines were exceeded in bouts 2 (1%: ~1 second), 3 (4%: ~5 seconds) and 4 (10%: ~12 seconds). Thus the time continuously sustained above the DBP guidelines for a continuous time period was minimal. It is suggested that due to this relatively short duration, and the fact that DBP returns to resting values within a few minutes (Humphreys and Lind, 1963), the increase in DBP above the guidelines is unlikely to cause any significant cardiovascular risk in the current participant group.

#### ***4.4.4 Potential limitations when prescribing wall squat exercise intensity from an incremental test***

It is proposed that the methods described above provide a sound isometric wall squat training prescription, however there appear to be a small number of limitations. First of all, the incremental test consisted of five finite stages designed to be completed to maximum. Of the forty incremental tests carried out, ten were fully completed. While these participants subjectively confirmed that they could not have completed an additional incremental stage, it may be beneficial to have a more standardised method to ascertain whether maximum levels have been attained. Indeed, previous isometric research has utilised ratings of perceived effort (Seals, 1993; Wiles et al., 2005). These scales are used to gauge a participant's level of effort, exertion, fatigue and pain (Borg, 1998). Therefore, all future incremental tests carried out within this thesis will employ such methods.

A second limitation of the incremental test is that isometric exercise can cause a certain amount of discomfort in the contracting muscle, particularly towards the point of fatigue (Lind, 2011). Participants must learn to overcome the discomfort so that this is not a limiting factor to the isometric exercise being completed to fatigue (Lind, 2011). If participants do not overcome this barrier, the incremental test may

end prematurely and thus the participant's true isometric  $HR_{peak}$  may not be attained, again leading to training being completed at a substandard intensity. There was not an objective method to determine whether a participant had completed the isometric incremental test to fatigue. However, completion to fatigue was assumed for four main reasons: 1) all participants volunteered to take part in the study, 2) there was a 0% drop out rate, suggesting that all participants accepted the study requirements, 3) the reliability data produced for the repeated incremental tests was good; criterion used by Gálvez et al. (2000). Finally, 4) all participants subjectively confirmed that they could not have sustained the isometric wall squat exercise position for any longer.

Finally, this study established the isometric wall squat training prescription method in young normotensive healthy males, as advised by Badrov et al. (2013a). However, this IET protocol may be most directly applied to hypertensive individuals. While the principles of the incremental test and the data collected should be reflected in any population, the specifics of translating this novel IET protocol to a hypertensive population may need further investigation. For instance, the maximal nature of the incremental test designed in this study may need to be addressed, as participants are required to complete several stages of increasing wall squat exercise intensity to maximum. While the BP levels attained by the normotensive participants utilised in this study were deemed to be safe, the pressor response may be greater with hypertensive individuals due to their higher initial BP levels (Ewing et al., 1973). Therefore it may be necessary for future research to develop a submaximal incremental isometric exercise test, as discussed in section 6.7 (page 172).

#### **4.5 Conclusion**

It is proposed that the incremental test and calculated target HR and BP ranges provide a means by which isometric wall squat exercise intensity can be reliably prescribed and monitored. It remains to be established whether wall squat exercise can reduce resting BP when utilised within a home-based training protocol.

## **CHAPTER 5: STUDY 3**

### **THE EFFECTS OF A FOUR WEEK HOME-BASED ISOMETRIC EXERCISE TRAINING PROGRAMME ON RESTING BLOOD PRESSURE AND OTHER CARDIOVASCULAR VARIABLES**

The work in this chapter was presented at the American College of Sports Medicine Annual Meeting (Goldring, Wiles and Coleman, 2012).

#### **5.1 Introduction**

As outlined in Chapter 1, (section 1.4.1, page 11), it is well established that IET causes a reduction in resting BP (Wiley et al., 1992; Ray and Carrasco, 2000; Howden et al., 2002; Taylor et al., 2003; Peters et al., 2006; McGowan et al., 2007a; 2007b; Millar et al., 2008; Devereux, Wiles and Swaine, 2010b; Wiles, Coleman and Swaine, 2010; Baross, Wiles and Swaine, 2012; Badrov et al., 2013a; 2013b; Millar et al., 2013a). However, despite the proven efficacy of IET, its application is somewhat limited as the majority of training studies have involved the use of expensive and/or laboratory-based equipment, which introduces a number of common barriers to physical activity and exercise, such as cost (Belza et al., 2004; Allison et al., 2005; Lascar et al., 2014) and time (Troost et al., 2002; Lascar et al., 2014) (see section 1.2, page 4). These are factors that could reduce the effectiveness of IET if used as a physical therapy for altering BP (Millar, Paashuis and McCartney, 2009b). It is suggested that the isometric wall squat exercise, which utilises simple, inexpensive equipment, could be prescribed within an accessible home-based training programme, in order to reduce some of these obstacles that are known to negatively impact the adoption and maintenance of exercise.

From the previous studies of this thesis it has been found that constant position isometric wall squat exercise intensity can be: 1) reliably adjusted by manipulating the knee joint angle, see study 1 (Chapter 3, page 91), and 2) accurately prescribed for training at a participant-specific knee joint angle to elicit a target HR (95% HR<sub>peak</sub>) from an incremental test, see study 2 (Chapter 4, page 109). Consequently this final study looked to establish whether constant position isometric wall squat exercise could actually reduce resting BP when utilised within a home-based training programme. To achieve this it is proposed that participants should complete a pre-training incremental test, based on the protocol designed by Wiles et al. (2008b), in order to establish a curvilinear relationship between knee joint angle and HR, as found in study 2 (see section 4.3.2, page 115). From this relationship, training intensity would then be prescribed to an individualised wall squat knee joint angle to attain a target HR, which is 95% of the HR<sub>peak</sub> achieved during the incremental test. Each session could then include four 2 minute isometric exercise bouts with 2 minutes rest in between (Wiles, Coleman and Swaine, 2010). Research suggests that a 2 minute exercise duration produces a large cardiovascular and autonomic stimulus, which could be an important factor for maximising BP adaptations (Millar, MacDonald and McCartney, 2011), as previously discussed in section 1.5.4 (page 30). Training sessions would then be completed 3 times a week over a 4 week period (Devereux, Wiles and Swaine, 2010b). It is proposed that a greater training stimulus will be elicited as wall squat exercise will be performed at a high intensity (95% HR<sub>peak</sub>) using a large muscle mass. It is anticipated that this will help to ensure that BP adaptations occur at a faster rate of 4 weeks, as found by Devereux, Wiles and Swaine (2010b) (see section 1.5.2b, page 27). Also, implementing a lower training

frequency (3 times a week), which would reduce the participant's time commitment, may help to overcome this known exercise barrier to increase adherence (DeMichele et al., 1997).

As well as establishing the efficacy of this novel home-based IET protocol for reducing resting BP, the clinical significance of any resting SBP and DBP reductions will also be determined. Traditionally research has often focused on the statistical significance of data (Page, 2014) and conclusions regarding the effectiveness of an intervention are typically based on the statistical comparisons between mean changes that result from different study conditions (Jacobson and Truax, 1991). However, the overall effectiveness of a treatment cannot be conveyed based on statistical significance alone (Brignardello-Petersen et al., 2013), as no clinical insight is provided in terms of the size or direction of the outcome (Page, 2014). Consequently, the literature suggests that research should also consider the data's clinical significance (Brignardello-Petersen et al., 2013), which relates to the practical importance of the intervention's result (Fethney, 2010). The clinical significance of an outcome is established by determining the minimal clinically important difference (MCID) (Page, 2014) and is described as the smallest change that is considered worthwhile or important to an individual (Copay et al., 2007). One method used to establish the MCID is the anchor-based approach, which compares the change score to another outcome value of interest (Fethney, 2010). Therefore it is important to consider that the main goal of any antihypertensive therapy is to ultimately lower cardiovascular related morbidity and mortality (Chobanian et al., 2003). There is limited data available to establish the MCID for resting BP reductions, however two recent IET review articles emphasised that even small decreases in resting BP could be clinically relevant (Millar et al., 2013b) and reduce hypertension-related morbidity and mortality (Lawrence et al., 2014). Indeed, it has previously been estimated that SBP or DBP reductions of 2 mmHg could reduce the risk of coronary heart disease, stroke and mortality (Cook et al., 1995; Neaton et al., 1995 cited in Stamler, 1997). However, while this may be the case, few IET studies have reported the percentage of participants that attained such clinically relevant BP reductions (Millar et al., 2013b).

Furthermore, the mechanisms that regulate a reduction in resting BP following IET are not well understood (Millar et al., 2009b). As MAP is determined by  $\dot{Q}$  and TPR (Hietanen, 1984), any reductions in BP are likely to be moderated primarily by either one or both of these variables (Wiley et al., 1992; Pescatello et al., 2004; Millar et al., 2013b) (see section 1.4.2, page 15). As  $\dot{Q}$  does not typically alter following this type of training, it is suggested that a reduction in BP would more likely be mediated by a reduction in TPR (Millar et al., 2013b); however the possibility of a change in  $\dot{Q}$  cannot be overlooked (Wiley et al., 1992). Despite the importance of these variables, only two studies to date have measured these parameters pre- and post-IET, however no statistically significant changes in  $\dot{Q}$  or TPR occurred despite the fact that resting BP was reduced (Devereux, Wiles and Swaine, 2010b; Wiles, Coleman and Swaine, 2010). Further research is required to ascertain whether one or both of these variables regulate a reduction in resting BP.

Therefore the primary aim of this study was to investigate whether a 4 week home-based isometric wall squat training programme could successfully reduce resting BP. Further to this, the secondary aim of the study was to explore the physiological variables that have been suggested to mediate a change in resting BP following IET, such as  $\dot{Q}$  and TPR.

## 5.2 Methods

### 5.2.1 Participants

Twenty-eight healthy males (age  $30 \pm 7$  years; stature  $1.78 \pm 0.05$  m; body mass  $78.7 \pm 11.1$  kg; SBP  $125 \pm 6$  mmHg; DBP  $78 \pm 5$  mmHg; mean  $\pm$  standard deviation) completed the study. Participants self-reported that they were physically active, being involved in exercise on average for approximately 10.6  $\pm$  10.7 hours per week. Typically their habitual exercise included walking, running, cycling, swimming, resistance training, football, hockey, rugby, cricket, volleyball, table tennis, badminton, golf, trampolining, fencing, wrestling, and taekwondo. All participants met the studies participant inclusion criteria as outlined in section 2.3.1 (page 48).

### 5.2.2 Sample size estimation

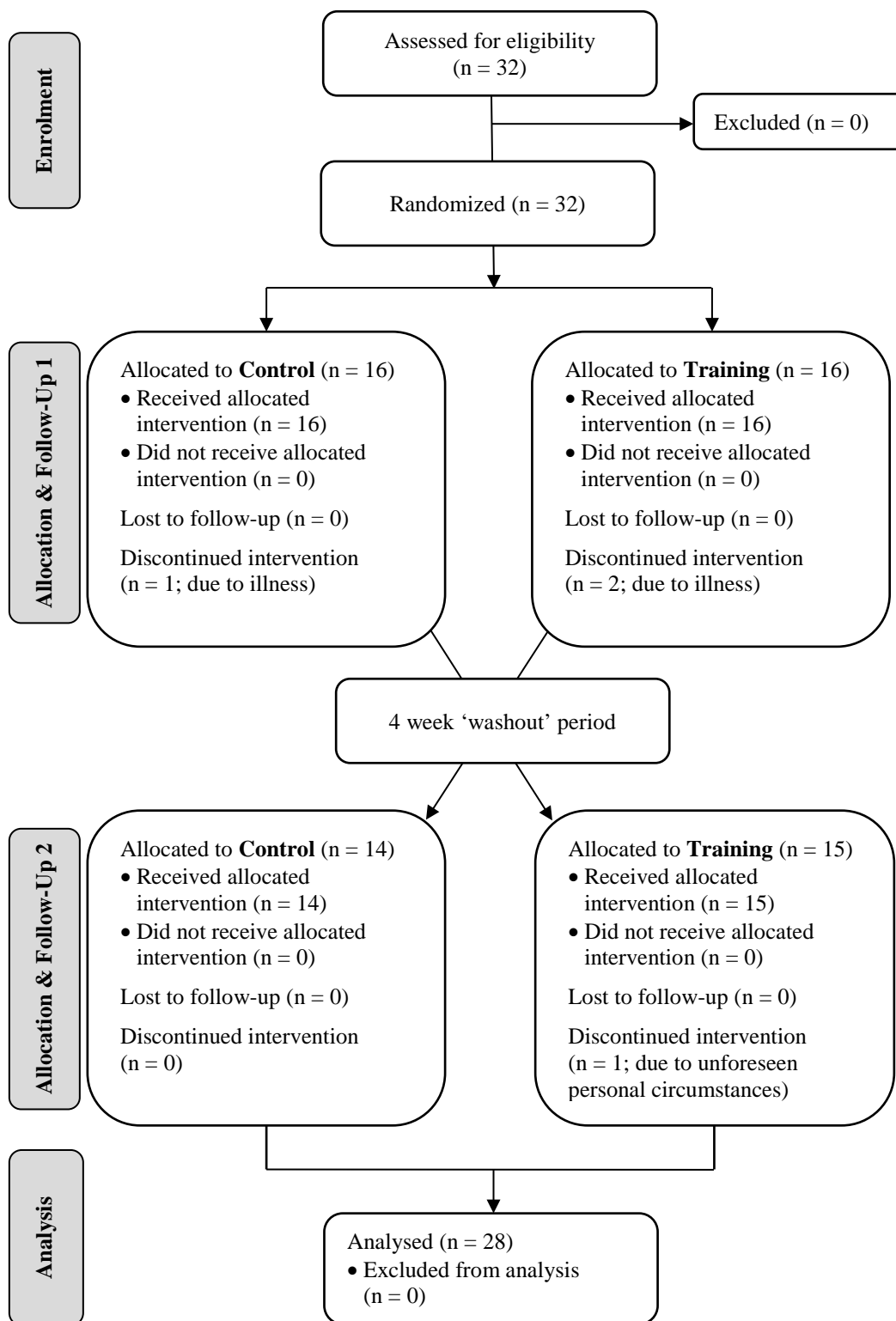
The participant sample size for this study was estimated using the equation,  $n = 16 (s^2/d^2)$  outlined by Hopkins (2001), as described in section 2.3.3 (page 49). In order to calculate the sample size, data was needed regarding the likely changes that occur to BP after isometric training. Published data acquired from within this laboratory was used to ascertain the smallest worthwhile change value ( $d$ ). Wiles, Coleman and Swaine (2010) found significant reductions in resting BP values after 8 weeks of isometric double-leg extension training and no statistically significant changes in  $\dot{Q}$ , TPR, HR and SV. The change scores were expressed as a percentage of the mean baseline value ( $[\text{change}/\text{mean}]100$ ) to be input into the sample size equation (see Table 5.1). To ensure that comparable reliability data was input into the equation, the 8 week control data from the Wiles, Coleman and Swaine (2010) study was used to calculate the coefficient of variation (CV) ( $s$ ) for each of the variables (J.D. Wiles, personal communication, August 2010). This data can be seen in Table 5.1 along with the estimated number of participants required to be recruited for study 3 ( $n$ ).

**Table 5.1.** The previously published data (Wiles, Coleman and Swaine, 2010) used for study 3's sample size calculation and smallest detectable change based upon the methods of Hopkins (2001).

	Change post isometric training	Baseline value	$d$ (% of mean score)	$s$ = resting CV	$n$ = no. of participants = $16 (s^2/d^2)$
SBP (mmHg)	-5	122	-4.3%	4.6%	18
DBP (mmHg)	-3	69	-3.8%	4.0%	18
MAP (mmHg)	-3	89	-2.8%	3.5%	25
$\dot{Q}$ (L $\cdot$ min $^{-1}$ )	0.21	7.22	2.9%	5.5%	57
TPR (mmHg $\cdot$ mL $^{-1}\cdot$ min $^{-1}$ )	-0.69	12.56	-5.5%	8.1%	35
HR (beats $\cdot$ min $^{-1}$ )	-3	71	-3.7%	9.6%	105
SV (mL)	7.33	103.52	7.1%	10.3%	34

The main focus of this study was the primary measure of BP pre- and post-isometric wall squat training and pre- and post-control. Thus taking into consideration the findings of previous research (Wiles, Coleman and Swaine, 2010), at least 25 participants were recruited based on the sample size estimation for SBP, DBP and MAP, as displayed in Table 5.1. While this number is below the estimated sample size

for the secondary variables  $\dot{Q}$ , TPR, HR and SV, these parameters were still measured in order to gain an insight into the potential mechanisms that regulate BP changes. Furthermore, it is important to note that the sample size selected for the current study ( $n = 25$ ) exceeds that used by the majority of previous IET studies ( $n \leq 17$ ) that have explored potential BP control mechanisms (Wiley et al., 1992; Ray and Carrasco, 2000; Taylor et al., 2003; McGowan et al., 2006; Peters et al., 2006; McGowan et al., 2007a; 2007b; Devereux, Wiles and Swaine, 2010b; Wiles, Coleman and Swaine, 2010; Baross, Wiles and Swaine, 2012; Stiller-Moldovan, Kenno and McGowan, 2012; Badrov et al., 2013a; 2013b; Millar et al., 2013a). In order to account for potential participant dropout, thirty-two participants were initially recruited. However, four participants discontinued an intervention due to either illness or unforeseen personal circumstances and therefore twenty-eight participants completed study 3 in total, as seen in Figure 5.1.



**Figure 5.1.** CONSORT diagram showing the participant numbers for study 3 during enrolment, allocation, follow-up, and analysis.



### 5.2.3 Equipment

#### *Laboratory-based testing equipment*

*Blood pressure:* All BP parameters (SBP, DBP and MAP) were measured during rest and exercise. Systolic and diastolic BPs were measured using a non-invasive hemodynamic monitor (Finometer, model 1, Finapres Medical Systems BV, Amsterdam, The Netherlands). The Finometer SBP and DBP data were interfaced with a Windows PC using an analog I/O box (Finapres Medical Systems BV, Amsterdam, The Netherlands) and a 16 channel data acquisition system (PowerLab/16SP, ML795, ADInstruments Pty Ltd, Castle Hill, Australia). The Finometer SBP and DBP data were then continuously displayed on a computer using LabChart Pro software (version 7.1, ADInstruments Pty Ltd, Castle Hill, Australia). Mean arterial pressure was also displayed on LabChart and was calculated instantaneously using the Finometer SBP and DBP data, which was input into the MAP equation. For further details see section 2.5.6 (page 59).

*Heart rate:* Heart rate was recorded during rest and exercise via ECG using a 16 channel data acquisition system (PowerLab/16SP, ML795, ADInstruments Pty Ltd, Castle Hill, Australia) and was continuously displayed on a computer using LabChart Pro software (version 7.1, ADInstruments Pty Ltd, Castle Hill, Australia). Participants were fitted with three single patient use ECG electrodes (Ambu® Blue Sensor R, Ambu A/S, Ballerup, Denmark), which were placed in a standard three-lead bipolar ECG arrangement. For further details see section 2.6.2 (page 64).

*Cardiac output:* Resting  $\dot{Q}$  was also measured using a non-invasive hemodynamic monitor (Finometer, model 1, Finapres Medical Systems BV, Amsterdam, The Netherlands) and continuously displayed on a computer using LabChart Pro software (version 7.1, ADInstruments Pty Ltd, Castle Hill, Australia). For further details see section 2.7.3 (page 75).

*Total peripheral resistance:* Resting TPR was estimated offline using the MAP and  $\dot{Q}$  data, which was entered into the TPR equation. For further details see sections 2.8.2 (page 77).

*Stroke volume:* Resting SV was estimated offline using the  $\dot{Q}$  and HR data, which was input into the SV equation. For further details see sections 2.9.2 (page 78).

*Wall squat knee joint angle:* Knee joint angle was measured during exercise using a clinical goniometer (MIE Clinical Goniometer, MIE Medical Research Ltd., Leeds, U.K.). For further details see section 2.10.2 (page 79).

*Rate of perceived discomfort:* The Borg CR10 scale was used to measure and rate discomfort specifically felt in the participant's upper legs during exercise in the laboratory and at home. For further details see section 2.11.2 (page 89).

#### *Home-based testing equipment*

*Heart rate:* During home-based exercise HR was measured with a HRM, which consisted of a Polar RS400 Computer (Polar RS400, Polar Electro Oy, Kempele, Finland) and a Polar WearLink transmitter (Wearlink V2, Polar Electro Oy, Kempele, Finland). For further details see section 2.6.4 (page 67).

*Wall squat knee joint angle:* During home-based testing the wall squat knee joint angle was set using the Bend and Squat device (made in-house, Department of Sport Science, Tourism and Leisure, Canterbury Christ Church University, Canterbury, United Kingdom). For further details see section 2.10.5 (page 83).

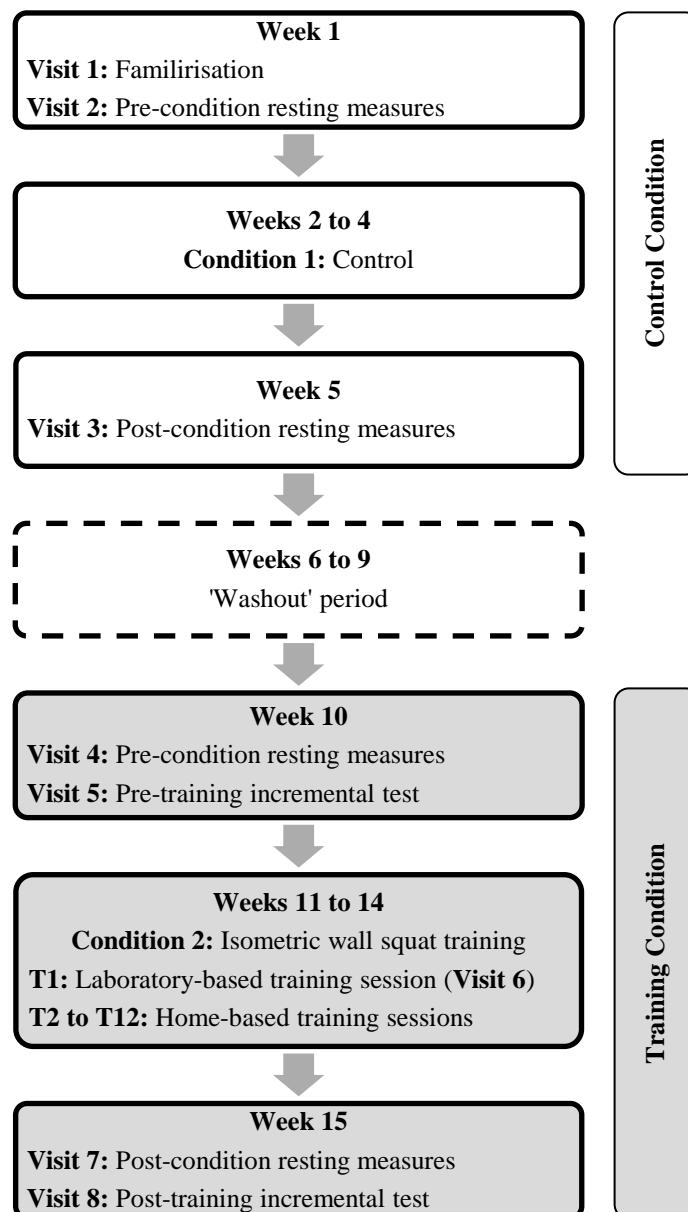
#### **5.2.4 Procedures**

##### *Familiarisation*

Prior to all data collection, participants were familiarised with the isometric wall squat exercise, the testing protocols and the measurement procedures, as outlined in section 2.3.5 (page 50). All participants adhered to the testing requirements, presented in section 2.3.4 (page 50), and this was verbally confirmed by the participants prior to the start of each testing session.

##### *Overall study design*

All participants were required to complete two conditions in a randomised crossover study design. Each participant acted as their own control group (condition one) and received a 4 week isometric training intervention (condition two). Random allocation determined the order in which participants received each treatment. Resting measures were taken pre- and post- both conditions. A four week 'washout' period was given between conditions during which time no treatment was appointed. Devereux (2010a) found that any evident reductions in BP following 4 weeks of IET at 95%HR<sub>peak</sub> were reversed to pre-training values within 7 days of detraining. Thus, it is suggested that the four week 'washout' period utilised in this study was more than adequate to diminish any residual effects from the previous treatment. A schematic of the overall design is presented in Figure 5.2. It can be seen that participants were required to make a total of 8 separate visits to the laboratory over a 15 week period.



**Figure 5.2.** Schematic illustration of study 3's overall design assuming the control condition was randomly selected first.

#### *Control condition*

During the control period participants were required to maintain their normal daily routine for a 4 week period. Participants were asked to refrain from any form of exercise they did not habitually perform. During this period of time participants did not visit the laboratory as no measures were taken. Pre- and post-control resting measures (BP,  $\dot{Q}$ , TPR, HR and SV) were taken in the laboratory.

#### *Training condition*

Before training participants were required to visit the laboratory twice for baseline resting measures (BP,  $\dot{Q}$ , TPR, HR and SV) to be taken and to complete an initial incremental test to determine the isometric training intensity. Participants then embarked on a four week home-based isometric wall squat training programme. All participants completed the first training session (T1) in the laboratory and after this time

all training sessions (T2 to T12) were home-based. Following this, participants visited the laboratory for post-training resting measures (BP,  $\dot{Q}$ , TPR, HR and SV). These measures were taken at least 72 hours after the participants final training session (Wiles, 2008a), due to the fact acute hypotension has been shown to persist for approximately up to 12 hours post exercise (Kenney and Seals, 1993). During a subsequent laboratory visit a post-training incremental test was completed.

#### *Resting measures*

Resting cardiovascular measures were taken before and after each condition and also at the start of all other laboratory visits. Upon arrival to the laboratory, participants rested in a seated position for 15 minutes. After an initial 10 minute period (Pickering et al., 2005), SBP, DBP and  $\dot{Q}$  were measured continuously for 5 minutes using the Finometer (Iellamo et al., 1994) with HR measured simultaneously via ECG. After this time, the mean SBP, DBP, MAP,  $\dot{Q}$ , TPR, HR and SV were calculated offline for the 5 minute period.

#### *Pre- and post-training incremental test protocol*

The incremental protocol used in this study was based upon the original work of Wiles et al. (2008b) in which an incremental isometric test was designed to determine training intensity for isometric double-leg extension exercise training. For the incremental isometric wall squat test in this study, participants were required to perform several isometric wall squat exercises in stages of increasing intensity, which was adjusted by manipulating the knee joint angle. The first stage began at 135° of knee flexion and participants were instructed to hold this position for 2 minutes. Once each stage was complete the knee joint angle was decreased by 10° as follows; 135°, 125°, 115°, 105°, to 95°. The exercise intensity was increased every 2 minutes until the participant reached the end of 95° stage to maximum, until the participant could no longer maintain the knee joint angle within 5° of the target value or to the point of volitional fatigue. The test was continuous so there was no rest between the incremental stages. Participants were given verbal instructions to ensure that each wall squat was held at the correct exercise position and also to ensure the proper timing of each incremental stage. Participants were asked to give their RPD at the end of each incremental stage and also upon cessation of the incremental test, which provided subjective evidence that the test had been completed to maximum.

Heart rate and BP were recorded continuously throughout the incremental test. For analysis, the mean for last 5 seconds of each 30 second period were calculated offline, as well as the mean for the last 30 seconds of each incremental stage. All isometric wall squat exercises were performed using the same technique as outlined in section 3.2.4 (page 95). Also, the position of the participant's feet and back positions were recorded for each incremental stage using a standard metre rule to the nearest centimetre. The feet position was measured as the direct distance from the back of the left heel to the wall (see Figure 2.15, page 87). The back position was measured as the direct distance from the ground to the lower back, which was defined as the last point of contact that the participant's back had with the wall (see Figure 2.15, page 87).

### *Prescribing the isometric wall squat training intensity*

The training protocol used in this study was based upon the procedure devised by Wiles, Coleman and Swaine (2010) and then utilised by Devereux, Wiles and Swaine (2010b) for isometric double-leg extension training. Using the participant's data from the initial pre-training incremental test, knee joint angle was plotted against the mean HR for the last 30 seconds of each incremental stage. This was possible as study 2 found that a 'steady-state' response was achieved during the last 30 seconds of each incremental work stage (section 4.3.2, page 115). The inverse curvilinear relationship produced was then used to calculate the participant-specific knee joint angle required to elicit a target HR. The target HR selected for training was 95%  $HR_{peak}$  as utilised by Devereux, Wiles and Swaine (2010b) and Wiles, Coleman and Swaine (2010). In the current study  $HR_{peak}$  was defined as the mean HR of the last 30 seconds achieved during the incremental test.

Further to this, each participant's individual THRR was calculated using the modified limits of agreement equation: target HR + bias  $\pm$  2.77 x CV (Hopkins, 2000). The reliability data (CV) of the  $HR_{peak}$  attained for repeated incremental tests in study 2 was utilised (INC1 vs. INC2; see section 4.3.2, page 115) and expressed in beats per minute related to each participant's individual target HR (CV[individual target HR/100] ) to input into the THRR equation. The bias value entered was the mean difference in the  $HR_{peak}$  values attained between repeated tests in study 2 (INC1 vs. INC2; see section 4.3.2, page 115). The  $HR_{peak}$  was utilised for the CV and bias values as the target HR was derived from this parameter.

### *Isometric wall squat exercise training*

Participants completed a 4 week home-based isometric wall squat training programme. Training was completed 3 days a week for 4 successive weeks (12 sessions in total) with at least 48 hours between training sessions. The first session was completed under supervision in the laboratory to allocate training equipment and also explain and demonstrate the training protocol to be followed. All training sessions thereafter were completed in a location of the participant's choice. Each training session was composed of four 2 minute bouts of isometric wall squat exercise with 2 minutes seated rest between bouts. All training sessions were completed at a participant-specific knee joint angle prescribed from the pre-training incremental test, relative to an individualised target HR (95%  $HR_{peak}$ ). The knee joint angle was set using the Bend and Squat device, as it was not deemed practical for a participant to measure knee joint angle with a goniometer whilst training unsupervised at home, as previously discussed in section 2.10.5, page 83).

Heart rate was recorded by the participants continuously throughout each training session using a HRM. Participants were asked to make a record of the last HR value attained for the four exercise bouts. This HR value was selected as study 2 previously found that HR reached a 'steady-state' during the last 30 seconds of exercise and also because this value was shown to more accurately reflect the prescribed target HR compared to the mean of the whole 2 minute bout (see section 4.3.3, page 119). This data was then communicated to the investigator after each training session. If the mean HR of the four exercise bouts deviated from the THRR for two consecutive sessions this indicated that the participant was training at a suboptimal intensity. Therefore the knee joint angle, and consequently training intensity, was altered by the investigator. When necessary this small adjustment was based upon the participant's HR and knee

joint angle curvilinear relationship established from the pre-training incremental test (see section 5.3.1, page 143) from which the change in knee joint angle required to correct the training HR discrepancy was interpolated. Accordingly, new settings for the Bend and Squat device's 'floor' and 'wall' arms were calculated from the linear relationships produced during the pre-training incremental test between knee joint angle and the participant's feet and back positions. The new measurements were subsequently communicated to the participant, who adjusted the Bend and Squat device accordingly. Following this adjustment, if the mean HR was still below the THRR during the next training session this indicated that the participant was still working at a suboptimal intensity. As a result, the participant completed an additional incremental test in the laboratory to re-determine their curvilinear relationship between HR and knee joint angle, from which the knee joint angle was re-prescribed and the intensity was increased; this was the case for six participants. It is important to note that in all 6 cases, the training HR had been below the required THRR, rather than above. Therefore while the participants previous training sessions may have been deemed suboptimal for BP adaptations to occur, the participants were still working at a safe level of cardiovascular stress.

The HR data were downloaded from the HRMs by the investigator at the end of each week. The mean HR for last 5 seconds of each 30 second period was calculated offline, as well as the mean HR for the last 30 seconds of each exercise bout. Further to this, participants also recorded their RPD at the end of each exercise bout to measure how hard the participants felt they were working, which was also communicated to the investigator after each session. This provided an additional subjective means of monitoring safe levels of physical exertion. A 'breathe' sign was given to all participants to place in front of them whilst training (see Appendix 8, page 242). This was to prompt the participants to keep a normal steady breathing pattern when exercising at home in order to avoid the Valsalva manoeuvre, which has been associated with extreme elevations in BP during some forms of resistance training (MacDougall et al., 1985).

#### *Initial laboratory-based training session*

During the first laboratory-based training session participants were assigned a Bend and Squat device and HRM. Participants also received a 'Training Manual' (see Appendix 8, pages 231-244), which detailed the training protocol to be followed and contained instructions for equipment (Bend and Squat device and HRM) and procedures (isometric wall squat exercise and sending data), as well as an RPD Borg CR10 scale and a 'breathe' sign. The training manual also contained a data sheet for HR and RPD to be recorded by the participant, a suggested training session timetable and an outline of the pre-training session requirements. Finally, a disclaimer was also included that advised the participant what to do and who to contact in the unlikely event of an adverse reaction occurring during a home-based exercise session (e.g. severe or unusual shortness of breath, dizziness, chest pain/discomfort).

During the initial session, participants completed three brief isometric wall squat exercises at their prescribed target knee joint angle, which was determined by the goniometer. Each wall squat was held for a maximum period of 10 seconds with a 30 second rest period between each exercise. During the 10 second period, the position of the participant's feet and back positions were recorded using a standard metre rule, as detailed in section 2.10.4b (page 81). The mean of the three feet and back measurements were calculated and the correct size Bend and Squat device was assigned to the participant; see section

2.10.6d (page 87) for available Bend and Squat sizes. The Bend and Squat device's 'floor' and 'wall' arms were adjusted based on the participant's mean feet and back measurements. Participants then completed one further 10 second isometric wall squat exercise using the Bend and Squat device to ensure that the actual knee joint angle matched the prescribed target. If the measured knee joint angle deviated by more than 3° then the Bend and Squat device was adjusted accordingly.

Once the Bend and Squat device was setup correctly, the first training session was completed. This initial training session was led by the participant and, if necessary, verbal instructions were given by the investigator relating to the timing of the exercise bouts and rest periods. All training sessions thereafter were completed in a location of the participant's choice. Participants were strongly encouraged to contact the investigator if they were unsure of the procedure at any stage.

### **5.2.5 Data analysis**

Before analysis, all data were checked for conformity with the parametric assumptions (Field, 2009). Where the parametric assumptions were met, a factorial repeated measures ANOVA was carried out on the incremental test (pre- and post-training) to explore the possible differences in the HR values over time. The LSD *post-hoc* test was used to explore any significant differences detected. Where data were not normally distributed, it was transformed and analysed in the same manner as study 1 (section 3.2.5, page 97). Data analysis was performed with IBM SPSS (BM SPSS Statistics for Windows, version 19.0, Armonk, NY: IBM Corporation).

The curvilinear relationships between knee joint angle and HR were explored through a one-phase exponential decay model using GraphPad Prism (GraphPad Prism version 5.01 for Windows, GraphPad Software, San Diego, CA). If the analysis was reported as being 'interrupted' then a linear relationship was considered to be a better fit, which was then explored using Pearson's product-moment correlation coefficient with Microsoft Excel software (Microsoft Excel 10, Microsoft Corporation, Redmond, WA). The linear relationships between knee joint angle and both the feet and back position were also explored using Pearson's product-moment correlation coefficient.

A factorial repeated measures ANOVA was also carried out, as detailed above, on the training session data to explore the possible differences in the HR values between training sessions (T1 to T12). Furthermore, the time in the THRR between the first two (T1 and T2) and final two training sessions (T11 and T12) were explored using a paired T-Test, which was carried out using Microsoft Excel software (Microsoft Excel 10, Microsoft Corporation, Redmond, WA). If normal distribution was not achieved, the non-parametric Wilcoxon signed ranks test was utilised. This analysis was also completed on the pre-and post-training value comparisons. Also, the non-parametric RPD training session data (T1 vs. T12) and incremental data (pre vs. post) was analysed using the non-parametric Wilcoxon signed ranks test.

An analysis of covariance (ANCOVA) was used with resting BP values as covariates to assess whether resting BP (SBP, DBP, MAP) changes following both the control and training conditions were influenced by the initial resting BP values, as previously found (Millar et al., 2007). For all other variables ( $\dot{Q}$ , TPR, HR and SV) differences in the change scores between the control and training data were assessed using a paired sample T-Test where data met the parametric assumptions; a Wilcoxon signed ranks test was used

when the data was non-parametric. Further to this, the clinical significance of the resting SBP and DBP reductions were determined by calculating the percentage of participants that achieved a BP reduction equal or greater than the minimal clinically important difference (MCID). The MCID was identified using an anchor-based approach (Fethney, 2010) and a 2 mmHg reduction was selected as the MCID based on the estimated reductions in risk for cardiovascular morbidity and mortality reported by Neaton et al. (1995 cited in Stamler, 1997) and Cook et al. (1995) for SBP and DBP, respectively. Within-participant variation, expressed as a coefficient of variation (CV), was calculated for all cardiovascular variables (SBP, DBP, MAP,  $\dot{Q}$ , TPR, HR and SV) at rest for the control group. The CV was derived by log-transformed two-way ANOVA as described by Atkinson and Nevill (2001), together with the 95% confidence intervals (CI) for a normal distribution (Tate and Klett, 1959).

For all tests, an alpha level of  $< 0.05$  was set as the threshold for statistical significance. All data are expressed as mean  $\pm$  standard deviation, unless otherwise indicated.

## 5.3 Results

### 5.3.1 Pre-training incremental test data

Of the twenty-eight pre-training incremental tests completed, six were fully completed. The mean final incremental stage reached but not completed was stage 4, the mean stage fully completed was 4 and the mean duration of the test was 8 minutes 21 seconds  $\pm$  70 seconds. Further to this the maximum RPD value attained during the pre-training incremental test was 10, which was attained during the final incremental stage reached for all participants.

It was important that HR reached a 'steady-state' during each stage of the incremental test (Wiles et al. 2008b) and this was found to occur during the last 30 seconds in study 2 (see section 4.3.2, page 115). Thus, the mean HR data collected during the pre-training incremental test for each 30 second time period were examined. This data was analysed only for those participants who fully completed the pre-training incremental test. It was found that there were no significant differences in the mean HR data when compared over time for the mean incremental data ( $P = 0.49$ ). Therefore all further data analysis on the incremental HR was assessed utilising the mean HR of the last 30 seconds, as in study 2 (section 4.3.2, page 115) as it appears that a 'steady-state' had been reached.

The mean HR data produced a significant inverse curvilinear relationship with wall squat knee joint angle during the pre-training incremental test ( $r$  value =  $-1.00$ ;  $P < 0.05$ ). When each individual HR and knee joint angle relationship was analysed it was found that the  $r$  values ranged from  $-0.96$  to  $-1.00$  ( $P < 0.05$ ). Of the twenty-eight pre-training incremental tests completed, seven produced a curvilinear relationship that was termed 'ambiguous' by GraphPad and two produced an 'interrupted' analysis, in which case a linear relationship was a better fit and thus used for analysis.

The mean  $HR_{peak}$  attained during the pre-training incremental test was  $122 \pm 19$  beats $\cdot$ min $^{-1}$ . Each participant's target HR (95%  $HR_{peak}$ ) was calculated from their individual  $HR_{peak}$ . The mean target HR for training was  $116 \pm 18$  beats $\cdot$ min $^{-1}$  and based on this a THRR was calculated; mean THRR was  $94 \pm 15$  beats $\cdot$ min $^{-1}$  to  $135 \pm 22$  beats $\cdot$ min $^{-1}$ . From the inverse curvilinear relationship produced between HR and



knee joint angle, the target knee joint angle for training was calculated based on the prescribed target HR. The mean training knee joint angle was  $105 \pm 6^\circ$ .

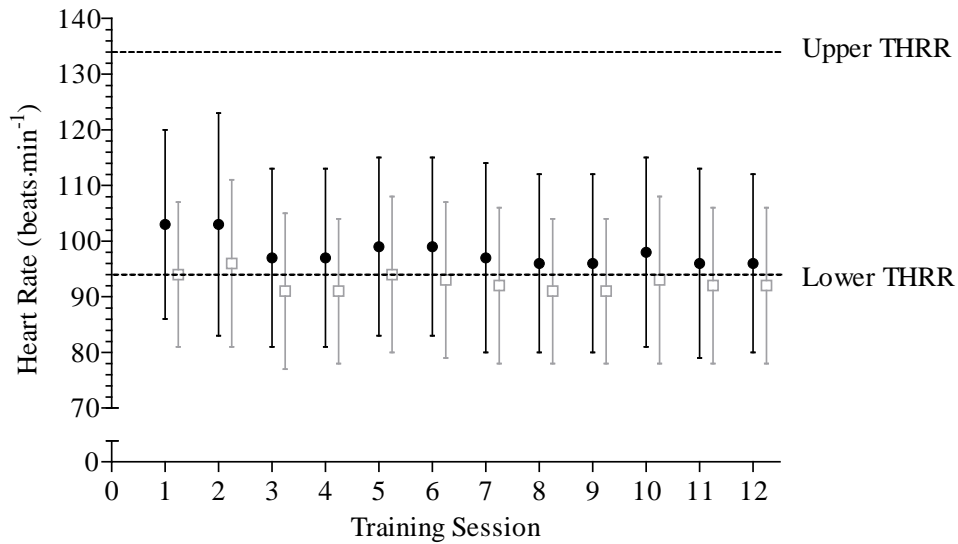
Furthermore, knee joint angle and the mean feet position data produced a significant inverse linear relationship ( $r = -1.00$ ;  $P < 0.05$ ) during the pre-training incremental test. When each participant's individual inverse linear relationship between wall squat knee joint angle and feet position was examined it was found that  $r$  ranged from  $-0.97$  to  $-1.00$  ( $P < 0.05$ ). Also, wall squat knee joint angle produced a significant linear relationship with the mean back position data ( $r = 0.99$ ;  $P < 0.05$ ). When each participant's individual linear relationship between wall squat knee joint angle and back position was examined it was found that  $r$  ranged from  $0.96$  to  $1.00$  ( $P < 0.05$ ).

### **5.3.2 Weekly training data**

All participants fully completed all of the isometric wall squat exercise training and control sessions. Of the 336 training sessions completed in total (28 participants completed 12 training sessions each), HR data was missing for 11 sessions due to participant issues with the HRMs. The training sessions were still completed on these occasions as verbally confirmed by the participants. However, analysis of the training data was completed for those 23 participants who had a full data set for all 12 training sessions.

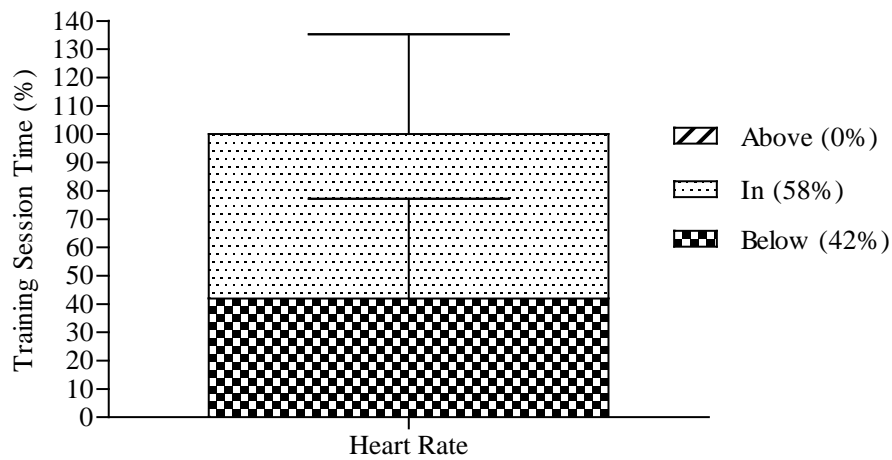
For all 12 training sessions, the mean HR was  $93 \pm 13$  beats·min<sup>-1</sup> for the whole training session data (mean of all four exercise bouts) and  $98 \pm 16$  beats·min<sup>-1</sup> for the last 30 seconds of each training session (mean of the last 30 seconds of all four exercise bouts). On comparing the actual HR values achieved during training and the expected target HR, it was found that there were significant differences ( $P < 0.001$ ) for both the whole training session data ( $-23 \pm 17$  beats·min<sup>-1</sup>) and for the last 30 seconds of training data ( $-17 \pm 16$  beats·min<sup>-1</sup>). When the HR values were compared between the 12 training sessions (T1 to T12) it was found that there were no significant differences for the whole training session data ( $P = 0.053$ ), however HR was significantly different for the last 30 seconds of training ( $P = 0.002$ ). The last 30 seconds HR data significantly decreased from T1 ( $103 \pm 17$  beats·min<sup>-1</sup>) to T7 ( $97 \pm 17$  beats·min<sup>-1</sup>) ( $P = 0.02$ ), however, there were no significant differences in any of the comparisons from T7 to T12 ( $96 \pm 16$  beats·min<sup>-1</sup>) ( $P \geq 0.198$ ). The success to which the participants maintained their HR within the target range over the 12 training sessions is demonstrated in Figure 5.3.

Further to this, there was a trend for the mean RPD to decrease over the training sessions from T1 (6.4) to T12 (5.0) ( $P < 0.001$ ).



**Figure 5.3.** The variation around the target heart rate range for each of the 12 training sessions for the mean of the last 30 seconds (●) and mean of the whole training session (□) for all 4 exercise bouts.

The amount of time each participant spent within their individual THRR during all training sessions was calculated. Figure 5.4 illustrates the mean percentage of time spent below, in and above the target ranges for HR during a whole training session (mean of all training sessions).



**Figure 5.4.** The mean percentage of time spent below, in and above the target heart rate range during a whole training session (mean data of all training sessions).

When the time spent below, in and above the THRR during the whole training session was compared between the first two and the final two training sessions (mean T1 and T2 vs. mean T11 and T12) it was found that there were no significant differences (see Table 5.2).

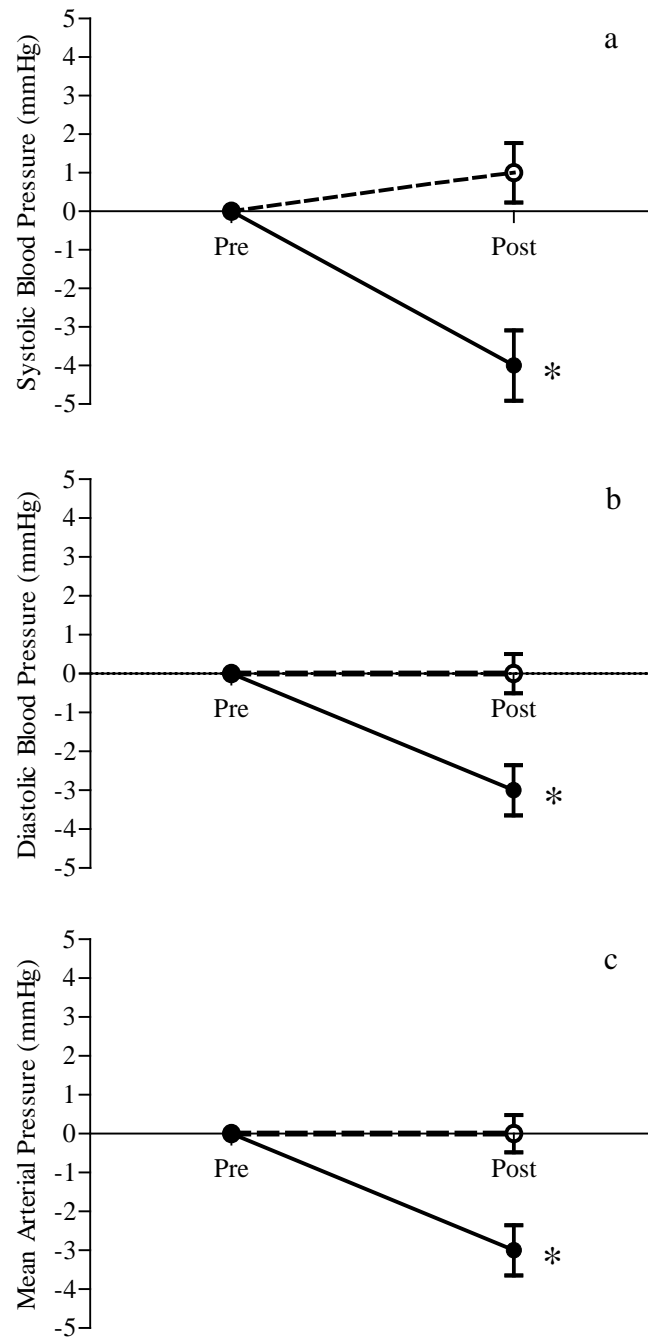
**Table 5.2.** The mean percentage of time spent below, in and above the target heart rate range at the start of training (mean T1 and T2) compared to the end of training (mean T11 and T12).

Variable	Time Spent	T1 and T2	T11 and T12	Significance
HR	Below	40 ± 33%	46 ± 33%	<i>P</i> = 0.13
	In	59 ± 33%	54 ± 33%	<i>P</i> = 0.12
	Above	1 ± 2%	0 ± 1%	<i>P</i> = 0.46

### 5.3.3 Training adaptations

#### *Resting blood pressure*

Four weeks of isometric wall squat exercise training resulted in a significant reduction in resting SBP ( $-4 \pm 5$  mmHg) compared to the control group ( $1 \pm 4$  mmHg) ( $P < 0.001$ ) as seen in Figure 5.5a. Of the 28 participants, 19 (68%) experienced a clinically relevant reduction ( $\geq 2$  mmHg) in SBP (Neaton et al., 1995 cited in Stamler, 1997). Diastolic BP also significantly reduced at rest pre- to post-training ( $-3 \pm 3$  mmHg) compared to the control group ( $0 \pm 3$  mmHg) ( $P < 0.001$ ) as seen in Figure 5.5b. Of the 28 participants, 20 (71%) experienced a clinically relevant reduction ( $\geq 2$  mmHg) in DBP (Cook et al., 1995). Finally, resting MAP decreased significantly following training ( $-3 \pm 3$  mmHg) compared to the control group ( $0 \pm 3$  mmHg) ( $P < 0.001$ ) as seen in Figure 5.5c.



**Figure 5.5.** The mean systolic (a), diastolic (b) and mean arterial (c) pressure change values at rest for the control (—○—) and training (—●—) conditions. Error bars indicate standard error of the mean.

\* = significant ( $P < 0.05$ ) difference in the control and training change value.

Table 5.3 demonstrates mean values for the BP parameters before and after both the control and training experimental conditions.

**Table 5.3.** Mean values for resting systolic (SBP), diastolic (DBP) and mean arterial (MAP) pressure before and after the control and training conditions.

BP Parameter	Control		Training	
	Pre	Post	Pre	Post
SBP (mmHg)	125 ± 6	126 ± 7	127 ± 7	123 ± 8 *
DBP (mmHg)	78 ± 5	78 ± 5	79 ± 5	76 ± 6 *
MAP (mmHg)	94 ± 5	94 ± 6	95 ± 5	92 ± 6 *

\* = significant ( $P < 0.05$ ) difference in the pre to post change value between the control and training conditions.

The reliability of resting measures for the control group (CV with 95% CI) were 2.3% (1.8-3.2%) for SBP, 2.4% (1.9-3.3%) for DBP and 1.9% (1.5-2.6%) for MAP.

*Resting cardiac output, total peripheral resistance, heart rate and stroke volume*

After four weeks of isometric wall squat exercise training there was a significant reduction in  $\dot{Q}$  ( $-0.54 \pm 0.66 \text{ L}\cdot\text{min}^{-1}$ ) in comparison to the control group ( $-0.04 \pm 0.63 \text{ L}\cdot\text{min}^{-1}$ ) ( $P = 0.01$ ) and also a significant reduction in resting HR after training ( $-5 \pm 7 \text{ beats}\cdot\text{min}^{-1}$ ) compared to the control group data ( $-1 \pm 4 \text{ beats}\cdot\text{min}^{-1}$ ) ( $P = 0.01$ ). However, there was no significant change in resting TPR with training ( $1.10 \pm 2.15 \text{ mmHg}\cdot\text{mL}^{-1}\cdot\text{min}^{-1}$ ) compared to the control data ( $-0.06 \pm 1.90 \text{ mmHg}\cdot\text{mL}^{-1}\cdot\text{min}^{-1}$ ) ( $P = 0.06$ ) and also no significant change in resting SV following training ( $-1.58 \pm 9.95 \text{ mL}$ ) compared to the control group ( $1.52 \pm 9.96 \text{ mL}$ ) ( $P = 0.19$ ). Table 5.4 demonstrates mean values for  $\dot{Q}$ , TPR, HR and SV before and after both experimental conditions.

**Table 5.4.** The mean values for resting cardiac output ( $\dot{Q}$ ), heart rate (HR), total peripheral resistance (TPR), and stroke volume (SV) before and after the control and training conditions.

Variable	Control		Training	
	Pre	Post	Pre	Post
$\dot{Q}$ ( $\text{L}\cdot\text{min}^{-1}$ )	5.66 ± 1.06	5.62 ± 0.94	5.81 ± 1.01	5.27 ± 0.86 *
TPR ( $\text{mmHg}\cdot\text{mL}^{-1}\cdot\text{min}^{-1}$ )	17.23 ± 3.65	17.17 ± 2.79	16.83 ± 2.87	17.94 ± 3.00
HR ( $\text{beats}\cdot\text{min}^{-1}$ )	64 ± 9	63 ± 9	65 ± 9	60 ± 9 *
SV (mL)	88.47 ± 12.00	89.99 ± 14.16	90.36 ± 13.61	88.79 ± 9.61

\* = significant ( $P < 0.05$ ) difference in the pre to post change value between the control and training conditions.

The reliability of resting measures for the control group (CV with 95% CI) were 7.9% (6.3-10.8%) for  $\dot{Q}$ , 8.0% (6.4-11.0%) for TPR, 4.7% (3.7-6.4%) for HR and 7.9% (6.3-10.8%) for SV.

### 5.3.4 Post-training incremental test data

Of the twenty-eight post-training incremental tests completed, nine were fully completed. The mean final incremental stage reached but not completed was stage 5 (not statistically significant from the pre-training test;  $P = 0.10$ ), the mean stage fully completed was 4 (not statistically significant from the pre-training test;  $P = 0.10$ ) and the mean duration of the test was 8 minutes 48 seconds  $\pm$  70 seconds, which was statistically significant compared to the pre-training test ( $P = 0.002$ ). Further to this the maximum RPD value attained during the post-training incremental test was 9 (statistically significant from the pre-training test;  $P = 0.02$ ), which was attained during the final incremental stage reached for all participants.

The mean HR data collected for each 30 second time period were examined for those participants who fully completed the post-training incremental test to analyse whether HR had reached a ‘steady-state’ (Wiles et al. 2008b). It was found that there were no significant differences in the mean HR data when compared over time for the mean incremental data ( $P = 0.656$ ). Therefore all further data analysis on the incremental data for HR was assessed utilising the mean of the last 30 seconds as it appears that a ‘steady-state’ had been reached.

The mean HR data produced a significant inverse curvilinear relationship with wall squat knee joint angle during the post-training incremental test ( $r$  value =  $-0.93$ ;  $P < 0.05$ ). When each participant’s individual HR and knee joint angle relationship was analysed it was found that the  $r$  values ranged from  $-0.89$  to  $-1.00$  ( $P < 0.05$ ). Of the twenty-eight pre-training incremental tests completed, four produced a curvilinear relationship that was termed ‘ambiguous’ by GraphPad and three produced an ‘interrupted’ analysis, in which case a linear relationship was a better fit and thus used for analysis.

The mean target HR and range and mean target knee joint angle produced from the post-training incremental test are displayed in Table 5.5. Compared to the pre-training incremental test it can be seen that only target knee joint angle changed significantly.

**Table 5.5.** The mean values for the training targets and ranges calculated from the pre- and post-training incremental tests.

	Incremental Test		Significance
	Pre-training	Post-training	
HR <sub>peak</sub> (beats·min <sup>-1</sup> )	122 $\pm$ 19	119 $\pm$ 22	$P = 0.36$
Target HR (beats·min <sup>-1</sup> )	116 $\pm$ 18	113 $\pm$ 20	$P = 0.36$
HR range (beats·min <sup>-1</sup> )	94-135	91-131	
Target Knee Joint Angle (degrees)	105 $\pm$ 6	103 $\pm$ 6	$P = 0.008$ *

\* = significant ( $P < 0.05$ ) difference in the calculated pre- and post-training value.

None of the participants reported any adverse symptoms, such as shortness of breath, dizziness, chest pain, light-headedness, etc., during any of the incremental tests or training sessions.

## 5.4 Discussion

### 5.4.1 *The effects of four weeks home-based isometric wall squat training on resting blood pressure*

The main aim of this study was to determine whether four weeks of home-based constant position isometric wall squat exercise training could successfully lower resting BP. The results confirmed that this was the case as all three resting BP parameters produced statistically significant reductions (SBP: -4 mmHg; DBP: -3 mmHg; MAP: -3 mmHg;  $P < 0.05$ ), as presented in section 5.3.3 (page 146). These BP adaptations are similar to those previously reported following IET that was partly laboratory-based performing constant force contractions (McGowan et al., 2007a; Millar et al., 2013a) and completely laboratory-based completing constant EMG contractions (Devereux, Wiles and Swaine, 2010b; Wiles, Coleman and Swaine, 2010). Therefore the isometric wall squat training protocol utilised within this study appears to provide a viable alternative home-based method for the reduction of resting BP. This accessible and potentially cost effective training programme may help to improve isometric exercise's efficacy as a physical therapy for altering BP. Furthermore, this is only the second study to show reductions in all three BP components (SBP, DBP, MAP) following 4 weeks of isometric leg training; the first being completed by Devereux, Wiles and Swaine (2010b). It is suggested that these chronic BP adaptations occurred at a faster rate as IET was performed utilising a larger muscle mass at a higher intensity than used in other investigations (Baross, Wiles and Swaine, 2012), which may provide a greater cardiovascular training stimulus as previously discussed in sections 1.5.2 and 1.5.3 (pages 25 and 28, respectively). Indeed, Baross, Wiles and Swaine (2012) found resting BP reductions after 8 weeks of isometric double-leg extension training. Leg extensions isolate the quadriceps (Delavier, 2010) and may use a smaller muscle mass in comparison to the wall squat exercise, which utilises the quadriceps as well as additional muscle groups (Contreras, 2014). Furthermore, Baross, Wiles and Swaine (2012) also prescribed the IET intensity at 85%  $HR_{peak}$ , whereas the current study prescribed a higher intensity of 95%  $HR_{peak}$ . However, since this study used a unique constant position isometric contraction style, direct comparisons to previous research, such as constant EMG isometric exercise (Baross, Wiles and Swaine, 2012), are difficult.

It may be suggested that the reductions in resting BP found in the current study are quite modest compared to some previous research, where reductions as large as 19 mmHg for SBP (Taylor et al., 2003) and 15 mmHg for DBP (Wiley et al., 1992) have been reported. However, these studies utilised either high-normal or hypertensive participants who therefore had a higher initial BP level, which is thought to increase an individual's capacity for BP adaptations (Stiller-Moldovan, Kenno and McGowan, 2012; Badrov et al., 2013a). Furthermore, as hypertension can be caused by a variety of underlying pathophysiological factors (Beevers, Lip and O'Brien, 2001), such as endothelial dysfunction (Bian, Doursout and Murad, 2008), the mechanisms that govern a BP reduction in a hypertensive population are likely to be different to those experienced in normotensive individuals (Baross, Wiles and Swaine, 2012); this potential difference will be discussed further in section 5.4.3 (page 152).

#### ***5.4.2 The clinical significance of resting blood pressure reductions following isometric wall squat training***

While the reductions in resting BP found in the present study were statistically significant, the magnitude of these changes were quite modest compared to some previous IET research, as reported in the preceding section, and may not be practically relevant. Consequently, it is also important to consider the data's clinical significance (Brignardello-Petersen et al., 2013), such as the smallest change considered worthwhile to an individual (Copay et al., 2007), which is known as the minimal clinically important difference (MCID) (Page, 2014). There is limited data available to establish the MCID for resting BP reductions following IET, however two key papers reported the likely health implications associated with BP reductions. Indeed, Cook et al. (1995) estimated that a DBP reduction of 2 mmHg can reduce the risk of hypertension (17%), coronary heart disease (6%) and stroke (15%). Furthermore, Neaton et al. (1995 cited in Stamler, 1997) estimated that a 2 mmHg SBP reduction could lower CVD (5%) and all-cause (3%) mortality. In the present study, these MCIDs were attained by 68% of the participants for SBP and by 71% for DBP, as reported in section 5.3.3 (page 146). This finding is important considering that the main goal of any antihypertensive therapy is to ultimately lower cardiovascular related morbidity and mortality (Chobanian et al., 2003). Furthermore, these response rates are similar to those presented in the paper of Millar et al. (2013b), which reviewed the BP reductions from published and unpublished studies. It was estimated that a 2 mmHg reduction was attained in 60% to 90% of normotensive and unmedicated hypertensive individuals (Peters et al., 2006; McGowan et al., 2007a; Millar et al., 2008) and 50% to 83% of medicated hypertensive participants (McGowan et al., 2006; McGowan et al., 2007b; Millar et al., 2007; Stiller-Moldovan, Kenno and McGowan, 2012; Badrov et al., 2013b). Further to this, the literature also suggests that another important indicator of clinical significance is effect size, which is a standardised measure (Copay et al., 2007) and reflects the magnitude of change between groups (Page, 2014). The effect size statistics calculated for the intervention within this study indicates that the IET protocol prescribed had a large effect on SBP and DBP reductions ( $d = 1.10$  and  $1.00$ , SBP and DBP respectively), based on Cohen's (1988) criteria (large effect  $\geq 0.8$ ). This further strengthens the practical relevance of the BP reductions reported in the present study, as it has been previously suggested that larger effect sizes are more likely to be clinically useful (Jacobson and Truax, 1991).

While the studies by Cook et al. (1995) and Neaton et al. (1995 cited in Stamler, 1997) provide useful indications for the likely magnitude of SBP and DBP reductions that are clinically relevant, it is acknowledged that there are several limitations when applying this research to the current study. First of all, these studies investigated older populations. Indeed, Cook et al. (1995) studied white men and women aged 35 to 64 years and Neaton et al. (1995 cited in Stamler, 1997) studied white men aged 35 to 57 years, whereas the participants in the current study were younger males ( $30 \pm 7$  years). Secondly, and most importantly, the decreased risks of morbidity and mortality associated with a reduction in resting BP was not measured directly. The percentage reductions in the incidence of CHD and stroke reported by Cook et al. (1995) were only estimated based on a hypothetical population of 100,000 individuals achieving an average 2 mmHg DBP reduction. This limitation is also present within the work of Neaton et al. (1995 cited in Stamler 1997), which also estimated the favourable effects of lowering the population average SBP by 2 mmHg on mortality rates. Finally, it is also important to note that Neaton et al. (1995 cited in Stamler 1997) specifically estimated the incidence of CVD and all-cause mortality due to a



hypothetical reduction in SBP with a lower daily sodium intake, rather than a BP reduction due to IET. Therefore, due to these limitations, it would be beneficial to conduct a large scale study using the specific target population and directly explore the relationships between the resting BP reductions achieved through IET and the incidence of CVD and mortality risks.

It also acknowledged that a 2 mmHg reduction in SBP and DBP is rather small and could have occurred in some participants due to natural variation, rather than an adaptation produced from IET. This is highlighted by the fact that the SBP and DBP values for control group in this study varied by 2.3% (~3 mmHg) and 2.4% (~2 mmHg), respectively (see section 5.3.3, page 146). While this may be the case, the mean SBP reduction reported for the IET group was 4 mmHg and this magnitude of reduction was achieved by 61% of participants, which may be associated with an even greater reduction in the CVD (9%) and mortality (6%) risk factors (Neaton et al., 1995 cited in Stamler, 1997). Furthermore, an even greater reduction in resting SBP of 6 mmHg relates to a 13% and 9% decreased risk of CVD and all-cause mortality, respectively (Neaton et al., 1995 cited in Stamler, 1997), which is a SBP reduction level attained by 43% of participants in the current study. Therefore it can be concluded that isometric wall squat exercise training can reduce resting BP and potentially produce important clinical health benefits, which is the definitive goal of any antihypertensive therapy (Chobanian et al., 2003). Furthermore, not only does a reduction in BP lower the risk of BP related illnesses, it also lessens the need for pharmacological intervention and consequently the probability of experiencing undesirable deleterious side effects known to occur with this type of therapy (Millar et al., 2013b).

#### ***5.4.3 Possible mechanisms responsible for the reduction in resting blood pressure following 4 weeks home-based isometric wall squat exercise***

The data presented also offers some explanation for the underlying physiological mechanisms responsible for the BP adaptations after 4 weeks of isometric wall squat training. As MAP is determined by  $\dot{Q}$  and TPR (Hietanen, 1984), a reduction in BP must be due to alterations to either one or both of these variables (Wiley et al., 1992; Pescatello et al., 2004; Millar et al., 2013b). It was found that significant reduction in  $\dot{Q}$  was produced alongside a reduction in resting BP, with no significant change in TPR (see section 5.3.3, page 146). This finding is contrary to the suggestion that reductions in BP following IET are more likely owing to a decrease in TPR (Millar et al., 2013b). Furthermore, the few previous IET studies that have measured  $\dot{Q}$  and TPR pre- and post-IET found no significant alterations to either variable alongside reductions in resting BP (Devereux, Wiles and Swaine, 2010b; Wiles, Coleman and Swaine, 2010).

Further to this, HR also significantly reduced following isometric wall squat training and this was combined with no significant alteration in SV (see section 5.3.3, page 146). As  $\dot{Q}$  is mediated by HR and SV (Smith and Fernhall, 2011), it is therefore likely that the decrease in  $\dot{Q}$  experienced in the present study was due to a concomitant reduction in HR. Previous IET research has also reported either a significant reduction in HR (-7 to -5 beats·min<sup>-1</sup>; Devereux, Wiles and Swaine, 2010b; Baross, Wiles and Swaine, 2012) and/or no significant change in SV (-0.2 to 18.52 mL; Devereux, Wiles and Swaine, 2010b; Wiles, Coleman and Swaine, 2010).

A decrease in HR following IET is potentially attributable to a combination of alterations from the ANS, such as a decrease in sympathetic activity and an increase in parasympathetic activity (Fleck, 2003).

While some IET research has found ANS activity modifications when studying a hypertensive population (Taylor et al., 2003; Millar et al., 2013a), this has not been the case for those with normal BP (Wiles, Coleman and Swaine, 2010; Badrov et al., 2013a). However, these normotensive studies generally produced relatively modest BP reductions and it has been suggested that the spectral measures of HRV, as used by Wiles, Coleman and Swaine (2010), may not be sensitive enough to detect any small changes in neurocardiac modulation (Millar et al., 2013a). As ANS activity was not measured in the present study, only speculative insights can be offered based on the HR data presented and the findings of previous research. From these it is suggested that isometric wall squat training may elicit cardiac neural adaptations that reduce resting HR, and consequently  $\dot{Q}$ , to bring about a reduction in resting BP.

It is suggested that TPR did not change following training for two main reasons; firstly due to the normotensive population studied, which may limit the capacity for functional vascular adaptations (Green et al., 2004), and secondly, because of the potential time course required for both functional and structural vascular adaptations (Tinken et al., 2008; 2010). While research has suggested that IET may bring about functional vascular adaptations in hypertensive participants, such as improved endothelial function (McGowan et al., 2007b) and improved oxidative stress (Peters et al., 2006), functional endothelial adaptations have not been observed in normotensive populations following this type of training (McGowan et al., 2006), which is likely due to these individuals having an already normal vascular function (Green et al., 2004). While one study has found improvements in resistance vessel endothelial function following IET with normotensive participants, these changes occurred after 8 weeks and therefore the 4 week duration of the present study may not have been long enough to induce such vascular adaptations to ultimately reduce TPR. Further to this, potential structural vascular adaptations, such as increased artery diameter, are also suggested to occur after a longer period of IET, between 4 to 8 weeks (Baross, Wiles and Swaine, 2012). Thus, based upon the current study's data and the previous research presented it appears unlikely that a reduction in resting BP following isometric wall squat training is due to a reduction in TPR. However, the lack of statistically significant TPR reductions should be contextualised in the fact that much research has found that vascular training adaptations occur locally in the muscle rather than systemically (McGowan et al., 2007b; Badrov et al., 2013a). Therefore as the calculation of TPR utilised in this thesis reflects systemic vascular resistance (Boone, 2014), localised improvements in vascular function cannot be ruled out.

Finally, it is also important to note that whilst the sample size selected in the current study had enough statistical power to detect any training induced adaptations to the primary variables, resting BP (SBP, DBP and MAP), the secondary measures (resting  $\dot{Q}$ , TPR, HR and SV) were underpowered. A substantial number of participants would have been required to be recruited to be fully confident in the secondary variable results, such as 57 and 105 participants for  $\dot{Q}$  and HR, respectively (see section 5.2.2, page 133), which was not deemed practical in terms of time constraints or appropriate due to the ethical issues concerning resources (Hopkins, 2006). Therefore it is acknowledged that further research is required utilising a larger sample size in order to gain adequate statistical power to fully elucidate the BP control mechanisms.

#### ***5.4.4 Reviewing the home-based isometric wall squat training protocol for the reduction of resting blood pressure***

While the IET protocol prescribed in the present study produced a significant and clinically relevant reduction in resting BP, there are a number of potential limitations that need to be reviewed. The target HR and range calculated in this study (116 [94-135] beats·min<sup>-1</sup>) was very similar to that produced in study 2 of this thesis (118 [96-138] beats·min<sup>-1</sup>) as was the target knee joint angle prescribed (study 2: 104° vs. study 3: 105°). Despite this fact, the actual mean HR value attained during training in the current study was approximately 9 and 12 beats·min<sup>-1</sup> lower when compared to study 2 for both the whole training session data (study 2: 102 beats·min<sup>-1</sup> vs. study 3: 93 beats·min<sup>-1</sup>) and the last 30 seconds of training data (study 2: 110 beats·min<sup>-1</sup> vs. study 3: 98 beats·min<sup>-1</sup>). Consequently, the actual HR values attained during training were statistically lower than the prescribed target HR, such that the mean HR for the whole training session was 23 beats·min<sup>-1</sup> lower and the last 30 second data was 17 beats·min<sup>-1</sup> lower. This affected the time spent in the THRR, which appears to be reduced in the current study (58%) in comparison to study 2 (67%), with more time being spent below the target range (study 2: 32% vs. study 3: 42%).

There are several potential explanations for such differences in the HR data between the two studies. First of all, the wall squat training sessions in study 2 were completed in the laboratory under the guidance of an investigator, whereas the current study was home-based with the training sessions being completed unsupervised. Therefore any unintentional or fatigue related alterations to the exercise position caused by the participant might not have been fully corrected. Furthermore, participants must be well motivated to complete the wall squat training sessions due to the known discomfort that is associated with isometric exercise (Lind, 2011). Thus there is a possibility that participants could have consciously or subconsciously modified the exercise position in an attempt to ease this discomfort. Such alterations in the exercise position could have contributed to a decrease in the IET intensity. Further to this, the methods used to set the knee joint angle were different between the two studies, as outlined in section 5.2.4 (page 137), which could have led to errors in knee joint angle measurement. Study 2 utilised a goniometer in which the investigator directly measured the knee joint angle. Whereas study 3 utilised the Bend and Squat device, which uses the relationship between knee joint angle and both the feet and back positions to indirectly set the exercise position. While a preliminary study did find the Bend and Squat device to be valid, it is possible that some measurement error may have occurred during translation (see section 2.10.6, page 85), which could have led to a suboptimal exercise intensity being completed.

Further to this when participants re-completed the incremental test post-training, it was found that participants lasted for a significantly longer duration (27 seconds) compared to the pre-training test. While this did not produce any statistically significant difference to the target HR prescribed, it was calculated that a different target knee joint angle would be required to obtain the prescribed target HR (see Table 5.5, page 149). This suggests that participants would need to work at a higher intensity to obtain the desired target HR. This may offer a further explanation as to why there was a discrepancy between the target HR and actual value attained during training, as participants may have been working at a slightly suboptimal intensity. This may be reflected in the training RPD recorded, which showed a statistically significant decrease from weeks 1 to 4 (see section 5.3.2, page 144) suggesting that

participants may have found the training sessions progressively easier; although this was not reflected in the mean HR value or time spent in the training range which remained unchanged from weeks 1 to 4. Furthermore, while there was a statistically significant difference in the knee joint angle prescribed between the pre- and post-training incremental tests, this difference was minimal ( $2^\circ$ ) and may not be practically relevant due to the fact that study 1 found no difference in the acute cardiovascular response when the wall squat knee position was changed by  $5^\circ$  (see section 3.3.2, page 97).

Furthermore, it is also worth noting that there appears to have been a statistically significant decrease in the maximum RPD recorded during the post-training incremental test (pre: 10 vs. post: 9). This may suggest that some participants did not reach their maximum and could potentially have completed a further incremental stage, which was not possible utilising the current protocol. Indeed,  $90^\circ$  was selected as the fifth and final incremental stage due to the fact that it has been subjectively observed that performing wall squats beyond  $90^\circ$  may change the application of the back's support force, which has been shown to alter the relative contribution of the contracting muscles (Blanpied, 1999); see section 3.2.4 (page 95). Therefore, to keep the nature of the exercise consistent at all wall squat intensities, increasing intensity beyond the  $90^\circ$  stage would require an alternative adjustment method, such as performing weighted wall squats in which increased quadriceps activity would be required to maintain the exercise position. However, it is suggested that over complicating the procedure at this stage by trying to establish a new isometric training protocol is unnecessary. This is particularly pertinent as the intended target population (hypertensive older individuals) are probably less physically active than the participants in the current study and are therefore extremely unlikely to complete the whole incremental test as currently presented.

## **5.5 Conclusion**

The data presented in this chapter has shown that 4 weeks of home-based isometric wall squat training reduces resting SBP, DBP, and MAP in healthy normotensive males. Such an accessible and cost effective IET programme may help reduce some of the key barriers known to reduce exercise adherence and may provide a more effective lifestyle modification for the prevention of hypertension. Further to this, it is suggested that such chronic BP adaptations are unlikely to be due to a change in TPR as previously thought, but are instead mediated by a reduction in  $\dot{Q}$ , which is primarily governed by a decrease in resting HR.



## **CHAPTER 6: GENERAL DISCUSSION**

### **6.1 Executive summary of findings**

In this thesis, three studies were carried out to inform the development of a unique home-based isometric training protocol utilising the novel constant position wall squat exercise; the experimental data from these studies were presented in Chapters 3, 4, and 5. The three studies were designed to: 1) establish a method for adjusting wall squat exercise intensity (Chapter 3); 2) determine a method for prescribing wall squat exercise intensity from an incremental test and the efficacy of monitoring intensity using a target range (Chapter 4), and 3) investigate whether the use of home-based isometric wall squat training could indeed reduce resting BP and, if so, explore the primary mechanism(s) responsible for such a reduction (Chapter 5).

The main findings reported from these studies include:

1. Constant position isometric wall squat exercise intensity can be altered by manipulating the knee joint angle as HR and BP both produce significant inverse relationships with knee joint angle between 135° and 90° (Study 1, Chapter 3).
2. The relationships between both HR and BP and knee joint angle can be established from an incremental test, from which wall squat intensity can be reliably prescribed at a participant-specific knee joint angle to elicit a target HR, in this case 95% HR<sub>peak</sub> (Study 2, Chapter 4).
3. The modified limits of agreement equation can be utilised to calculate an appropriate target heart rate range enabling the intensity of an isometric wall squat training session to be monitored (Study 2, Chapter 4).
4. Four weeks of home-based isometric wall squat exercise training elicited statistically significant and clinically relevant resting BP reductions in normotensive males (Study 3, Chapter 5).
5. The reduction in resting BP following isometric wall squat training is possibly mediated by a reduction in resting  $\dot{Q}$ , which may be governed by a decrease in resting HR (Study 3, Chapter 5).

### **6.2 Establishing a method for altering and prescribing constant position isometric wall squat exercise intensity, as explored in Chapters 3 and 4**

The initial studies within this thesis successfully validate a novel isometric contraction style and mode, constant position wall squat exercise, which was essential in the development of an inexpensive home-based IET protocol. Previous research associated with isometric exercise for the reduction of resting BP has typically utilised constant force (%MVC) handgrip contractions or more recently constant EMG (%EMG<sub>peak</sub>) double-leg extensions. However, these isometric contraction styles and exercise modes require the use of expensive and/or laboratory-based equipment. For example, a number of studies required participants to complete double-leg extension isometric exercise at an individualised %EMG<sub>peak</sub> to attain a prescribed target HR (Devereux, Wiles and Swaine, 2010b; Wiles, Coleman and Swaine, 2010; Baross, Wiles and Swaine, 2012). This constant EMG isometric contraction style is suggested to produce an attenuated cardiovascular response in comparison to constant force work (Schibye et al., 1981; Franke, Boettger and McLean, 2000) and may produce a more accurate IET prescription and accompanying cardiovascular stress (Wiles et al., 2008b). However, it is far from practical for this contraction style to be

completed in the home as this would currently require the use of a laboratory-based isokinetic dynamometer and expensive EMG equipment. For this type of exercise to be accessible for the general population it would ultimately require the individual to travel to and from a facility to complete training using the specialist equipment while under supervision. This introduces the common physical activity and exercise barriers of transportation (Belza et al., 2004), lack of time (Trost et al., 2002; Lascar et al., 2014) and inaccessibility of facilities (Allison et al., 2005; Lascar et al., 2014). These factors are all likely to reduce adherence and consequently affect the potential effectiveness of this isometric therapy for producing BP reductions.

Alongside this, there is a growing body of research that has utilised a more accessible training method for constant force IHG exercise. Indeed, a programmable handgrip device has been utilised in a series of studies that have successfully lowered resting BP (Taylor et al., 2003; McGowan et al., 2006; Peters et al., 2006; McGowan et al., 2007a; 2007b; Badrov 2013a; 2013b; Millar et al., 2013a). This digital handgrip device guides the user through all steps of the IHG training protocol from performing a MVC for setting the IET intensity, to completing a 12 minute exercise session (Abe and Bisognano, 2011). Theoretically the instructions provided by the device would help to negate the need for supervision whilst allowing individuals to achieve the optimal training effects (Millar et al., 2009b). Furthermore, this device is compact and portable, so could easily be used in a location of the participant's choice. Indeed, the majority of IET studies that utilised this device were partly laboratory-based, with one or two training sessions out of three being completed in the participant's home (McGowan et al., 2006; 2007b; Badrov 2013a; 2013b; Millar et al., 2013a). However, despite the efficacy and ease of use, the device is currently on the market in the UK from £299 to £449 (Zona Health, 2014). Whilst it is acknowledged that compared to the costs of long-term pharmacological treatments this is relatively inexpensive (Millar et al., 2008), it is suggested that this level of financial outlay is still relatively excessive for many individuals; thus making the device inaccessible to a large proportion of the general population. At the other extreme one study successfully lowered resting BP by implementing constant force IHG training using an inexpensive spring-loaded handgrip device (Millar et al., 2008). While this device only costs approximately \$2 (Millar et al., 2008) (~ £1; XE, 2014), due to the protocols simplicity the IHG training was not set at a precise intensity. Training was completed at an approximate resistance level between 30-40% MVC without any indication of the participant's level of cardiovascular stress, such as RPE or HR. Therefore intensity was not rigorously controlled, which is fundamental in the safe prescription of isometric exercise (Wiles et al., 2005).

In order to make isometric exercise more accessible to the general population, it was essential to devise a mode of exercise and contraction style that could be easily completed at home with little cost, as well as a method to monitor the IET intensity. To this end isometric wall squat exercise was selected as a suitable mode of exercise since, in its most basic form, an individual is only required to perform a squat with their back resting against a wall (Escamilla et al., 2009a; 2009b). Furthermore, it is suggested that an isometric exercise that utilises a larger muscle mass may bring about optimal BP adaptations (Lawrence et al., 2014) due to the fact that the size of the muscle mass is suggested to affect the magnitude of the acute cardiovascular response to isometric exercise (Mitchell et al., 1980; Seals et al., 1983; Lewis et al., 1985; Iellamo et al., 1999; Franke, Boettger and McLean, 2000; Gálvez et al., 2000). Since the wall squat exercise requires an individual to maintain the knee joint at a given angle, typically 90°-110° (Escamilla

et al., 2009a; 2009b), it appeared that this isometric contraction style was best aligned with the term constant position, in which a given joint angle is maintained while supporting an inertial load (Hunter et al., 2002). However, for this novel isometric exercise mode and contraction style to be utilised within an IET protocol, it was essential to devise a valid method for adjusting and prescribing intensity.

To this end the first major finding of this thesis was that knee joint angle reliably produced an inverse curvilinear relationship with HR and an inverse linear relationship with BP from completing individual bouts of wall squat exercise (Study 1, Chapter 3), such that an increase in knee flexion produced increases in both HR and BP. This was suggested to occur because squatting exercise performed with greater knee flexion presented higher levels of EMG activity (Escamilla, 2001; Kvist and Gillquist, 2001; Bevilacqua-Grossi et al., 2005), which will likely increase the cardiovascular response due to greater central command (Franke, Boettger and McLean, 2000) and/or the exercise pressor reflex (Gálvez et al., 2000). Furthermore, it is suggested that static muscular contractions mechanically compress the intramuscular blood vessels and consequently hinder blood flow (Lind, 2011). This may cause an imbalance in the muscle's supply-to-demand ratio of oxygen and consequently require greater anaerobic resynthesis of ATP (Sinoway et al., 1989). This could cause metabolites to accumulate and metaboreceptors to be activated (Mostoufi-Moab et al., 1998), which would consequently increase the cardiovascular response.

The second key finding of this thesis was that these significant relationships between knee joint angle and both HR and BP could be reproduced by completing an incremental isometric wall squat test (Study 2, Chapter 4). The incremental test was based on the protocol designed by Wiles et al. (2008b) and included five 2 minute incremental stages at fixed knee joint angles (135°, 125°, 115°, 105° and 95°). The incremental test was continued until either the final 95° was completed to maximum, the participant failed to maintain the desired knee joint angle ( $\pm 5^\circ$ ) or to the point of volitional fatigue. This was an important finding as the methods of Wiles, Coleman and Swaine (2010) could be then be adapted to prescribe isometric wall squat exercise intensity. Based on the curvilinear relationship established from the incremental test between knee joint angle and HR, an individualised wall squat position (knee joint angle) could be calculated for a participant to complete during training in order to achieve the required target HR (95%  $HR_{peak}$ ).

Establishing these methods to adjust and prescribe isometric wall squat exercise intensity were paramount in the development of the home-based protocol; however it was also essential to utilise portable and relatively inexpensive equipment to ensure accessibility for the general population. While a goniometer is relatively low cost to purchase at approximately £8 (Amazon, 2014), this device was not suitable for unsupervised, home-based use due to the impracticality of a participant measuring their own knee joint angle while performing the wall squat exercise. Furthermore, an individual must have the skill of palpitation and knowledge of anatomy in order to locate any bony landmarks and accurately align the goniometer on the required joint (Clarkson, 2005). Therefore it was also necessary to develop a simple device for setting the wall squat position.

Preliminary research found that wall squat knee joint angle produced an inverse relationship with feet position and a linear relationship with back position (section 2.10.6, page 85), such that increasing knee flexion required the feet to be positioned further away from the wall and the back to move lower down the wall. Consequently it was possible to design and make a device that could position the feet and back so



that the required knee joint angle and wall squat position were attained. It is difficult to estimate what the unit price of this device would be if it was sold commercially as it was made in-house (Department of Sport Science, Tourism and Leisure, Canterbury Christ Church University, Canterbury, United Kingdom). However, it is estimated that each individual Bend and Squat device cost approximately £20; this price is for raw materials only and excludes the cost of labour and tools. If mass produced the overall cost per unit would likely reduce (Koren, 2010). A HRM was also required for home-based training so that the intensity could be monitored, which can be purchased from as little as £5 (Amazon, 2014). Thus, altogether the equipment required for isometric wall squat training could cost as little as £25. It is suggested that utilising such inexpensive equipment that can be used in a location of the participant's choice may help to reduce physical activity and exercise barriers, such as cost (Belza et al., 2004; Allison et al., 2005; Lascar et al., 2014) and lack of time (Trost et al., 2002; Lascar et al., 2014) and thus help to make isometric exercise more accessible to the general population and increase the efficacy of IET (Millar, Paashuis and McCartney, 2009b). While this may be the case, these are only a few of the many factors that may affect participation in physical activity and exercise (Bauman et al., 2002) and therefore other factors need to be explored in relation to IET. Further to this, it is also acknowledged that the behaviour change concept should be considered when developing an intervention to ensure its successful application (Michie, van Stralen and West, 2011); this notion will be explored further in section 6.7 (page 172).

### **6.3 Utilising the limits of agreement as a method to create a target heart rate range and enable intensity to be monitored during home-based training, as explored in Chapter 4**

A further aim of this thesis was to establish a viable method to continuously monitor the isometric exercise intensity for unsupervised home-based training. This was deemed to be essential to ensure that participants experienced a suitable (but safe) cardiovascular stimulus (Wiles et al., 2005). Whilst the majority of previous research has ensured that training is maintained at the required isometric intensity by measuring the constant force (%MVC), none of these studies have monitored the participant's level of cardiovascular stress (Wiley et al., 1992; Ray and Carrasco, 2000; Howden et al., 2002; Taylor et al., 2003; McGowan et al., 2006; Peters et al., 2006; McGowan et al., 2007a; 2007b; Millar et al., 2008; Stiller-Moldovan, Kenno and McGowan, 2012; Badrov et al., 2013a; 2013b; Millar et al., 2013a). As described in the preceding section 6.2 (page 157), the methods utilised in this thesis do allow for such cardiovascular monitoring as the exercise intensity is set according to a precise target HR. However, due to the variable nature of HR (Scott, Randolph and Leier, 1989; Stanforth et al., 2000; Højgaard et al., 2005) it is more appropriate to use a THRR rather than trying to attain one precise target HR value.

In light of this, the studies within this thesis calculated THRR utilising the limits of agreement method (Hopkins, 2000; Coleman et al., 2005), which was found to represent a realistic range to be achieved and maintained during isometric wall squat training (see Study 2, section 4.4.3, page 127). It is proposed that this novel method produces a more objective range than that prescribed in preceding isometric training studies, which utilised  $\pm 5\%$  of the individual target HR value (Devereux, Wiles and Swaine, 2010b; Wiles, Coleman and Swaine, 2010). This  $\pm 5\%$  range appears to be rather small and somewhat arbitrary; particularly as the reliability of the  $HR_{peak}$  within the current thesis was 6.3% (CV), which was the value from which the target HR was calculated. Therefore, to take into consideration the variable nature of HR,

the studies within this thesis calculated a participant's THRR using the modified limits of agreement method (Hopkins, 2000; Coleman et al., 2005), which described the likely difference between repeated test for 95% of the sample population (Atkinson and Nevill, 1998). This was deemed more appropriate than CV, which only covers 52% of the population (Hopkins, 2001). Calculating the THRR using a method that considers the reliability of a variable enables a 'real' change to be identified between repeated tests (Harding et al., 1988; Eliasziw et al., 1994). In the context of this thesis, this means that if the training value fell within the THRR then it was deemed that HR simply fluctuated due to either natural variability or measurement error. However, if the mean HR value fell outside the prescribed THRR then the training intensity was altered for the following session, as it was deemed that a 'real' change in HR had occurred possibly due to training adaptations. Monitoring HR in this manner can help to detect and prevent large errors in individual training intensity (Achten and Jeukendrup, 2003). Therefore by utilising the limits of agreement method to set THRR, this thesis has developed a novel, more objective method by which HR can be monitored. This is a key principle in the development of a home-based isometric training protocol to ensure that a safe and effective cardiovascular stimulus is utilised to induce BP adaptations.

While HR may provide a quantitative measure of cardiovascular stress, it is acknowledged that there may be some shortcomings in its application to IET. For instance, HR was in the THRR for 58% of a whole training session and consequently HR was below the THRR for 42% of the time, which may indicate that HR is not an optimal indicator of IET intensity. Indeed, Devereux, Wiles and Swaine (2011) examined the markers of isometric training intensity that best reflect subsequent reductions in resting BP. These authors reported that reductions in resting SBP and MAP were not related to training HR and it was suggested that using  $\%HR_{peak}$  may not be the most prudent method to prescribe IET for the reduction of resting BP. However, the authors did acknowledge that HR is useful as an indication of overall cardiovascular stress. Instead, markers related to EMG and torque were reported to best reflect the association between BP reductions and training intensity (Devereux, Wiles and Swaine, 2011). Although, it is noteworthy that such indicators are not suitable for use within a home-based IET protocol due to the expensive equipment required for measurement, as previously discussed in section 1.5.1c (page 24). Therefore, while HR may not be the most suitable marker of intensity to reflect reductions in resting BP with IET, at this moment in time it appears to be the most appropriate measure of intensity for home-based protocols. It is proposed that future research might explore the use of RPE to monitor isometric exercise intensity.

#### **6.4 The effectiveness of home-based isometric wall squat exercise training for reducing resting blood pressure, as explored in Chapter 5**

The final major aim of the thesis was to determine whether the methods established in studies 1 and 2 (Chapters 3 and 4 respectively) could be effectively utilised within a home-based constant position isometric wall squat training protocol to reduce resting BP (Study 3, Chapter 5). After participants completed 4 weeks of training, it was found that this novel home-based protocol significantly reduced resting BP in all 3 parameters (SBP: -4 mmHg; DBP: -3 mmHg; MAP: -3 mmHg). These BP reductions are similar in magnitude to those reported in previous isometric training research that have used a variety

of different protocols (McGowan et al., 2007a; Devereux, Wiles and Swaine, 2010b; Wiles, Coleman and Swaine, 2010; Millar et al., 2013a).

First of all, McGowan et al. (2007a) and Millar et al. (2013a) both utilised a traditional isometric training protocol to produce reductions in resting BP. In these studies, participants were required to complete constant force IHG contractions at 30% MVC 3 times a week for 8 weeks. Both studies found that SBP reduced by 5 mmHg, however no significant reduction was found in DBP; Millar et al. (2013a) also found a significant reduction in MAP (-3 mmHg). The protocol prescribed in these studies had the potential to be home-based as handgrip contractions were performed using a programmable handgrip dynamometer. However, only Millar et al. (2013a) partly utilised this feature by asking participants to complete one training session out of the three independently in the home; in the study of McGowan et al. (2007a) all training sessions took place under supervision in the laboratory. Further to this, the magnitude of BP reductions in the current study are also comparable to those produced using the alternative isometric training protocol prescribed by Devereux, Wiles and Swaine (2010b) and Wiles, Coleman and Swaine (2010). Within these studies, participants completed laboratory-based isometric double-leg extension training 3 times a week at an individualised constant EMG value (% EMG<sub>peak</sub>) in order to achieve a target HR (95% HR<sub>peak</sub>). Both training studies produced significant reductions in all resting BP parameters (SBP: -5 mmHg; DBP: -3 mmHg; MAP: -3 mmHg), however Wiles, Coleman and Swaine (2010) implemented an 8 week protocol, whereas Devereux, Wiles and Swaine (2010b) prescribed only 4 weeks.

Overall, the isometric training protocol developed within this thesis not only challenged some of the exercise barriers imposed by previous isometric training protocols, such as time and cost, but also effectively reduced resting BP. Indeed, this is the first isometric training research of its kind to produce significant BP reductions utilising: 1) a constant position contraction style to elicit a target HR; 2) an isometric wall squat exercise mode, and; 3) a fully home-based protocol. Employing such novel methods could have important implications for the use of isometric training by the general population. The equipment utilised to set the wall squat exercise position (Bend and Squat device) and monitor intensity (HRM) was inexpensive, which also reduces the associated cost of isometric exercise. Furthermore, the time required to complete a training session was only 14 minutes (4 x 2 minute exercise bouts with 2 minutes rest) and no time was required to travel to and from a facility. The training equipment was both simple and portable so that an exercise session could be completed in a location of the participant's choice. Altogether, the data presented in this thesis suggest that home-based constant position isometric wall squat training may provide a more cost and time effective protocol for the reduction of resting BP, which could reduce the barriers to exercise to improve adherence (Carlson et al., 2014) and ultimately increase the efficacy of isometric training.

While this thesis found a statistically significant decrease in resting BP following 4 weeks of isometric wall squat training, the pattern of BP reduction beyond this point is unknown as IET studies of a longer duration have found conflicting results (Millar et al., 2007). Millar et al. (2007) consolidated the data from three previous IHG training studies of medicated hypertensives (Taylor et al., 2003; McGowan et al., 2004; 2006) to examine the longitudinal effects on resting BP. In these studies participants completed four 2 minute IHG contractions at 30% MVC 3 times a week for 8 weeks and resting BP was measured twice weekly before training. The results of hierarchical linear modelling showed a negative linear pattern

of BP decline over time, such that SBP decreased by a rate of  $-0.32$  mmHg per session and DBP by  $-0.20$  mmHg (Millar et al., 2007). Furthermore, the results also indicated that 8 weeks of IHG training may not have produced maximal BP adaptations and suggested that resting BP could decrease further after a longer period of training. However, contrary to this finding Badrov et al. (2013a) reported that resting BP significantly decreased following 4 weeks of IHG training at 30% MVC 5 times a week, with no further BP reductions after completing another 4 weeks of training; this may suggest that maximal BP adaptations had been achieved by week 4. However, the increased training frequency (5 vs. 3 sessions per week) may have had a temporal effect on the BP adaptations produced (Badrov et al., 2013a). Within the same study participants also completed IHG training at 30% MVC 3 times a week and significant BP reductions were not found until week 8 (Badrov et al., 2013a). Similarly, from the data presented by Wiles, Coleman and Swaine (2010) it appears that most of the resting SBP adaptations following isometric double-leg extension training were produced within the first 4 weeks ( $-4.8$  mmHg) when completed at a high intensity ( $95\% HR_{peak}$ ) 3 times a week. Minimal additional resting SBP reductions occurred between weeks 4 and 8 ( $-0.3$  mmHg), although the resting SBP reductions were not actually statistically significant until week 8. Furthermore, this study also suggests an intensity-dependent temporal effect on BP adaptations due to the fact that when training was completed at a lower intensity ( $75\% HR_{peak}$ ) 3 times a week significant BP reductions were only clearly apparent at week 8. It therefore appears that the ability to achieve maximal BP adaptations may depend on the IET dose prescribed, which is likely affected by the programme variables that alter the magnitude of the cardiovascular response, such as exercise mode (muscle mass), intensity and duration, or exposure to the training stimulus, such as frequency, as previously discussed in section 1.5 (page 20). Further research is required to ascertain the intervention length and dose required to achieve maximal BP adaptations following isometric wall squat training.

### **6.5 The possible mechanisms responsible for reductions in resting blood pressure following isometric wall squat training, as explored in Chapter 5**

This thesis offers a new insight into the potential mechanisms that govern a reduction in resting BP. The isometric training study completed within this thesis was the first of its kind to report that reductions in resting BP were associated with a significant decrease in  $\dot{Q}$  in conjunction with no significant change to TPR (Study 3, Chapter 5). Whilst it is widely acknowledged that a change in MAP is likely due to an alteration to  $\dot{Q}$  and/or TPR (Wiley et al., 1992; Pescatello et al., 2004; Millar et al., 2013b), very few studies have actually measured these variables and those that did found no significant changes in either parameter (Devereux, Wiles and Swaine, 2010b; Wiles, Coleman and Swaine, 2010). It is suggested that this thesis found a reduction in  $\dot{Q}$  when other studies had not due to the larger sample size that was used ( $n = 28$ ) in comparison to previous research ( $n \leq 13$ ) (Devereux, Wiles and Swaine, 2010b; Wiles, Coleman and Swaine, 2010). This is evidenced by a recalculation of participant sample size inputting the control and training data obtained from study 3 into the Hopkins (2001) equation, from which it was estimated that only 11 participants were required to detect a change in  $\dot{Q}$  and 25 participants for TPR; see Table 5.1 (page 133) for the original sample size calculation for study 3.

The findings of this thesis add to the increasing body of research attempting to unravel the regulatory mechanisms that lower resting BP following isometric training. While few studies have measured  $\dot{Q}$  and

TPR directly, several studies have explored the different regulatory pathways that could modulate a change in  $\dot{Q}$  and/or TPR to produce BP reductions. These include autonomic function (Ray and Carrasco, 2000; Taylor et al., 2003; Wiles, Coleman and Swaine, 2010; Stiller-Moldovan, Kenno and McGowan, 2012; Badrov et al., 2013a; Millar et al., 2013a), endothelial function (McGowan et al., 2007a; 2007b; Badrov et al., 2013a), oxidative stress (Peters et al., 2006), and structural vasculature adaptations (Baross, Wiles and Swaine, 2012). The following sections will discuss these regulatory mechanisms in light of the findings presented within this thesis. Furthermore, this discussion will also consider two important observations that may provide additional understanding of the potential BP control mechanisms: 1) due to the underlying disease associated with hypertension, such as endothelial dysfunction (Bian, Doursout and Murad, 2008), different pathways may regulate BP reductions in individuals with high BP compared to normotensives (Baross, Wiles and Swaine, 2012), and 2) the physiological adaptations reported by previous studies may be misinterpreted due to the period of measurement utilised, such as 4 weeks or 8 weeks (Tinken et al., 2008). Indeed, it has previously been suggested that BP reductions may be due to a temporal sequence of alterations that initially change cardiovascular function and are subsequently superseded by longer term structural adaptations (Millar et al., 2013b). Such a biphasic pattern of adaptation has previously been reported following both aerobic (Tinken et al., 2008) and IET (Tinken et al., 2010). Further to this, animal studies also provide an insight into the time course of training adaptations and suggest that training-induced benefits could even be multiphasic (Masson et al., 2014). Indeed, Masson et al. (2014) investigated the time course changes of cardiovascular parameters in spontaneously hypertensive rats during 8 weeks of low intensity treadmill training (1 hour at 50-60% of maximal exercise capacity, 5 times per week). Within the first 2 weeks of training, early adaptive responses were reported such as normalization of baroreceptor reflex control and reductions in the pro-inflammatory and pro-oxidant profiles. In week 4 these responses were followed by an increase in the vagal component of HRV and decrease in resting HR. Finally after 8 weeks of training, the vasomotor component of BP variability reduced and resting MAP decreased. These findings suggest that an array of regulatory mechanisms appear sequentially to control reductions in resting BP over time. Therefore when discussing the potential pathways that regulate BP reductions following IET it is important to consider: 1) the BP classification of the participants being studied, and 2) the time period within the intervention that the BP control mechanism is being measured.

From the results reported in the training study within this thesis, it is suggested that the BP reductions were likely due to IET induced adaptations to the nervous system. As  $\dot{Q}$  is governed by HR and SV (Smith and Fernhall, 2011), the reduction in resting  $\dot{Q}$  following isometric wall squat training is most likely to have occurred due to the concomitant decrease in resting HR that was reported alongside no change in resting SV. From the recalculation of sample size using the data obtained in study 3, it was estimated that only 6 participants were required to detect a change in HR; however, statistical inferences about SV cannot be made as the recalculation continued to indicate that the sample size was too small ( $n = 315$ ). A reduction in resting HR would typically be mediated by increased parasympathetic and decreased sympathetic nervous system activity (Fleck, 2003). Indeed, HR has previously been reported as an indicator of sympathetic tone, as resting supine HR has been correlated with both plasma noradrenaline and MSNA (Grassi et al., 1998). While markers of ANS activity were not studied within this thesis, previous IET research has measured both linear HRV (Taylor et al., 2003; Wiles, Coleman and

Swaine, 2010; Stiller-Moldovan, Kenno and McGowan, 2012; Badrov et al., 2013a; Millar et al., 2013a) and nonlinear HRV (Badrov et al., 2013a; Millar et al., 2013a), however the results have been somewhat equivocal (Lawrence et al., 2014).

Both Taylor et al. (2003) and Millar et al. (2013a) studied medicated hypertensive participants and found that 10 weeks and 8 weeks of IHG training, respectively, elicited reductions in both SBP and MAP alongside alterations in HRV. Taylor et al. (2003) utilised the more traditional spectral analysis to measure HRV and reported a decrease in the low- to high-frequency ratio, which suggested a simultaneous decrease in sympathetic modulation and an increase in vagal modulation. Furthermore Millar et al. (2013a) found improvements in nonlinear HRV such that sample entropy increased and fractal scaling distance score decreased, which reflected improved sympathovagal balance; although it is important to note that no difference was detected in the linear measure of HRV in this study. Such improvements in the cardiac autonomic function following IET could reduce resting HR to modulate a reduction in resting BP via  $\dot{Q}$ ; although this was not found to be the case with the medicated hypertensive individuals studied as no statistically significant change in HR was reported (Taylor et al., 2003; Millar et al., 2013a). Furthermore, Stiller-Moldovan, Kenno and McGowan (2012) also studied medicated hypertensive individuals but conversely found no significant changes to either resting BP, linear HRV or HR following 8 weeks of IHG training. It was suggested that maximum autonomic improvements may have already been experienced due to the antihypertensive medication being taken by participants and thus these well-controlled medicated hypertensive individuals may have had a limited capacity for BP reductions (Stiller-Moldovan, Kenno and McGowan, 2012). It seems logical to suggest that a similar effect could be experienced with normotensive participants who may also have optimal autonomic function. Improvements in resting BP and autonomic function may have been possible in the studies completed by Taylor et al. (2003) and Millar et al. (2013a) due to the fact that the participants had higher initial resting BP levels (Taylor et al., 2003; Millar et al., 2013a) and that not all participants were medicated (25%; Taylor et al., 2003). The findings of these studies together suggest that IET has the potential to induce cardiac neural adaptations in medicated hypertensive individuals that may modulate resting BP reductions through a reduction in resting HR. Although alterations to HRV have been detected when studying medicated hypertensive participants, this has not been the case with normotensive individuals (Wiles, Coleman and Swaine, 2010; Badrov et al., 2013a), which were the sample population utilised in the studies within this thesis.

Wiles, Coleman and Swaine (2010) reported significant reductions in all three resting BP parameters (SBP: -5 mmHg; DBP: -3 mmHg; MAP: -3 mmHg) following 8 weeks of high intensity (95%  $HR_{peak}$ ) isometric double-leg extension training; however no significant differences in HR or the linear measures of HRV were found. Furthermore, Badrov et al. (2013a) found that SBP significantly decreased (-6 mmHg) following 8 weeks IHG training but again found no changes in HR nor either linear or nonlinear indices of HRV. However, it is suggested that such a modest decrease in BP would likely be mediated by a small change in HRV that the traditional spectral analysis may not be sensitive enough to detect (Millar et al., 2013a), particularly as there are many well-known environmental factors that affect data recording (Lawrence et al., 2014). Furthermore, it is suggested that the IET study within this thesis found significant resting HR reductions for normotensive participants when other research has not due to the fact that a larger sample size was selected enabling more statistical power. Finally, it is also worth considering that a

decrease in resting HR may have been detected in the current research due to the intervention length and consequent time period of measurement. Indeed, Wiles, Coleman and Swaine (2010) measured post-training resting HR (week 8) but did not report resting HR mid-term (week 4). It is a possibility that there may be a time course for HR alterations, such that HR initially decreases due to a change in autonomic function, as suggested by Masson et al. (2014), which may then be superseded by alternative BP control mechanisms in the longer term. In support of this, Devereux, Wiles and Swaine (2010b) found a statistically significant decrease in resting HR ( $-7 \text{ beats}\cdot\text{min}^{-1}$ ) following 4 weeks of high intensity (95%  $\text{HR}_{\text{peak}}$ ) isometric double-leg extension training; although this must be viewed with some caution as Devereux, Wiles and Swaine (2010b) also reported a statistically significant decrease in the control group's resting HR ( $-4 \text{ beats}\cdot\text{min}^{-1}$ ). In light of the research presented, a decrease in resting HR, such as that reported following 4 weeks of isometric wall squat training, may suggest the BP reductions found at that time point were mediated by a change in autonomic function. To fully understand the relationship between autonomic function and resting BP reductions in normotensive participants, further research is required that: 1) utilises a large enough sample size to ensure sufficient statistical power (Badrov et al., 2013a), 2) measures both linear and nonlinear indices of HRV, and 3) examines potential time course change in the mechanisms underlying resting BP reductions.

An alternative indicator of ANS activity that could help explain a reduction in resting BP following IET is an alteration in baroreflex function. The arterial baroreceptors monitor changes in BP and consequently mediate adjustments to the cardiovascular system accordingly via the ANS (Fadel, Smith and Gallagher, 2004). It was initially hypothesised by Kiveloff and Huber (1971) that the baroreceptors in the carotid sinus and aortic arch may be stimulated during isometric exercise, which could cause a reflex reduction in HR to consequently reduce BP. Further to this Wiley et al. (1992) also implied that the repeated exposure to the pressor response caused by the significant increase in MAP during isometric training may stimulate baroreceptor resetting. While some authors have hinted at the possibility of such a link between BP reductions and baroreflex function, to date only one training study appears to have measured baroreflex function pre- and post-IET (Devereux, 2010a). In the doctoral thesis of Devereux (2010a), it was reported that 4 weeks of isometric double-leg extension training in normotensive participants produced reductions in all three BP parameters, however this was not associated with any significant alterations to baroreflex sensitivity, HR or  $\dot{Q}$ . This finding suggests that adjustments to baroreflex function do not play a role in BP adaptations following IET (Devereux, 2010a). However it was acknowledged that the lack of significant finding for baroreflex sensitivity may have been due to the inherent 'noise' of the measure, as a high level of test-retest variance was found during an initial reliability study (Devereux, 2010a). As such, it remains unclear whether baroreflex function has an important role to play in the reduction of resting BP, particularly as the majority of insights are merely speculative; further research is required to gain a clearer understanding.

Whilst the preceding sections may infer that the reductions in resting BP following 4 weeks of isometric wall squat training could be 'centrally' mediated through a reduction of  $\dot{Q}$  via the ANS modulation of HR, this is in opposition to the common suggestion that BP reductions following IET occur through a decrease in TPR (Millar et al., 2013b). Indeed  $\dot{Q}$  is thought to remain unchanged as any HR reduction is often offset by an increase in SV (Fagard and Cornelissen, 2007). It is therefore also important to discuss the possibility that an alteration to autonomic balance could moderate changes in TPR to regulate resting

BP; however there is limited data to explore the impact of isometric training on the neural regulation of vascular tone (Millar et al., 2013b). Alongside moderations in HRV, Taylor et al. (2003) also found that a reduction in SBP and MAP following 10 weeks of IHG was accompanied by a decrease in the low- to high-frequency area ratio of SBP variability in medicated hypertensive participants. It has previously been proposed that a reduction in the low frequency component of SBP variability may reflect a change in the baroreflex-mediated efferent sympathetic regulation of the peripheral vasculature (Pagani et al., 1988, 1997). Such an attenuation in the sympathetic vasoconstrictor activity may serve to reduce resting BP (Millar et al., 2013b), presumably through an increase in the blood vessel diameter which reduces TPR (Tortora and Derrickson, 2012). However it is unlikely that this was the case with the normotensive participants utilised within this thesis since no significant changes in TPR were found. Indeed this is supported by the research of Ray and Carrasco (2000), who found that 5 weeks of IHG training produced reductions in resting DBP and MAP in normotensive participants, in the absence of any significant change in resting efferent MSNA. These results may imply that alterations in central efferent sympathetic outflow to skeletal muscle are not a prerequisite to BP adaptations following IET in this population (Millar et al., 2013b). However, this could be due to the fact that the normotensive participants studied did not have an elevated resting MSNA in comparison to the values typically documented for hypertensive individuals (Millar et al., 2013b) and therefore the normotensive individuals may have had a limited capacity for MSNA adjustments. Indeed, hypertension is associated with impaired metaboreflex control of MSNA (Rondon et al., 2006) and thus alterations to resting efferent MSNA may modulate BP adaptations in this population. Furthermore, there may also be a time course for IET induced neural alterations of vascular tone as Taylor et al. (2003) reported beneficial changes to a marker of peripheral sympathetic nerve activity following IET at 10 weeks, but Ray and Carrasco (2000) did not after 5 weeks. This notion is supported by the work of Masson et al. (2014), which did not find changes to the low frequency component of systolic arterial pressure variability until week 8 when investigating the effects of low intensity treadmill training with hypertensive rats. Thus, due to the potential time course of adaptation, it is plausible to suggest that the intervention length utilised for isometric wall squat training within this thesis (4 weeks) may have not have been long enough to alter sympathetic vasomotor tone, which may explain the lack of significant change to TPR. Ray and Carrasco (2000) concluded that other mechanisms must be responsible for the BP adaptations following 5 weeks of IET in normotensive individuals and it was postulated that a decrease in resting BP could instead be due to peripheral vascular adaptations, such as improvements in endothelial function.

Ray and Carrasco (2000) initially proposed that the extreme pressor response experienced during isometric exercise may increase the exposure to systemic shear stress on the blood vessels throughout the entire body and consequently increase the release of endothelium-derived nitric oxide. To this end, McGowan et al. (2007b) examined the hypothesis that IHG would induce improvements in systemic endothelial function, which would reduce TPR to lower resting BP. Participants who were medicated for hypertension were randomly assigned to complete either a bilateral or unilateral 8 week IHG protocol. Resting BP was measured pre-and post-training as well as flow-mediated dilation (FMD), which is an index of endothelial-dependent dilation. Both bilateral and unilateral IHG training produced significant reductions in resting SBP. However, the bilateral protocol found improvements in brachial artery FMD in both arms, whereas in contrast, the unilateral protocol only improved brachial artery FMD in the trained



arm. This suggests that improvements in endothelial-dependent vasodilation are localised rather than systemic (McGowan et al., 2007b). It is unknown whether such localised improvements in vascular function would consequently affect TPR as the study did not measure this variable. Whilst systemic endothelial function has not been shown to change following IHG, Green et al. (2004) proposed that shear stress mediated improvements in nitric oxide function may be dependent on the size of the muscle mass subjected to training, presumably due to the greater pressor response experienced during isometric exercise of a larger muscle mass (Mitchell et al., 1980; Seals et al., 1983; Lewis et al., 1985; Iellamo et al., 1999; Franke, Boettger and McLean, 2000; Gálvez et al., 2000). It is suggested that the muscle mass recruited or hemodynamic response associated with IHG exercise, may not be sufficient to induce a generalized benefit (Green et al., 2004), and this may explain why no systemic improvement in endothelial function was found by McGowan et al. (2006). Despite this fact, no change in TPR was reported in the training study within this thesis utilising the isometric wall squat exercise, which primarily uses the larger quadriceps muscles (Contreras, 2014), which suggests that improvements in systemic endothelial function do not regulate reductions in resting BP following 4 weeks of IET in a normotensive population.

The concept that IET increases the bioavailability of nitric oxide to reduce BP is supported by the study completed by Peters et al. (2006) which examined the effect of 6 weeks IHG training on BP and markers of oxidative stress in hypertensive participants. It was found that SBP significantly lowered and this was regulated by favourable changes in markers of oxidative stress, such as a dramatic decrease in exercise-induced oxygen centred radicals (-266%) and an increase in the ratio between resting whole blood glutathione to oxidized glutathione (+61%). Such a decrease in oxidative stress is important as an excess in reactive oxygen species is thought to enhance nitric oxide deactivation and impair endothelial function (Higashi et al., 2009), which is thought to play a critical role in the pathogenesis of hypertension (Cai and Harrison, 2000). Therefore a shift towards increased antioxidant protection may be another mechanism that could be responsible for reductions in BP following IET due to a potential improvement endothelium-dependent dilation (Millar et al., 2009b).

While the research of McGowan et al. (2007b) and Peters et al. (2006) may suggest that improved endothelial function plays an important role in producing BP adaptations following IET in hypertensive individuals, this may not be the case for normotensive participants. Indeed, Green et al. (2004) proposed that exercise training in healthy participants may not induce improvements nitric oxide dependent vasodilation since the endothelial function is already normal and, as indicated earlier, benefits may be more probable in those with antecedent endothelial dysfunction, such as those with hypertension (Bian, Doursout and Murad, 2008). This is supported by the work of McGowan et al. (2007a) that found reductions in resting SBP in a normotensive population following 8 weeks unilateral IHG training but no improvement in either local or systemic endothelium-dependent vasodilation. Therefore, this may explain why the normotensive participants within this thesis experienced no alteration to TPR following IET induced reductions in resting BP. However, the calculation of TPR utilised in this thesis reflects systemic vascular resistance (Boone, 2014) and is at best an estimate; thus localised changes cannot be ruled out.

As well as considering the BP status of the participants (normotensive vs. hypertensive) in relation to the likely endothelial function changes experienced following IET, it is also important to examine the time

course of arterial adaptations since previous research suggests that changes in endothelial function occur at around 4 weeks and subside by week 8 (Tinken et al., 2008; 2010). Therefore this may also explain why McGowan et al. (2007a) found no change in endothelial function after normotensive participants completed 8 weeks of IHG training. Indeed, in a series of studies, Tinken and colleagues explored the theory that there is a time course for arterial adaptations (Tinken et al., 2008; 2010). Tinken et al. (2008) first investigated the changes in artery function and structure in response to 8 weeks cycle and treadmill aerobic exercise training in participants that were not hypertensive. From the findings of the study it was proposed that an initial increase in vascular function occurs in the first 2 to 4 weeks, which is nitric oxide mediated, and then following a longer period of 8 weeks training the vasculature begins to remodel in an attempt to normalise the shear stress (Tinken et al., 2008). It appeared that the endothelial functional changes peaked at around 4 weeks and then returned to near baseline levels by week 8; whereas structural adaptations began at week 2 and continued to increase throughout training (Tinken et al., 2008). However, it is important to note that no statistically significant change in BP was detected when pre- and post-training values were compared (0 vs. 8 weeks) and TPR was not measured. A later study by Tinken et al. (2010) found that IHG training over an 8 week period also brought about time-dependent changes in both arterial function and remodelling with normotensive participants. It was again proposed that IHG training is initially associated with functional adaptations, such as increased brachial artery nitric oxide dependent function, which is subsequently superseded by other adaptations, such as resistance vessel arterial remodelling. Although once again, no statistically significant change in BP was reported and TPR was not measured. While the research by Tinken and colleagues may suggest a time-dependent change in endothelial function at around 4 weeks, the IHG research discussed thus far does not necessarily support this theory (McGowan et al., 2007a; 2007b). Indeed, McGowan et al. (2007b) found improvements in endothelial-dependent vasodilation at 8 weeks when studying hypertensive individuals, whereas Tinken and colleagues found that nitric oxide mediated function had returned to baseline by this time (Tinken et al., 2008; 2010). This variance may be due to different initial BP status of the participants studied (hypertensive vs. normotensive, respectively), which may suggest a different time-course of arterial adaptation in hypertensive individuals, possibly due to inherent endothelial dysfunction (Bian, Doursout and Murad, 2008). However, McGowan et al. (2007a) did study normotensive participants but found no change in endothelial function alongside no statistically significant decrease in SBP from baseline to week 4 (-3.8 mmHg). Furthermore, the arterial adaptations reported by Tinken and colleagues were not associated with changes in BP (Tinken et al., 2008; 2010). Thus, from the research presented it is suggested that the reduction in resting BP following 4 weeks of isometric wall squat training completed by normotensive participants may not be mediated by improvements in local or systemic endothelial function.

Up until now, the studies discussed have focused specifically on endothelial-dependent function (McGowan et al., 2007a; 2007b), as few studies have explored the effects of IET on endothelial-independent vasodilation, which is an indicator of smooth muscle function (McGowan et al., 2006). However, McGowan et al. (2006) investigated the effects of 8 weeks of IHG training on both brachial artery FMD (an indicator of endothelium-independent vasodilation) and nitroglycerine-mediated maximal vasodilation (an indicator of endothelial-independent vasodilation) in medicated hypertensives. It was reported that endothelium-dependent vasodilation improved following IHG training, however

endothelium-independent vasodilation remained unchanged. Thus it is suggested that IET may have the potential to enhance endothelium-dependent vasodilation in medicated hypertensive individuals, possibly due to a shear stress related increase in the release of nitric oxide (McGowan et al., 2006; McGowan et al., 2007b), but may not alter the vascular smooth muscle's dilatory capacity (McGowan et al., 2006). Interestingly, evidence is accumulating to suggest that dietary nitrate, from vegetables such as beetroot, may have beneficial effects on blood pressure and endothelial function (Hobbs, George, Lovegrove, 2013a). Specifically, dietary nitrate may mediate reductions in BP by increased endothelium-independent vasodilation (Hobbs, George, Lovegrove, 2013a) via the sequential reduction of nitrate to nitrite and further to nitric oxide in the blood vessels (Hobbs et al., 2013b). Therefore it may be beneficial for future research to investigate whether a combined intervention of IET and dietary nitrates could produce greater improvements in endothelial function, and consequently BP reductions, due to the potential combined effects of these interventions on endothelium-dependent and -independent vasodilation, respectively.

It is also important to note that the endothelial function research discussed thus far has examined the effects of IHG training on the larger conduit arteries (McGowan et al., 2007a; 2007b), however hypertension is also associated with the narrowing of the smaller resistance vessels (Oparil, Zaman and Calhoun, 2003). To this end Badrov et al. (2013a) studied the effects of 8 weeks IHG training on resting BP and the resistance vessel vasculature in a normotensive population. It was found that SBP significantly decreased alongside an increase in the dilatory capacity of the resistance vessels. However, the resistance vessel adaptations were only apparent after 8 weeks of IET, not 4 weeks, and thus are not likely to be a key mechanism responsible for the BP adaptations reported following isometric wall squat training in this thesis.

It has also been proposed that structural adaptations, such as an increase in lumen diameter, may bring about BP adaptations after isometric training (McGowan et al., 2007a). As previously discussed, the current consensus is that any structural adaptations occur towards the latter end of training between weeks 4 and 8 (Tinken et al., 2008; 2010). Indeed, Leaf et al. (2003) reported that after 6 weeks of IHG training at approximately 25% to 35% MVC there was a significant increase in the lumen size of the cephalic vein in the exercising limb. Unfortunately BP was not measured in this study, however the training duration and intensity used was similar to previous IET studies that have successfully reduced resting BP. Therefore it is suggested that the increase in the size of the lumen could potentially have a positive effect on BP, due to its concomitant effect upon TPR. A later study by Baross, Wiles and Swaine (2012) investigated whether resting BP reductions following IET were associated with adaptations in the muscle vasculature. To this end, participants with high-normal BP completed 8 weeks of high intensity (85%  $HR_{peak}$ ) isometric double-leg extension training. Following this training, statistically significant reductions in resting SBP and MAP were reported. These resting BP reductions were accompanied by localised vascular adaptations in the trained limb, which comprised of increased resting femoral artery diameter, blood flow, blood velocity, and vascular conductance. However, these vascular adaptations occurred during the latter stages of training (between weeks 4 and 8), which supports that suggestion that such structural changes are sequentially time-dependent (Tinken et al., 2008; 2010). Taking this research into consideration, it is extremely unlikely that structural vascular adaptations were responsible for the BP reductions reported following isometric wall squat exercise as the training protocol was only 4 weeks in duration. While this may be supported by the fact that no change in TPR was found, this inference must

still be made with some caution since this parameter was not measured directly in the current thesis. Furthermore, the vascular adaptations reported by Baross, Wiles and Swaine (2012) occurred in the trained limb, and thus the systemic calculation of TPR utilised within this thesis may not reflect changes in the local vasculature as previously suggested.

Based upon the mechanistic research presented within this section, it is suggested that the BP reductions found following 4 weeks of isometric wall squat training in a normotensive population may have been due to a decrease in HR that consequently lowered  $\dot{Q}$ . It is suggested that such an alteration to resting HR may reflect an initial 'centrally' mediated change in autonomic regulation; although it is acknowledged that further research is required that specifically examines such regulatory pathways. As well as measuring linear and nonlinear HRV, it is suggested that future IET studies should also investigate alternative indices of autonomic function such as BP variability, MSNA, noradrenaline and/or baroreflex sensitivity (Badrov et al., 2013a). Furthermore, due to the fact that TPR did not change following 4 weeks of isometric wall squat training, it appears unlikely that 'peripheral' mechanisms, such as improved endothelial function or vascular remodelling, mediated the BP reductions in the normotensive population studied. However due to the limited evidence available and the fact that these regulatory pathways were not directly measured within this thesis, alterations to the vascular structure and function following IET cannot be ruled out. Finally, it appears highly likely that the BP control mechanisms are determined by an intricate interplay of many factors, such as an individual's initial BP level and the time course of adaptations. It would therefore be beneficial for future IET research to explore the potential multiphasic nature of BP regulation by measuring a variety of different control mechanisms, such as autonomic function, endothelial function, and structural vasculature adaptations, at various stages throughout training.

## **6.6 Contextualising the reductions in resting blood pressure following home-based isometric wall squat training in relation to the potential health and economic impact**

Developing an accessible lifestyle modification that has the potential to help prevent and control resting BP, such as the home-based isometric wall squat training protocol presented within this thesis, is of great importance due to the inordinate public health impact and economic burden that hypertension represents (Hodgson and Cai, 2001). First and foremost, high BP is a major problem due to the fact that it is highly prevalent and an associated modifiable risk factor for cardiovascular and kidney disease (He and Whelton, 1997). To this end, the major goal of any antihypertensive therapy is to lower cardiovascular and renal related morbidity and mortality (Chobanian et al., 2003). The beneficial health implications associated with a reduction in resting BP are suggested to occur even for a relatively modest BP decrease (Millar et al., 2013b). Indeed, a 2 mmHg reduction in SBP or DBP could lead to a decreased risk of hypertension (17%), coronary heart disease (5-6%), stroke (15%) and all-cause mortality (3%) (Cook et al., 1995; Neaton et al., 1995 cited in Stamler, 1997), although it is important to consider the limitations of these estimated risk reductions as previously acknowledged (see section 5.4.2, page 151). Despite this fact, the IET training study within this thesis may have produced clinically relevant resting BP reductions for over two-thirds of the sample population (SBP: 68%; DBP: 71%). Such clinically relevant BP reductions are particularly pertinent for the normotensive participants studied with this thesis (125/78 mmHg) as the associated risk of CVD begins to appear from BP levels as low as 115/75 mmHg,

SBP/DBP respectively (Lewington et al., 2002). Thus while the training study within this thesis did not ascertain whether isometric wall squat training can effectively treat hypertension, it has demonstrated that this relatively simple lifestyle modification can effectively lower resting BP to potentially reduce the prevalence of hypertension and the concomitant risk of cardiovascular and renal disease. Before this novel home-based IET protocol can be applied as an antihypertensive treatment, it is fundamental to first repeat the stringent processes completed in this thesis with a hypertensive population. Although the percentage change in BP during isometric exercise is not different for hypertensive individuals, the BP values attained may be greater due to the higher initial BP levels (Ewing et al., 1973). For this reason, the IET protocol may need to be adapted to ensure that the prescription method is still safe and effective for a hypertensive population, as discussed in section 6.7 (page 172).

Further to this, hypertension not only imposes significant health implications but also a substantial economic burden (Hodgson and Cai, 2001). In 2010 it was estimated that the direct and indirect cost of hypertension was \$46.4 billion in the United States alone, which was estimated to increase to \$274 billion by 2030 (Go et al., 2014). The direct healthcare costs for the treatment of hypertension include expenditures related to antihypertensive medication, office visits for the management of BP, laboratory tests and in-hospital costs required for the treatment of adverse drug reactions (Elliott, 2003). Of these expenditures, drug costs represent the greatest direct medical cost (Tarride et al., 2009). In the UK, the clinical management of hypertension is one of the most common primary care interventions and in 2006 antihypertensive drug therapies alone cost approximately £1 billion (NICE, 2011). However, it is important to remember that there are also indirect costs associated with hypertension related to loss of productivity (Alcocer and Cueto, 2008) due to morbidity or mortality, which can also cost the economy billions (Heidenreich et al., 2011). In addition to this, the enormous economic burden of hypertension is further compounded due to the cost of healthcare resources required to diagnose and treat chronic conditions for which high BP is a risk factor such as cardiovascular and renal disease (Hodgson and Cai, 2001; Elliott, 2003). In 1998 it was suggested that 33% of adults in the UK had not reached their target BP level (< 140/90 mmHg) and it was estimated that failure to achieve this goal resulted in 58,000 major cardiovascular events, which was predicted to cost the NHS £97.2 million (2000/01 prices) (Lloyd, Schmieder and Marchant, 2003). Taken together, it is suggested that successful efforts to prevent and treat hypertension will not only reduce the prevalence of hypertension but also decrease any associated cost. Therefore lifestyle modifications, such as the home-based isometric wall squat training protocol, may help to substantially reduce both the health implications and economic burden of hypertension. Furthermore, the IET protocol developed within this thesis provides an alternative cost-effective lifestyle modification as it requires the use of inexpensive equipment such as a HRM and Bend and Squat device, which together only cost approximately £25 (see section 6.2, page 157).

## **6.7 Future directions**

This thesis has successfully developed a home-based isometric wall squat training protocol for the safe and effective reduction of resting BP in normotensive individuals. Whilst this research has important implications as a lifestyle modification for the prevention of high BP, as outlined in section 6.6 (page 171), it is currently unknown whether this mode of isometric training would successfully and safely lower resting BP in a hypertensive population. However, based upon the successful use of other forms of IET,

such as constant force IHG training, with individuals who have high-normal or high BP (Wiley et al., 1992; Taylor et al., 2003; Peters et al., 2006; McGowan et al., 2007b; Badrov et al., 2013b; Millar et al., 2013a), it is likely that the hypotensive benefits of isometric wall squat training experienced with normotensive participants may also extend to those individuals with hypertension. Indeed, previous IET studies have found significant reductions in resting BP following IHG training with high-normal (Wiley et al., 1992), hypertensive (Peters et al., 2006) and medicated hypertensive participants (Taylor et al., 2003; McGowan et al., 2007b; Badrov et al., 2013b; Millar et al., 2013a); one study also found significant BP reductions after participants with high-normal BP completed constant EMG isometric double-leg extension training (Baross, Wiles and Swaine, 2012). Further to this, previous research has also shown that pre-training SBP is negatively correlated with BP reductions following IHG training (Millar et al., 2007). Therefore not only does isometric wall squat training have the potential to lower BP in a hypertensive population, but could in fact produce even greater BP adaptations than those experienced with the normotensive population studied within this thesis. If isometric wall squat training can in fact reduce resting BP in a hypertensive population this would be of substantial benefit. Lifestyle modifications that successfully lower resting BP in hypertensive individuals will not only provide beneficial health improvements (Cook et al., 1995; Neaton et al., 1995 cited in Stamler, 1997) and potentially reduce the associated economic burden (Lloyd, Schmieder and Marchant, 2003), as described in section 6.6 (page 171), but also lessen the need for antihypertensive drug therapies that can be accompanied by adverse side effects (Millar et al., 2013b).

To further contextualise the potential for IET in BP management, it is important to discuss the use of antihypertensive drug therapies for the reduction of resting BP and any potential limitations of this treatment method. Antihypertensive drug treatments are prescribed to: 1) individuals under 80 years with SBP/DBP  $\geq$  140/90 mmHg and have target organ damage, established CVD, renal disease, diabetes, or 10-year cardiovascular risk  $\geq$  20% and, 2) people of any age with SBP/DBP  $\geq$  160/100 mmHg (NICE, 2011). While antihypertensive drugs successfully lower BP and consequently decrease the risks of stroke, coronary heart disease, and major cardiovascular events (Neal, MacMahon and Chapman, 2000; Turnbull, 2003), this therapy is also unfortunately associated with some common side effects, such as headache, dizziness, coughing and fatigue (Cheung, Wong and Lau, 2005; Khurshid et al., 2012). While these side effects seem relatively minor, such adverse drug reactions can have a huge impact on a person's normal functioning (Cohen, 2001) and subsequently their quality of life (Bloom, 1998). This is further compounded by the fact that hypertension itself generally has few symptoms (Bloom, 1998; Cohen, 2001; Cheung, Wong and Lau, 2005) and thus through taking antihypertensive medication an individual may actually feel subjectively worse than they did before treatment (Cohen, 2001). These associated side effects consequently affect the tolerability and compliance to antihypertensive medication (Cheung, Wong and Lau, 2005) and can cause many individuals to discontinue therapy (Bloom, 1998). Indeed, it has been reported that after six months of antihypertensive treatment between 35% to 50% of patients will discontinue therapy (Bloom, 1998; Vrijens et al., 2008). Furthermore, an observation study reported that after 10 years approximately 39% of individuals continuously used antihypertensive drugs during this period, 22% temporarily discontinued and restarted treatment, and 39% of individuals discontinued permanently (Van Wijk et al., 2005). If a hypertensive individual does discontinue their drug therapy then the BP lowering benefits can no longer be gained (Grégoire et al., 2002) and therefore poor adherence to

antihypertensive medication is a major barrier of BP control (Panjabi et al., 2013; Grégoire et al., 2002). It has previously been reported that up to 50% of medicated hypertensive individuals do not achieve their recommended target BP (Brown, 1997; Hajjar and Kotchen, 2003). Further to this, antihypertensive drug treatment has also been associated with morbidity and in some cases even mortality (Liamis, Milionis and Elisaf, 2008). This is due to the rare but serious potentially life-threatening adverse drug reactions, including angioedema (Brown and Vaughan, 1998), hyperkalaemia (Liamis, Milionis and Elisaf, 2008) and renal failure (McDowell et al., 2010) to name a few. Furthermore, the side effects of antihypertensive medication not only produce potential health problems but also pose an economic burden (Khurshid et al., 2012) due to the associated in-office or in-hospital costs of treating adverse drug reactions (Elliott, 2003). The highlighted limitations of antihypertensive medication clearly emphasise the need for alternative BP lowering regimes. Lifestyle modifications are an important BP reduction strategy that may reduce the amount of antihypertensive medication required (Blumenthal et al., 2002) and even diminish the need for drug therapy altogether (Beevers, Lip and O'Brien, 2001). Therefore it is clear that further research is required to establish a safe and effective lifestyle modification that can be used for the reduction of resting BP as either an alternative or adjunctive therapy to antihypertensive medication.

To this end, it has previously been proposed that isometric training, specifically involving handgrip exercise, may offer a relatively inexpensive and safer alternative method to produce resting BP reductions compared to the more traditional antihypertensive medication (Abe and Bisognano, 2011). Indeed constant force IHG training has most commonly been used to produce resting BP reductions in high-normal or hypertensive populations (Wiley et al., 1992; Taylor et al., 2003; Peters et al., 2006; McGowan et al., 2007b; Badrov et al., 2013a; Millar et al., 2013a). Only one study has utilised a different IET protocol to produce hypotensive adaptations in a high-normal population, which included a constant EMG isometric contraction style and leg based exercise mode (Baross, Wiles and Swaine, 2012). In this study participants completed 8 weeks of double-leg extension training at an individualised constant EMG value to achieve a specific target HR (85% HR<sub>peak</sub>). It was reported that high-normal participants achieved significant resting BP reductions (SBP: -11 mmHg; MAP: -5 mmHg). Furthermore, no adverse reactions have reported either during or following IET, such as unfavourable clinical events or lasting physical impairments (Millar et al., 2013b), and therefore it appears that IET is an exceptionally well-tolerated procedure. However, to date, no research has investigated whether constant position isometric wall squat exercise training at a target HR could produce BP adaptations in individuals with high resting BP. In order for this novel training protocol to be safely and effectively prescribed for a hypertensive population it is suggested that two main areas require further exploration: 1) the intensity that training is to be completed at, and 2) the method used to prescribe the training intensity.

It is well known that the pressor response experienced during isometric exercise is exaggerated (Mitchell and Wildenthal, 1974) and this may be further exacerbated with hypertensive individuals due to the higher initial resting BP levels (Ewing et al., 1973). When participants with normal BP completed isometric wall squat training within this thesis, the time that BP was above the ACSM exercise termination guidelines (Whaley, Brubaker and Otto, 2006) was limited. Indeed, during a wall squat training session it was found that, on average, SBP spent no time above the ACSM guidelines (SBP > 250 mmHg) and DBP spent only a small duration of time (4%, ~19 seconds) above the guidelines (DBP > 115 mmHg) (Whaley, Brubaker and Otto, 2006). However, while the BP response in normotensive

participants appears to remain at safe levels, this may not be the case for hypertensive individuals, as the higher initial BP level may cause a more exaggerated pressor response during wall squat training and consequently lead to the ACSM exercise termination guidelines being exceeded for a longer duration. As the cardiovascular response is related to the intensity of the isometric exercise performed (Lind et al., 1964; Iellamo et al., 1999), it is suggested that it may be more suitable for wall squat training to be completed at a lower intensity than that prescribed within this thesis (95%  $HR_{peak}$ ). Indeed, the study completed by Baross, Wiles and Swaine (2012) utilised a slightly lower training intensity (85%  $HR_{peak}$ ; equivalent to ~14% MVC) when investigating high-normal individuals and still produced statistically significant BP reductions. For a comparative perspective, performing double-leg extension exercise at 95%  $HR_{peak}$  has previously been suggested to be equivalent to approximately 21-24% MVC (Devereux, Wiles and Swaine, 2010b; Wiles, Coleman and Swaine, 2010). It is proposed that the lower training intensity utilised by Baross, Wiles and Swaine (2012) would have likely produced an attenuated pressor response in comparison to the intensity utilised within this study (95%  $HR_{peak}$ ) while still producing the required hypotensive adaptations. Therefore if isometric wall squat training is to be completed by hypertensive individuals, it may be more suitable to prescribe exercise at a lower intensity as the attenuated pressor response may help to compensate for the higher initial BP levels and thus help to ensure that the ACSM exercise termination guidelines are not exceeded. Although it is important to consider that when participants trained at 95%  $HR_{peak}$  in the current study, HR was in the THRR for 58% of a training session. Lowering the intensity could possibly reduce the time spent in the THRR, however the exact training dose required to create a reduction in resting BP is unknown. It is possible that a longer intervention length may be required than that utilised within this thesis (4 weeks) if isometric wall squat training is to be completed at a lower intensity, as Baross, Wiles and Swaine (2012) did not find significant BP reductions until week 8. Furthermore, Baross, Wiles and Swaine (2012) also implemented an even lower intensity (70%  $HR_{peak}$ ) and found no significant BP reductions after 8 weeks of training. This finding may suggest that there could be an intensity threshold at which BP adaptations occur (Millar et al., 2013b). Therefore before recommending constant position isometric wall squat exercise to individuals with high BP, it is imperative to study the acute BP response to training at a range of intensities, such as 70%, 75%, 80%, 85%, and 90%  $HR_{peak}$ . The BP values obtained should then be compared to the ACSM exercise terminations guidelines or an individual specific BP limit prescribed by a medical practitioner to establish the relative safety of the pressor response. Furthermore, isometric wall squat training should be carried out at the intensities deemed to be suitable in order to establish the effectiveness of each intensity inducing resting BP reductions.

In addition to evaluating the isometric wall squat training intensity for hypertensive individuals, the method of prescribing intensity also needs to be reviewed for this population. In order to accurately determine the intensity for wall squat training, an individual would be required to complete a pre-training incremental isometric wall squat test under the supervision of an exercise specialist. During the incremental test participants would complete several work stages of increasing isometric wall squat exercise intensity (135°, 125°, 115°, 105° and 95°) to maximum, as completed within this thesis, from which  $HR_{peak}$  can be determined as well as the curvilinear relationship between HR and knee joint angle. From this an individualised wall squat knee joint angle can be prescribed in order to attain a specified percentage of  $HR_{peak}$  during training. However, maximal exercise tests such as this have several



limitations, one of which being the high level of motivation required for an individual to continue exercising until fatigue (Noonan and Dean, 2000). Furthermore, and more importantly, such a strenuous test may pose a safety risk for individuals with contraindications to exercise (Noonan and Dean, 2000), such as those suffering from hypertension (Whaley, Brubaker and Otto, 2006). One particular concern of an incremental isometric test would be the potential extreme pressor response experienced during the final stage completed at maximum intensity. For the normotensive participants studied within this thesis, the BP response to incremental wall squat exercise was deemed safe as SBP stayed below the ACSM exercise termination guidelines (< 250 mmHg) and DBP exceeded the upper level for only a limited duration (> 115 mmHg; Whaley, Brubaker and Otto, 2006). However, if this incremental test is to be completed by high-normal or hypertensive participants, these BP guidelines may be exceeded due to the exaggerated pressor response known to be experienced by individuals with higher initial resting BP levels (Ewing et al., 1973), see section 1.3.1 (page 6). To this end, it may be more appropriate for hypertensive individuals to complete a submaximal incremental isometric exercise test to predict maximum, as used with aerobic fitness tests (McArdle, Katch and Katch, 2010), however such a test has not previously been devised or utilised for isometric exercise and thus requires further investigation.

During submaximal aerobic tests, individuals complete several stages of aerobic exercise in increasing intensity from light to relatively heavy (McArdle, Katch and Katch, 2010). Assuming a linear relationship exists between HR and  $\dot{V}O_2$ , these values are plotted on a graph for each submaximal intensity and a line of best-fit is drawn through to the participant's assumed  $HR_{max}$  (McArdle, Katch and Katch, 2010). From the linear HR-  $\dot{V}O_2$  line drawn the required values can be extrapolated, such as  $\dot{V}O_{2max}$  (McArdle, Katch and Katch, 2010). A similar protocol could be utilised to devise a submaximal incremental isometric wall squat exercise test. It is suggested that participants could complete three stages of wall squat exercise (135°, 125° and 115°) and HR could be plotted for each knee joint angle. A curvilinear line could then be interpolated to a predicted  $HR_{peak}$ , from which the knee joint angle for the target training HR (%  $HR_{peak}$ ) could be extrapolated. It is important to highlight that  $HR_{peak}$  would be utilised rather than  $HR_{max}$ , as isometric exercise has been reported to produce submaximal, modest increases in HR in comparison to aerobic exercise (Lind, 2011). A generalised  $HR_{peak}$  predication equation would likely consider age, as does the traditional  $HR_{max}$  equation ( $HR_{max} = 220 - age$ ; Robergs and Landwehr, 2002), as  $HR_{max}$  has been found to decline with age (Tanaka, Monahan and Seals, 2001). Utilising a similar protocol to Tanaka, Monahan and Seals (2001), a  $HR_{peak}$  predication equation could be devised by a range of participants aged 20 to 80 completing a continuous, incremental isometric wall squat test until volitional exhaustion;  $HR_{peak}$  would then be plotted against age to calculate the  $HR_{peak}$  regression equation. Separate  $HR_{peak}$  predication equations may need to be created for normotensive and hypertensive participants who may produce a different cardiovascular response. While this proposed submaximal incremental isometric wall squat test appears to be a viable alternative method to predict  $HR_{peak}$  and consequently calculate the training intensity, research is required to establish the validity and reliability of this method.

A further point to consider is that while this thesis found significant reductions in resting BP following 4 weeks of isometric wall squat training in a normotensive population, the longevity of these BP adaptations was not established. To date it appears that three studies have reported detraining data following IET (Wiley et al., 1992; Howden et al., 2002; Devereux, 2010a). Wiley et al. (1992) was the first to report that the hypotensive effect of IET was reversible. Following 5 weeks of IHG, Wiley et al.

(1992) found significant reductions in resting BP, however 2 weeks after training had ceased BP had significantly increased and by week 5 gradually increased further so that BP had returned to pre-training values. These results suggested that BP adaptations were reversed by a length of time equal to the training intervention (Lawrence et al., 2014). However, Howden et al. (2002) reported that the BP adaptations following 5 weeks of leg and arm training had disappeared after only 10 days. Finally, detraining data was also reported in the doctoral thesis of Devereux (2010a) in which participants completed isometric double-leg extension exercise 3 times a week for 4 weeks at a constant EMG value prescribed to elicit a target HR of 95%  $HR_{peak}$ . While all BP parameters (SBP, DBP and MAP) significantly decreased following IET, these reductions were not evident 1 week after the training intervention ceased. The detraining BP values were reported to be significantly higher than the post-training BP and were not significantly different to the pre-training resting measures (Devereux, 2010a). Future research should look to establish the minimum training requirements to maintain the important BP adaptations after a significant BP reduction has been achieved. Lawrence et al. (2014) proposes that it may be possible to adapt the IET protocol so that the overall volume and/or intensity is reduced, while still maintaining the improved BP level.

Another possible consideration for future research is the actual application of isometric exercise as an intervention for the prevention and treatment of hypertension. While the home-based IET protocol developed within this thesis successfully reduced resting BP, there may be some limitations when translating this research into practice. Although there is a growing body of research demonstrating that IET can reduce resting BP in normotensive (Ray and Carrasco, 2000; McGowan et al., 2007a; Millar et al., 2008; Devereux, Wiles and Swaine, 2010b; Wiles, Coleman and Swaine, 2010), high-normal (Wiley et al., 1992; McGowan et al., 2007b; Baross, Wiles and Swaine, 2012) and hypertensive (Taylor et al., 2003; Peters et al., 2006; McGowan et al., 2007b; Millar et al., 2013a) populations, knowledge of this health benefit may not be sufficient to engage people with this form of exercise. Indeed, despite the widely acknowledged health benefits of aerobic and resistance exercise (Department of Health, 2004), a large proportion of the population still do not complete enough physical activity to meet the UK's recommendations. Indeed, the 2012 Health Survey for England (Scholes and Mindell, 2013) indicated that only 33% of men and 23% of women achieved both the aerobic and muscle-strengthening activity guidelines. It is recognised that there are clear gaps between the Government recommendations and the self-reported levels of activity (Bock, Jarczok and Litaker, 2014). Thus it is clear that the development of more effective interventions to encourage the adoption and maintenance of regular exercise is an important challenge that needs to be faced (Bélanger-Gravel, Godin and Amireault, 2013).

To this end, the inexpensive home-based programme outlined in this thesis was developed to provide a more accessible IET protocol for the reduction of resting BP and potentially reduce some of the well-known barriers to physical activity and exercise, such as cost (Belza et al., 2004; Allison et al., 2005; Lascar et al., 2014) and lack of time (Troost et al., 2002; Lascar et al., 2014). Such barriers may have been imposed by previous research due to the expensive equipment utilised and/or laboratory-based nature of the protocols (Ray and Carrasco, 2000; Taylor et al., 2003; McGowan et al., 2007a; 2007b; Devereux, Wiles and Swaine, 2010b; Wiles, Coleman and Swaine, 2010; Baross, Wiles and Swaine, 2012; Badrov et al., 2013a; 2013b; Stiller-Moldovan, Kenno and McGowan, 2012; Millar et al., 2013a). It is interesting to note that the dropout rate for the IET training programme developed within this thesis was low at 12.5%,

with only 4 out of 32 participants discontinuing the intervention. Further to this, the level of compliance was high (100%) as the 28 participants that completed the study reported that they performed all of the 12 training sessions prescribed. It is suggested that these figures reflect the accessibility of the IET developed within this thesis. However, it is possible that the dropout rate and compliance level may vary if the protocol were to be applied to a different population, such as older hypertensive individuals, or on a larger scale. In addition, while the home-based IET protocol developed within this thesis may have challenged the exercise barriers of cost and lack of time, as discussed in section 6.2 (page 157), it is acknowledged that these are only two of the many factors that may affect participation in physical activity and exercise (Bauman et al., 2002) and other factors may need to be explored in future research.

Furthermore, it has been suggested that a critical step in the development of any successful intervention involves the consideration of behaviour change (Michie, van Stralen and West, 2011). Certainly, behaviour can have a large effect on an individual's health (NICE, 2007; Abraham et al., 2009). However, as the 2012 Health Survey for England (Scholes and Mindell, 2013) statistics indicate above, attempts to change people's behaviour have often been unsuccessful, or only partially successful, and this is likely due to the fact that many approaches do not consider the key theories and principles required to plan and deliver an effective intervention (NICE, 2007). Three factors have been identified as important intervention characteristics that may influence behaviour: 1) the theoretical basis of the intervention; 2) the behaviour change technique; 3) the mode of delivery (Webb et al., 2010). First of all, many theoretical approaches have been applied to understand the adoption and maintenance of physical activity and the most common theories used are the Theory Planned Behaviour, Transtheoretical Model of Change and Social Cognitive Theory (Davis et al., 2014). Applying such theories may maximise the effectiveness of interventions (Michie and Prestwich, 2010; Davis et al., 2014) by identifying and targeting the causal determinants of behaviour change (Hardeman et al., 2005). To this end Michie and Prestwich (2010) developed a Theory Coding Scheme to describe and evaluate the theoretical basis of interventions. Secondly, behaviour change techniques have also been associated with the effectiveness of an intervention (Michie et al., 2009; Webb et al., 2010). Behaviour change techniques refer to the approaches utilised to promote behaviour change within an intervention, such as self-monitoring and barrier identification (Webb et al., 2010), to name a few. Abraham and Michie (2008) developed a taxonomy to facilitate the identification of effective behaviour change techniques for inclusion within an intervention; this taxonomy was later refined and improved for physical activity and healthy eating behaviours (Michie et al., 2011). Finally, the mode of delivery has also been shown to affect the success of an intervention (Webb et al., 2010) and includes many different methods for physical activity and exercise, such as public campaigns, face-to-face interaction, and email or telephone mediated interventions (Bock, Jarczok and Litaker, 2014). It is therefore acknowledged that in order to develop an effective intervention in the fight against hypertension, future IET protocols should incorporate the concept of behaviour change by including theory-based interventions that identify and utilise specific behaviour change techniques and modes of delivery. Developing an understanding of these concepts could be key to ensuring the effective adoption and maintenance of isometric exercise as an intervention for the prevention and treatment of hypertension.

Finally, it is also suggested that future research should investigate the potential for resting BP reductions to be gained when isometric work is completed as a form of physical activity. As highlighted at the

beginning of this thesis (section 1.1.2, page 2), physical activity and exercise are terms that describe different concepts (Caspersen, Powell and Christenson, 1985). Physical activity is any movement that results in energy expenditure, whereas exercise is a subcategory involving planned and structured activity to maintain or improve physical fitness (WHO, 2015). Traditionally physical activity guidelines have focused on structured exercise programmes for the attainment of health benefits (Troiano, Macera and Ballard-Barbash, 2001). For example, 30 minutes of moderate-intensity, aerobic exercise on most days of the week has been prescribed for the management of hypertension (Pescatello et al., 2004). However, this represents only 1.5% of an individual's week (Katzmarzyk, 2010). While exercise is still recommended, the importance of physical activity within an individual's daily routine is now also emphasised (Troiano, Macera and Ballard-Barbash, 2001), as highlighted in the recent Public Health England (2014) physical activity framework 'Everybody active, every day'. Examples of physical activity that can be built into someone's daily routine include taking the stairs not the lift and active travel, such as walking or cycling to the shops (Public Health England, 2014). This paradigm shift to focus on physical inactivity is mainly due to the risks associated with sedentary behaviour (Ekblom-Bak, Hellénus and Ekblom, 2010), such as obesity, type 2 diabetes, metabolic syndrome and cardiovascular disease (Hamilton, Hamilton and Zderic, 2007). It is proposed that the development of future guidelines should not only focus on exercise, but also encourage individuals to increase the amount of non-exercise daily activities (Ekblom-Bak, Hellénus and Ekblom, 2010). To this end, it is suggested that future research should not only investigate the efficacy of IET protocols, but also explore the potential for resting BP reductions to be attained when isometric contractions are completed within someone's daily routine. Such activities could include grasping, lifting, holding and pushing heavy items (Lind, 1970; Lind, 2011) along with contractions against immovable, fixed objects (Mitchell and Wildenthal, 1974). In fact this idea has already been partially explored in the seminal study by Buck and Donner (1985), which showed that jobs involving moderate or heavy occupational isometric activity reduced the incidence of hypertension among 4,273 men. Embedding activity as part of an individual's everyday routine may strengthen the degree of automaticity as the behaviour is repeated as part of everyday life and could lead to the formation of a habit (Verplanken and Melkevik, 2008). The concept of habit has been undervalued in the behavioural sciences (Verplanken and Melkevik, 2008), but may play an important role in the continuation of physical activity (Rhodes, de Bruijn and Matheson, 2010). To inform the development of future physical activity and hypertension guidelines, research should explore the potential for non-exercise isometric activity to reduce resting BP when performed in either isolation or alongside a structured IET protocol.

## **6.8 Conclusion**

Overall the work completed in this thesis led to the development of an accessible home-based isometric training protocol that successfully and safely lowered resting BP in a normotensive population. This finding adds to an increasing body of research which suggests that IET can produce significant reductions in resting BP (Wiley et al., 1992; Ray and Carrasco, 2000; Howden et al., 2002; Taylor et al., 2003; Peters et al., 2006; McGowan et al., 2007a; 2007b; Millar et al., 2008; Devereux, Wiles and Swaine, 2010b; Wiles, Coleman and Swaine, 2010; Baross, Wiles and Swaine, 2012; Badrov et al., 2013a; 2013b; Millar et al., 2013a). Furthermore, the new protocol designed also challenges some of the common exercise barriers, such as cost and lack of time, which have previously been imposed by IET studies due to the expensive and/or laboratory-based equipment used. The home-based programme developed within

this thesis prescribed a unique contraction style and exercise mode: constant position wall squat exercise, which required the use of relatively simple, inexpensive equipment. Due to this fact, it is suggested that the novel home-based IET protocol developed may be more time and cost effective than those previously implemented, which may consequently increase adherence and have a positive impact on the efficacy of IET.

In conclusion, the home-based isometric wall squat exercise could be used as a lifestyle modification for the prevention of high BP, which may help to reduce the health impact and economic burden that exists due to hypertension. It is highly recommended that future research should investigate the potential for isometric wall squat training to be utilised as an alternative treatment method to lower resting BP in a hypertensive population.

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**APPENDIX 1**

**HEALTH AND MEDICAL QUESTIONNAIRE**

**Name:** .....

**Date of Birth:** .....      **Age:** .....      **Sex:** .....

**Contact Details**

**Address:**  
.....  
.....

**Telephone Number:** .....

**Mobile Number:** .....

**Email Address:** .....

Please answer the following questions by **circling** the appropriate response and if necessary providing extra information in the spaces provided.

**ANY INFORMATION CONTAINED HEREIN WILL BE TREATED AS CONFIDENTIAL**

1. How would you describe your present bodyweight?  
Underweight / Ideal / Slightly overweight / Very overweight
2. How would you describe your smoking habits?  
Non smoker / Previous smoker / Currently smoking
3. If you were a previous smoker, how long ago did you quit? .....  
(If you were not a previous smoker please move on to question 4)
4. How would you describe your alcohol intake?  
Never Drink / An occasional drink / A drink every day / More than one drink a day  
(Note 1 drink = 1 unit)
5. Have you had to consult your doctor within the last six months? **Yes / No**  
If you have answered **yes**, please give details: .....
6. Are you presently taking any form of medication? **Yes / No**  
If you have answered **yes**, please give details: .....

7. Do you suffer or have you ever suffered from any of the following?
- |                                |          |   |          |
|--------------------------------|----------|---|----------|
| a. Diabetes                    | Yes / No | b. Asthma   | Yes / No |
| c. Epilepsy                    | Yes / No | d. Bronchitis                                     | Yes / No |
| e. Any form of heart complaint | Yes / No | f. Serious Back or Neck Injury                    | Yes / No |
| g. High blood pressure         | Yes / No | h. Aneurysm <sup>1</sup> or Embolism <sup>2</sup> | Yes / No |
- 1: Arterial wall weakness causing dilation.                      2: Obstruction in the Artery.
8. Is there a history of heart complaint in your family? Yes / No  
 If you have answered **yes**, please give details .....
9. Do you have any allergies? Yes / No  
 If you have answered **yes**, please give details: .....
10. Do you currently have any form of muscle or joint injury? Yes / No  
 If you have answered **yes**, please give details: .....
11. Have you had to suspend your normal training/physical activity in the last two weeks? Yes / No  
 If you have answered **yes**, please give details: .....

**Signature of Participant:** ..... **Date:** .....

<u>To be completed by the researcher</u>	
<b>Resting systolic blood pressure (mmHg):</b>	.....
<b>Resting diastolic blood pressure (mmHg):</b>	.....
<b>Blood pressure category (Williams et al., 2004):</b>	.....
<b>Resting heart rate (beats·min<sup>-1</sup>):</b>	.....
<b>Signature of Researcher:</b> ..... <b>Date:</b> .....	

Williams, B., Poulter, N. R., Brown, M. J., Davis, M., McInnes, G. T., Potter, J. F., Sever, P. S. and McG Thom, S. (2004) 'Guidelines for management of hypertension: report of the fourth working party of the British Hypertension Society, 2004-BHS IV', Journal of Human Hypertension, 18 (3), pp. 139–85.

## **APPENDIX 2**

“The acute effects of isometric wall squat exercise on heart rate and blood pressure”

### **STUDY 1 PARTICIPANT INFORMATION**

This research study is being conducted at Canterbury Christ Church University (CCCU), as part of a PhD thesis by Natalie Goldring. Dr Jonathan Wiles, Senior Lecturer in Sport and Exercise Physiology at CCCU, is my 1<sup>st</sup> supervisor and Dr Damian Coleman, Principal Lecturer at CCCU, is my 2<sup>nd</sup> supervisor.

#### **Background**

Cardiovascular disease (CVD) is a major cause of death and ill health; high blood pressure (hypertension) is associated with increased risk of CVD. It is generally acknowledged that isometric exercise can cause a reduction in resting blood pressure and consequently decrease the risk of CVD. Isometric exercise is a type of resistance training that is performed in a static position in which the joint angle and muscle length do not change during the contraction (see Figure 1). Previous research conducted within this Department has demonstrated significant reductions in resting blood pressure after just 4 weeks of isometric exercise. However this research was laboratory-based and has not established the effectiveness of this type of exercise training in the privacy and comfort of the participant’s home. Furthermore there has been no previous work examining the efficacy of isometric exercise training when performing a basic exercise such as an isometric wall squat. In order for an isometric wall squat exercise to be prescribed in the home safely and effectively, it is essential to determine a means by which the intensity of exercise can be adjusted to elicit beneficial physiological adaptations, such as a decrease in resting blood pressure. The aim of this study is to determine the relationship between heart rate, blood pressure and exercise intensity during an isometric wall squat.

#### **What would you be required to do?**

If you decide to participate you will be asked to visit the Sport Science laboratory at Canterbury Christ Church University, North Holmes Road (room Ag86), for 30 minutes on 16 separate occasions on days that are convenient to you.

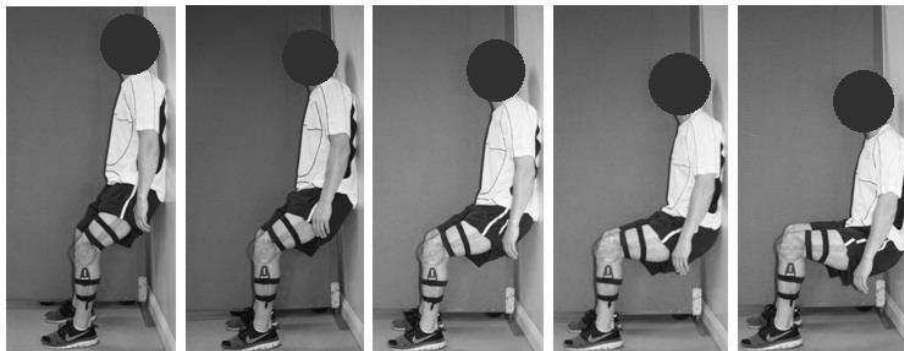
#### **Visit 1: Familiarisation**

During the first visit you will be introduced to the isometric wall squat technique (see Figure 1), as well as the protocol, equipment and testing procedures to be used in the study. You will also be required to fill in a short questionnaire about your current health status. Then your resting blood pressure and heart rate will be measured. Your blood pressure will be compared to current UK guidelines (British Hypertension Society, 2004). If, for any reason, your blood pressure level is high it will be recommended that you have your blood pressure status confirmed by a qualified medical practitioner. In order to facilitate this process you will be produced with a standard feedback letter detailing your blood pressure results. Should a qualified medical practitioner diagnose high blood pressure then you will be unable to participate in this particular research study.

Once the preliminary health screening has been successfully completed you will be given the opportunity to raise any questions you may have regarding the nature of the study before being asked to sign an informed consent form.

### Visits 2 to 6: Isometric wall squat exercise

At the start of each visit you will be required to rest for 10 minutes after which time resting heart rate and blood pressure will be taken. You will then be required to perform one isometric wall squat lasting 2 minutes or until you reach fatigue i.e. the point at which you cannot carry on. During each visit the wall squat position will be changed by manipulating the knee angle (see Figure 1). One of the following knee angles will be randomly assigned each visit; 135°, 130°, 125°, 120°, 115°, 110°, 105°, 100°, 95°, 90°. During the first ten visits all ten knee angles will be completed. Over the remaining five visits one of the aforementioned knee angles will be randomly assigned and repeated.



**Figure 1.** Different wall squat knee joint angles displayed in order of increasing knee flexion: 135°, 125°, 115°, 105°, 95° (left to right).

### Testing requirements

Pre-assessment requirements are:

- ❖ No caffeine (tea, coffee, fizzy drinks, chocolate) within 4 hours of the assessment
- ❖ No alcohol within 12 hours of the assessment
- ❖ No strenuous physical exercise within 24 hours of the assessment. If you feel fatigued prior to testing please do not hesitate to inform me straight away and I will rearrange your visit
- ❖ No food within 2 hours of the assessment
- ❖ Maintain regular dietary habits and levels of physical activity throughout the testing period
- ❖ Not to be taking any medication that may affect cardiovascular function
- ❖ Participants must be non-smokers

It is also imperative that participants are free from any medical condition that could conceivably affect their performance. As such if you fall ill or get injured during the study, please do not hesitate to inform me straight away and I will rearrange your visits accordingly.

Listed below are measures that will be recorded during the assessment. Some of the terms may be new to you. If you would like detailed descriptions of any of the measurements do not hesitate to contact me.

The assessment will involve:

- ❖ ECG (measurement of your heart rate)
- ❖ Blood pressure measurement
- ❖ Knee joint angle measurement

What to Wear

Light, comfortable clothing should be worn. Due to the fitting of monitoring equipment it will be necessary to wear shorts and a t-shirt for all tests.

### **Benefits**

The completion of a standard health screen, which includes the measurement of blood pressure and heart rate, provides you with an ideal opportunity to discuss the health benefits of exercise with a qualified Sport Scientist. You will also learn how to perform isometric exercise and gain knowledge about the potential health benefits associated with isometric exercise. Additionally, there will be further opportunities (if you so wish) to become involved in a subsequent research study where you will be personally trained using a structured isometric exercise program with regular feedback on your progress.

### **Potential risks**

Isometric exercise is known to be associated with a rise in blood pressure and heart rate during exercise, but there is currently no evidence to suggest that this presents an risk to healthy individuals. Furthermore for those unaccustomed to isometric exercise training, this type of activity may be perceived as being uncomfortable and may also lead to some muscle soreness in the following 48 hour period. This is perfectly normal and will have no long lasting effects. This study has been approved by the Canterbury Christ Church University Ethics Committee and all procedures were conducted according to the Declaration of Helsinki.

### **Feedback**

After your involvement in the study is complete, you will receive feedback on your assessment results.

### **Confidentiality**

All measurements (data) and personal information will be stored securely within CCCU at the Department of Sport Science, Tourism and Leisure. Data can only be accessed by Natalie Goldring and the two supervisors Dr Jonathan Wiles and Dr Damian Coleman. After completion of the study all data will be made anonymous (i.e. all personal information associated with the data will be removed).

### **Dissemination of results**

The results of the study may be published, however all participants will be made anonymous.

**Deciding whether to participate**

You should take a few days to read and digest the information in this document. If you have any questions or concerns about the nature, procedures or requirements for participation do not hesitate to contact me on the telephone number or e-mail address listed below. Participation in this study is entirely voluntary, and you may withdraw at any time during the study period.

Please contact:

Natalie Goldring

**Tel:** 01227 767700 ext. 3198

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### **APPENDIX 3**

“The relationship between exercise intensity, heart rate, and blood pressure during an incremental isometric wall squat exercise test”

#### **STUDY 2 PARTICIPANT INFORMATION**

This research study is being conducted at Canterbury Christ Church University (CCCU), as part of a PhD thesis by Natalie Goldring. Dr Jonathan Wiles, Senior Lecturer in Sport and Exercise Physiology at CCCU, is the 1<sup>st</sup> supervisor and Dr Damian Coleman, Principal Lecturer at CCCU, is the 2<sup>nd</sup> supervisor.

#### **Background**

Cardiovascular disease (CVD) is a major cause of death and ill health; high blood pressure (hypertension) is associated with increased risk of CVD. It is generally acknowledged that isometric exercise can cause a reduction in resting blood pressure and consequently decrease the risk of CVD. Isometric exercise is a type of resistance training that is performed in a static position in which the joint angle and muscle length do not change during the contraction (see Figure 1). Previous research conducted within the Department of Sport Science, Tourism & Leisure has demonstrated significant reductions in resting blood pressure after just 4 weeks of isometric exercise. However this research was purely laboratory-based and has not established the effectiveness of this type of exercise training when conducted in the privacy and comfort of the participant’s home. Furthermore there has been no previous work to establish the efficacy of the isometric wall squat as a valid method of performing isometric exercise training. In order for isometric wall squat exercise training to be completed in the home safely and effectively, it is essential to determine a means by which the intensity of exercise can be prescribed to elicit beneficial physiological adaptations, such as a decrease in resting blood pressure. The aim of this study is to determine the relationship between heart rate, blood pressure and exercise intensity during an incremental isometric wall squat exercise test.

#### **What would you be required to do?**

If you decide to participate you will be asked to visit the Sport Science laboratory at Canterbury Christ Church University, North Holmes Road (room Ag86), on 5 separate occasions. Each visit will last no longer than 45 minutes.

#### **Visit 1: Familiarisation**

During the first visit you will be introduced to the isometric wall squat technique (see Figure 1), as well as the protocol, equipment and testing procedures to be used in the study. You will also be required to fill in a short questionnaire about your current health status. Then your resting blood pressure and heart rate will be measured. Your blood pressure will be compared to current UK guidelines (British Hypertension Society 2004). If, for any reason, your blood pressure level is high it will be recommended that you have your blood pressure status confirmed by a qualified medical practitioner. In order to facilitate this process you will be produced with a standard feedback letter detailing your blood pressure results. Should a

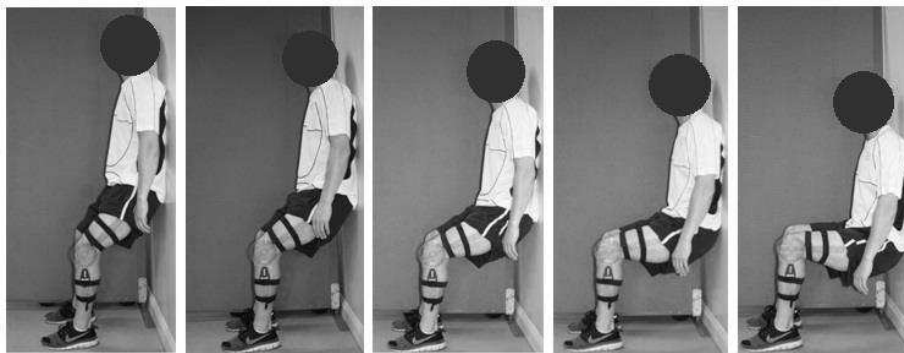


qualified medical practitioner diagnose high blood pressure then you will be unable to participate in this particular research study.

Once the preliminary health screening has been successfully completed you will be given the opportunity to raise any questions you may have regarding the nature of the study before being asked to sign an informed consent form.

### **Visits 2 and 3: Incremental isometric wall squat exercise test**

Upon visiting the laboratory you will be required to rest for 10 minutes after which time resting heart rate and blood pressure will be taken. You will then be required to perform an incremental isometric wall squat exercise test (see Figure 1). This test consists of 5 continuous stages in which the wall squat exercise intensity will be altered in descending order (knee joint angles of 135°, 125°, 115°, 105°, 95°). Each stage will last 2 minutes or until you reach voluntary fatigue i.e. the point at which you cannot carry on. Throughout each stage heart rate and blood pressure will be monitored and recorded.



**Figure 1.** Different wall squat knee joint angles displayed in order of increasing knee flexion: 135°, 125°, 115°, 105°, 95° (left to right).

### **Visits 4 and 5: Isometric wall squat exercise training**

Upon visiting the laboratory you will be required to rest for 10 minutes after which time resting heart rate and blood pressure will be taken. You will then be required to perform four isometric wall squats exercises. Each exercise will last 2 minutes or until you reach voluntary fatigue i.e. the point at which you decide that you cannot carry on. You will be given 2 minutes rest between each wall squat exercise. During the wall squat exercises you will be working at a precise knee joint angle which will be calculated from the incremental isometric wall squat exercise test completed in visits 1 and 2.

### **Testing requirements**

Pre-assessment requirements are:

- ❖ No caffeine (tea, coffee, fizzy drinks, chocolate) within 4 hours of the assessment
- ❖ No alcohol within 12 hours of the assessment
- ❖ No strenuous physical exercise within 24 hours of the assessment. If you feel fatigued prior to testing please do not hesitate to inform me straight away and I will rearrange your visit

- ❖ No food within 2 hours of the assessment
- ❖ Maintain regular dietary habits and levels of physical activity throughout the testing period
- ❖ Not to be taking any medication that may affect cardiovascular function
- ❖ Participants must be non-smokers

It is also imperative that participants are free from any medical condition that could conceivably affect their performance. As such if you fall ill or get injured during the study, please do not hesitate to inform me straight away and I will rearrange your visits accordingly.

Listed below are measures that will be recorded during the assessment. Some of the terms may be new to you. If you would like detailed descriptions of any of the measurements do not hesitate to contact me.

The assessment will involve:

- ❖ ECG (measurement of your heart rate)
- ❖ Blood pressure measurement
- ❖ Knee joint angle measurement

What to Wear

Light, comfortable clothing should be worn. Due to the fitting of monitoring equipment it will be necessary to wear shorts and a t-shirt for all tests.

### **Benefits**

The completion of a standard health screen, which includes the measurement of blood pressure and heart rate, provides you with an ideal opportunity to discuss the health benefits of exercise with a qualified Sport Scientist. You will also learn how to perform isometric exercise and gain knowledge about the potential health benefits associated with isometric exercise. Additionally, there will be further opportunities (if you so wish) to become involved in a subsequent research study where you will be personally trained using a structured isometric exercise program with regular feedback on your progress.

### **Potential risks**

Isometric exercise is known to be associated with a rise in blood pressure and heart rate during exercise, but there is currently no evidence to suggest that this presents an risk to healthy individuals. Furthermore for those unaccustomed to isometric exercise training, this type of activity may be perceived as being uncomfortable and may also lead to some muscle soreness in the following 48 hour period. This is perfectly normal and will have no long lasting effects. This study has been approved by the Canterbury Christ Church University Ethics Committee and all procedures were conducted according to the Declaration of Helsinki.

### **Feedback**

After your involvement in the study is complete, you will receive feedback on your assessment results.

**Confidentiality**

All measurements (data) and personal information will be stored securely within CCCU at the Department of Sport Science, Tourism and Leisure. Data can only be accessed by Natalie Goldring and the two supervisors Dr Jonathan Wiles and Dr Damian Coleman. After completion of the study all data will be made anonymous (i.e. all personal information associated with the data will be removed).

**Dissemination of results**

The results of the study may be published, however all participants will be made anonymous.

**Deciding whether to participate**

You should take a few days to read and digest the information in this document. If you have any questions or concerns about the nature, procedures or requirements for participation do not hesitate to contact me on the telephone number or e-mail address listed below. Participation in this study is entirely voluntary, and you may withdraw at any time during the study period.

Please contact:

Natalie Goldring

**Tel:** 01227 767700 ext. 3198

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Supervisor information:

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## **APPENDIX 4**

“The effects of a four week home-based isometric exercise training programme on resting blood pressure and other cardiovascular variables”

### **STUDY 3 PARTICIPANT INFORMATION**

A research study is being conducted at Canterbury Christ Church University (CCCU) as part of a thesis by Natalie Goldring. Dr Jonathan Wiles, Senior Lecturer in Sport and Exercise Physiology at CCCU, is my 1<sup>st</sup> supervisor and Dr Damian Coleman, Principal Lecturer at CCCU, is my 2<sup>nd</sup> supervisor.

#### **Background**

The beneficial effects of continuous aerobic exercise such as walking, jogging or cycling upon cardiovascular health are well documented. However, the effect of regular isometric exercise (the production of force without movement, i.e. a static muscle contraction) on cardiovascular parameters is less well understood. It is generally acknowledged that isometric exercise can cause a reduction in resting blood pressure; however this research is laboratory-based and the effectiveness of this type of isometric exercise training in the privacy and comfort of someone’s home has not been established. Furthermore there has been no previous work using the simple isometric wall squat (see Figure 1) as an exercise for isometric training. As a result, this study aims to determine whether the simple wall squat exercise can be successfully used to reduce resting blood pressure after 4 weeks of home-based isometric training.

#### **What will you be required to do?**

If you decide to participate in this study, you will be asked to visit the Sport Science laboratory at Canterbury Christ Church University, North Holmes Road (room Ag86), for 30-45 minutes on 8 separate occasions and complete a 4 week home-based isometric training programme.

To obtain the necessary data for analysis in this study, participants need to be willing to perform:

1. An initial familiarisation visit (30 minutes).
2. A 4 week resting period with cardiovascular variables measured before and after the 4 week rest period.
3. An incremental isometric wall squat exercise test (approximately 10 minutes of exercise).
4. An individual home-based isometric training programme, (8 minutes of exercise, 3 times per week for 4 consecutive weeks) with cardiovascular variables measured before and after the 4 week training period.

#### **To participate in this research you must:**

- Be aged 18 to 45.
- Be a healthy male, non smoker.
- Not have a musculoskeletal injury.
- Have no known medical problems that may impair your ability to participate in the study in any way.

- Have been free from illness/infection for the preceding 2 weeks to testing.
- Not be receiving any treatment for any medical conditions.
- Not be on any drugs or medication that might interfere with the physiological measures of the study and/or not to have been on medication for the preceding 4 weeks prior to testing.
- Have blood pressure < 140 mmHg systolic and < 90 mmHg diastolic.

### **Procedures**

#### **Familiarisation**

Upon arrival to the Sport Science laboratory you will be asked to complete a standard health and medical questionnaire and will then have your resting blood pressure taken. Before starting any exercise testing, you will be informed of your resting blood pressure in relation to current UK guidelines (British Hypertension Society 2004). If, for any reason, your blood pressure level is high it will be recommended that you have your blood pressure status confirmed by a qualified medical practitioner. In order to facilitate this process you will be issued with a standard feedback letter detailing your blood pressure results. Should a qualified medical practitioner diagnose high blood pressure then you will be unable to participate in this particular research study.

Once the preliminary health screening has been successfully completed you will be given the opportunity to raise any questions you may have regarding the nature of the study before being asked to sign an informed consent form. Following this you will be introduced to the isometric wall squat exercise, as well being familiarised with the protocol, equipment and testing procedures to be used in the study.

#### **Four week resting period**

During this 4 week rest period you will NOT be required to visit the Sport Science Laboratory. During this rest period you will just be asked to refrain from isometric exercise and any form of exercise that you are not accustomed to.

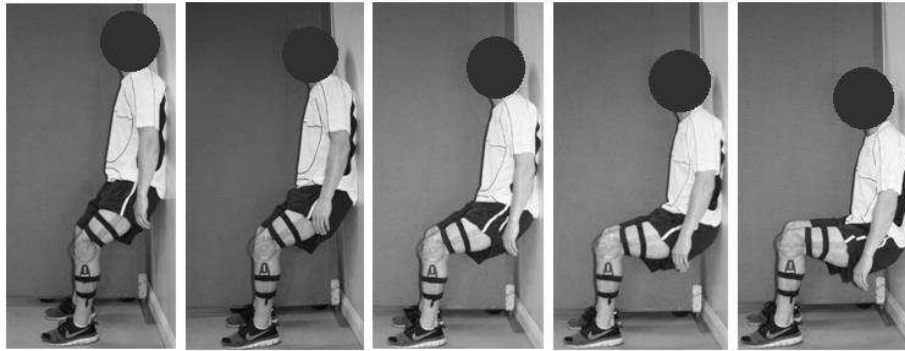
You will be required to come to the Sport Science Laboratory before and after the 4 week rest period to have resting measures of several cardiovascular variables, such as blood pressure and heart rate.

#### **Incremental isometric wall squat exercise test**

You will be required to visit the Sport Science laboratory to complete an initial incremental isometric wall squat exercise test, which will last approximately 10 minutes. This test will be used to determine how hard you have to work during the 4 week home-based isometric training programme.

The incremental test is split into 2 minute stages and over time the exercise will get harder. You will begin the incremental test at an easy exercise position of 135° knee joint angle, see Figure 1. This position will be held for 2 minutes. After this 2 minute stage the exercise will gradually get harder; the knee joint angle will be decreased by 10°. The exercise will get harder every 2 minutes until you reach the last stage

(see Figure 1) or until you feel you cannot exercise any longer. It is a continuous test so there will be no rest between stages. Heart rate and blood pressure will be recorded throughout the exercise.



**Figure 1.** Different wall squat knee joint angles displayed in order of increasing knee flexion: 135°, 125°, 115°, 105°, 95° (left to right).

#### **Four week home-based isometric training sessions**

You will be required to complete a 4 week home-based isometric exercise training programme. Training will be completed 3 days a week (12 training sessions in total). The first training session will be completed in the Sport Science laboratory; thereafter all training sessions will be completed in a location of your choice. Each training session will consist of 4 isometric wall squats at a fixed exercise position. Each isometric wall squat will last 2 minutes and there will be 2 minutes of seated rest between each exercise.

You will be required to come to the Sport Science laboratory before and after the 4 week training period to have resting measures of several cardiovascular variables, such as blood pressure and heart rate.

#### **Testing requirements**

Pre-assessment requirements are:

- ❖ No caffeine (tea, coffee, fizzy drinks, chocolate) within 4 hours of the assessment
- ❖ No alcohol within 12 hours of the assessment
- ❖ No strenuous physical exercise within 24 hours of the assessment. If you feel fatigued prior to testing please do not hesitate to inform me straight away and I will rearrange your visit
- ❖ No food within 2 hours of the assessment
- ❖ Maintain regular dietary habits and levels of physical activity throughout the testing period

It is also imperative that participants are free from any medical condition that could conceivably affect their performance. As such if you fall ill or get injured during the study, please do not hesitate to inform me straight away and I will rearrange your visits accordingly.

Listed below are measures that will be recorded during the assessment. Some of the terms may be new to you. If you would like detailed descriptions of any of the measurements do not hesitate to contact me.

The assessment will involve:

- ❖ ECG (measurement of your heart rate)
- ❖ Blood pressure measurement
- ❖ Other cardiovascular variables such as cardiac output, total peripheral resistance and stroke volume, will also be measured.
- ❖ Knee joint angle measurement

What to Wear

Light, comfortable clothing should be worn. Due to the fitting of monitoring equipment it will be necessary to wear shorts and a t-shirt for all tests.

### **Benefits**

The completion of a standardized health screen, which includes the measurement of blood pressure, provides you with an ideal opportunity to discuss the health and fitness benefits of exercise with a qualified Sport Scientist. Over the 4 week training period you may well experience improvements in isometric leg strength and cardiovascular variables associated with long term health.

Since this is a training study you will receive personal training using a structured isometric exercise programme along with regular feedback on your progress. You will also experience firsthand how to use scientific principles to inform your own training and learn how to exercise at appropriate levels of intensity.

Additionally there will be further opportunities (if you so wish) to become involved in future research investigations with similar benefits.

### **Potential risks**

Isometric exercise is known to be associated with a rise in blood pressure and heart rate during exercise, but there is currently no evidence to suggest that this presents a risk to healthy individuals. Furthermore for those unaccustomed to isometric exercise training, this type of activity may be perceived as being uncomfortable and may also lead to some muscle soreness in the following 48 hour period. This is perfectly normal and will have no long lasting effects. This study has been approved by the Canterbury Christ Church University Ethics Committee and all procedures were conducted according to the Declaration of Helsinki.

### **Feedback**

After your involvement in the study is complete, you will receive feedback on your assessment results.

### **Confidentiality**

All data and personal information will be stored securely within CCCU at the Department of Sport Science, Tourism and Leisure in accordance with the Data Protection Act 1998 and the University's own

data protection requirements. Data can only be accessed by Natalie Goldring and the two supervisors Dr Jonathan Wiles and Dr Damian Coleman. After completion of the study, all data will be made anonymous (i.e. all personal information associated with the data will be removed).

**Dissemination of results**

The results of the study may be published, however all participants will be made anonymous.

**Deciding whether to participate**

If you have any questions or concerns about the nature, procedures or requirements for participation do not hesitate to contact me. Should you decide to participate, you will be free to withdraw at any time without having to give a reason.

**Any questions?**

Please contact Natalie Goldring:

**Address:** Ag53, Department of Sport Science, Tourism and Leisure, Canterbury Christ Church University, North Holmes Road, Canterbury, Kent, CT1 1QU

**Tel:** 01227 767700 ext. 3198

**Email:** natalie.goldring@canterbury.ac.uk





**APPENDIX 5**

“The acute effects of isometric wall squat exercise on heart rate and blood pressure”

**INFORMED CONSENT**

The full details of the above study have been explained to me. I am clear about what will be involved and I am aware of the purpose of the assessments.

I understand that all assessments are non-medical and are not for diagnosis of any medical condition.

I know that I am not obliged to complete the assessments. I am free to stop the assessments at any point and for any reason, without explanation.

I know that I can withdraw from the study at any point and for any reason, without explanation.

I am aware of no medical condition that might put me at increased risk during my participation in the exercise protocols as described to me.

Signature of Participant: .....

Printed Name of Participant: .....

Date: .....

Signature of Researcher: .....



## APPENDIX 6

### INFORMED CONSENT

**Title of Project:** The effects of a four week home-based isometric exercise training programme on resting blood pressure and other cardiovascular variables

**Name of Researcher:** Miss Natalie Goldring

**Contact details:**

**Address:** Ag53, Department of Sport Science, Leisure and Tourism  
Canterbury Christ Church University  
North Holmes Road  
Canterbury  
Kent  
CT1 1QU

**Tel:** 01227 767700 ext. 3198

**Email:** natalie.goldring@canterbury.ac.uk

**Please initial box**

- |   |                          |
|---|--------------------------|
| 1. I confirm that I have read and understand the information sheet for the above study and have had the opportunity to ask questions. | <input type="checkbox"/> |
| 2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason.             | <input type="checkbox"/> |
| 3. I understand that any personal information that I provide to the researchers will be kept strictly confidential                    | <input type="checkbox"/> |
| 4. I agree to take part in the above study.   | <input type="checkbox"/> |

Name of Participant	Date	Signature

Name of Person taking consent (if different from researcher)	Date	Signature

Researcher	Date	Signature



**APPENDIX 7**

Miss Natalie Goldring  
Ag53  
Department of Sport Science, Tourism and Leisure  
Canterbury Christ Church University  
North Holmes Road  
Canterbury  
Kent  
CT1 1QU  
Tel: 01227 767700 ext. 3198  
Email: natalie.goldring@canterbury.ac.uk

Dear Sir/Madam

**RE: (PARTICIPANT NAME) BLOOD PRESSURE LEVEL**

The above individual volunteered to take part in a study at Canterbury Christ Church University. A prerequisite of the study is having a resting blood pressure < 140 mmHg systolic and < 90 mmHg diastolic in accordance with the British Hypertension Society guidelines (2004). Blood pressure measurements were taken using an automated BP monitor (Dinamap Pro 200, GE Medical Systems). The participant had been resting for 10 minutes in a seated position prior to measurement. The participant's measures are recorded below and it was recommended that they arrange an appointment to confirm these measurements.

<b>Date</b>	
<b>Time</b>	
<b>Average BP (mmHg)</b>	
<b>Maximum BP (mmHg)</b>	
<b>Minimum BP (mmHg)</b>	

If you require any more information please do not hesitate to contact me at the above address.

Yours sincerely,

Miss Natalie Goldring

BSc (Hons) Sport and Exercise Science



## APPENDIX 8

### TRAINING MANUAL

Name: ..... Participant I.D: .....

#### **Training Session Information**

- You will complete 12 training sessions in total over a 4 week period (3 sessions per week).
- Each training session requires you to perform a total of 4 wall squat exercises each lasting 2 minutes.
- Each wall squat will be performed at a specific angle (calculated from your incremental test) so that you reach your target heart rate.
- There will be 2 minutes seated rest between each wall squat.
- Each training session will last 14 minutes in total (see Exercise Protocol, *section 3*).

**Your wall squat training angle is:** .....

**Your target heart rate is:** .....

- You must leave 48 hours between each training session to ensure adequate recovery.
- You should try to ensure that all training sessions are at the same time of the day (*see Training Timetable, section 9*).
- You must adhere to the pre-training session requirements (*see section 4*).

#### **Equipment**

You will be given the following equipment to use whilst exercising at home:

##### **1. Bend and Squat Device**

- The Bend & Squat is a piece of exercise equipment designed to ensure that you are squatting at the correct angle.
- You will need to adjust the Bend & Squat for your specific training angle (*see Bend & Squat Instructions, section 5*).
- Your Bend & Squat measurements are: **WALL:** ..... **FLOOR:** .....
- You must ensure that the Bend & Squat is always set to these measurements before use.
- For instructions on how to use the Bend & Squat to perform the Isometric Wall Squat Exercise see *section 6*.

##### **2. Heart Rate Monitor**

- You will record heart rate throughout the wall squat using the heart rate monitor provided (*see Heart Rate Monitor Instructions, section 7*).
- At the end of every 2 minute wall squat you need to write down your heart rate on the Data Sheet provided (*see section 1*).
- At the end of every training session you will need to text or email Natalie Goldring your heart rate data for the 4 exercises (*see Sending Data, section 8*).
- Your heart rate monitor will be replaced at the end of each week so that your data can be downloaded.

##### **3. Rate of Perceived Discomfort (RPD) Scale**

- You will be provided with an RPD scale (*see section 2*). This scale is used to measure how much discomfort you feel there is in your legs.
- At the end of every 2 minute wall squat you need to write down your RPD on the Data Sheet provided (*see section 1*). \*You do **NOT** need to text or email your RPD data.



**SECTIONS**

1. Data Sheet
2. Rate of Perceived Discomfort (RPD) Scale
3. Exercise Protocol
4. Pre-Training Session Requirements
5. Bend & Squat Instructions
6. Isometric Wall Squat Exercise
7. Heart Rate Monitor Instructions
8. Sending Data
9. Training Session Timetable
10. Breathe Sign
11. Disclaimer

SECTION 1: DATA SHEET

- Please record your heart rate and RPD at the end of **EVERY 2 minute wall squat exercise**.
- Please send me your **heart rate** data after **EVERY TRAINING SESSION**

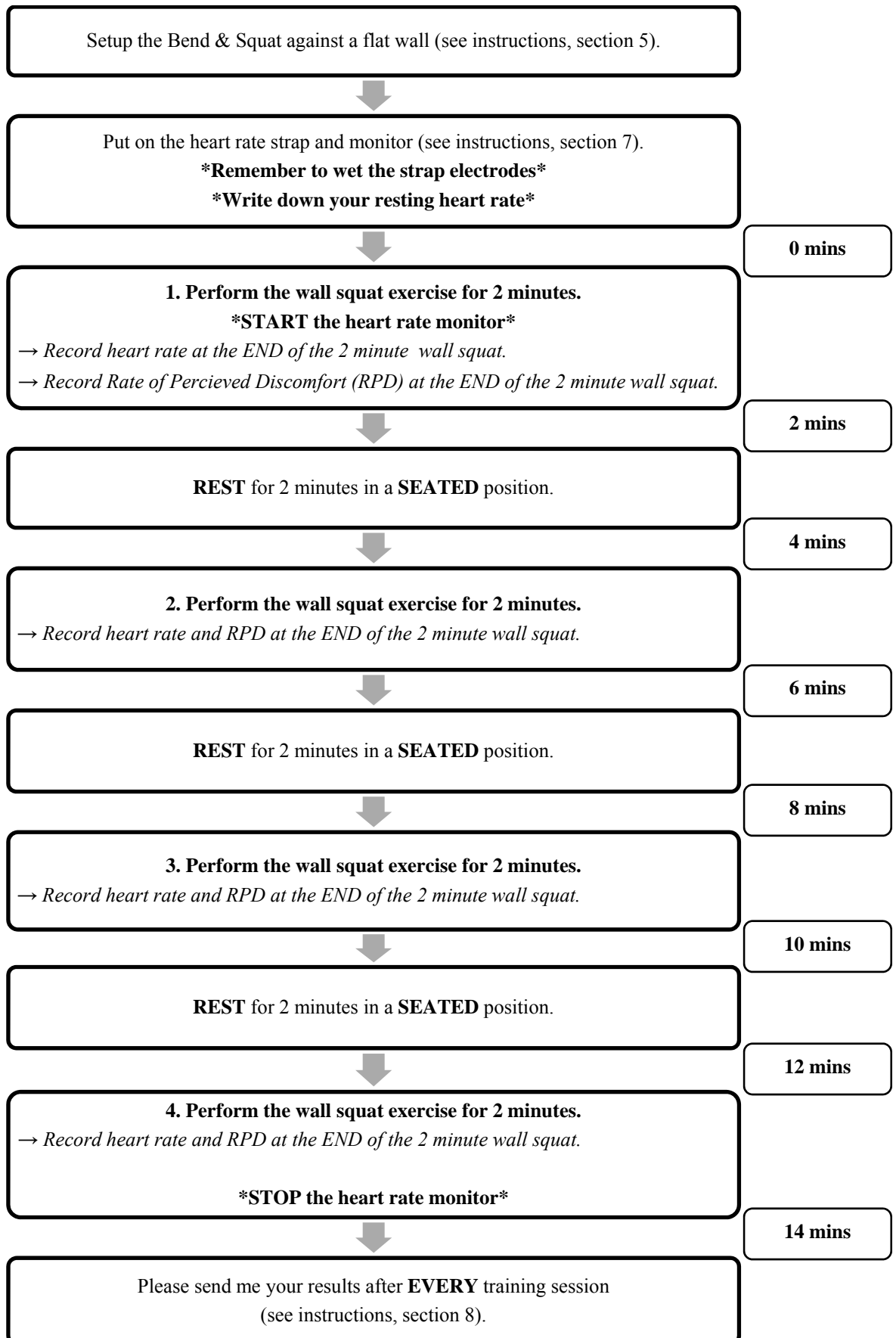
	Training Session	Resting Heart Rate	Exercise 1		Exercise 2		Exercise 3		Exercise 4	
			Heart Rate	RPD	Heart Rate	RPD	Heart Rate	RPD	Heart Rate	RPD
W E E K 1	1									
	2									
	3									
W E E K 2	4									
	5									
	6									
W E E K 3	7									
	8									
	9									
W E E K 4	10									
	11									
	12									

**SECTION 2: RATE OF PERCEIVED DISCOMFORT (RPD) SCALE**

This scale is used to measure how much discomfort you feel there is in your legs.

0	Nothing at all	“No P”
0.3		
0.5	Extremely weak	Just noticeable
1	Very weak	
1.5		
2	Weak	Light
2.5		
3	Moderate	
4		
5	Strong	Heavy
6		
7	Very Strong	
8		
9		
<b>10</b>	<b>Extremely strong</b>	<b>“Max P”</b>
11		
‡		
●	Absolute maximum	Highest possible

## SECTION 3: EXERCISE PROTOCOL



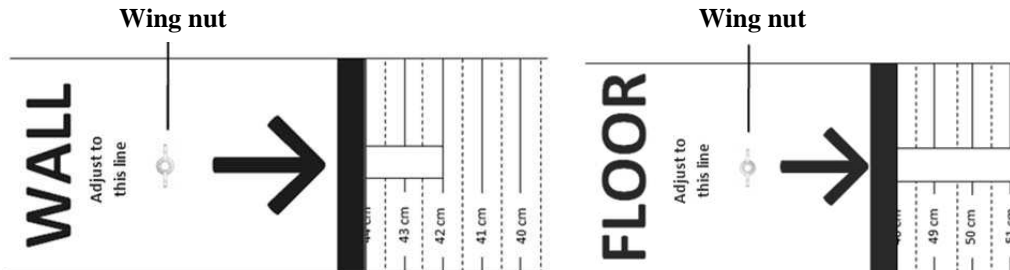
**SECTION 4: PRE-TRAINING SESSION REQUIREMENTS**

Please adhere to the following before EVERY training session:

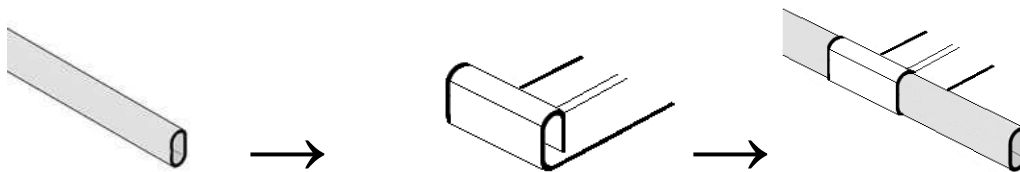
- No caffeine (tea, coffee, fizzy drinks, chocolate) 4 hours before a training session
- No alcohol 12 hours before a training session
- No strenuous physical exercise 24 hours before a training session. If you feel fatigued prior to training please do not hesitate to contact Natalie Goldring for advice.
- No food 2 hours before a training session, however you are allowed to drink water.

SECTION 5: BEND & SQUAT INSTRUCTIONS

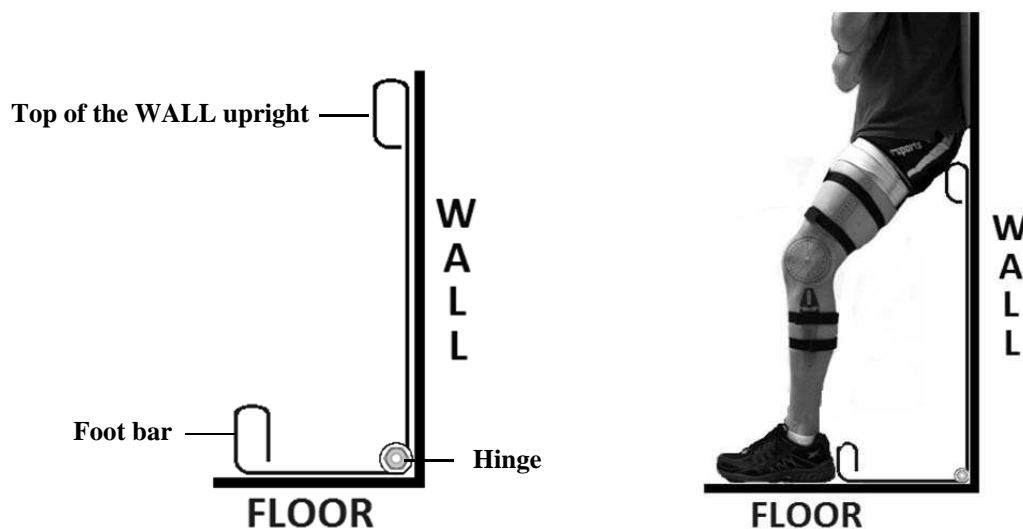
1. Adjust the **WALL** arm to the required length by loosening wing nut (*turn anticlockwise*). Then slide the **blue** line to the required measurement and tighten the wing nut (*turn clockwise*). Make sure that the **WALL** arm is secure and cannot move.



2. Adjust the **FLOOR** arm to the required length by loosening wing nut (*turn anticlockwise*). Then slide the **red** line to the required measurement and tighten the wing nut (*turn clockwise*). Make sure that the **FLOOR** arm is secure and cannot move.
3. Insert the bar into the slot at the end of the **FLOOR** arm.



4. Put the bend and squat at a 90 degree angle against a flat wall, making sure that the hinge is in the corner between the wall and the floor.



## SECTION 6: ISOMETRIC WALL SQUAT EXERCISE

- Stand with your head and back firmly against a flat, sturdy wall that supports the full weight of your body.
- Position your feet shoulder-width apart against the **Bend & Squat** bar with your toes facing forward. Make sure your feet are firmly on the floor, as you may find that they slide forward.
- To perform a wall squat, slowly bend your knees and allow your back to slide down the wall until your bottom is touching the upright of the **Bend & Squat**. **\*DO NOT** use the **Bend & Squat** as a seat. It should **NOT** support your body weight\*
- Look straight forward and hold this position for 2 minutes.
- Keep your arms crossed (or by your side) throughout the exercise and breathe steadily. **\*DO NOT** hold your breath.\* Put the laminated **BREATHE** sign in front of you whilst squatting as a reminder.
- When you have completed the 2 minute wall squat, use your hands to push yourself away from the wall.

**Do:**

- ✓ Make sure the **Bend & Squat** is set up correctly.
- ✓ Keep your feet shoulder width apart.
- ✓ Hold the exercise position for 2 minutes.
- ✓ Breathe steadily throughout the exercise.

**Do NOT:**

- ✗ Sit on the **Bend & Squat**.
- ✗ Slide down/up the wall.
- ✗ Move your feet.
- ✗ Hold your breath.

**SECTION 7: HEART RATE MONITOR INSTRUCTIONS****Putting on the heart rate chest strap**

1. Wet the electrode areas of the strap under running water and make sure that they are well moistened. *Do not get the transmitter wet.*
2. Adjust the strap length to fit snugly and comfortably.
3. Put the strap around your chest, just below the chest muscles, and attach the hook to the other end of the strap.
4. Check that the wet electrode areas are firmly against your skin and that the number is in a central, upright position.

**Using the heart rate monitor**

1. Secure the heart rate watch to your wrist.
2. Start the heart rate measurement by pressing the red “OK” button.
3. Hold the watch close chest strap and within 15 seconds, your heart rate will appear on the display screen.
4. Write down the heart rate displayed on your Data Sheet (*section 1*). This is your resting heart rate.
5. When you are in the wall squat position start recording heart rate by pressing the red “OK” button.
6. When exercising, the information that appears on the display is your calories burned, time spent exercising and current heart rate.
7. Keep the heart rate monitor recording throughout the 14 minute training session. **\*DO NOT** stop and start the heart rate monitor for every wall squat.\*
8. Stop recording heart rate at the end of the last wall squat by pressing the “STOP” button, (the bottom button on the left).
9. Press stop again. This will return you to the home screen.
10. Your heart rate data for the training session is now saved.

*Your heart rate monitor will be replaced once a week so that your data can be downloaded.*



**SECTION 8: SENDING DATA**

After **EVERY** training session you will need to text **OR** email your heart rate data to Natalie Goldring.

This is to ensure that you are working at the correct intensity.

➤ **Text:**

Here is a suggested layout for your text (R stands for rest and E stands for exercise):

- HR data for training session ?. R ???, E1: ???, E2: ???, E3: ???, E4: ???.
- *For example: HR data for training session 1. R: 50, E1: 62, E2: 71, E3: 101, E4: 118.*

➤ **Email:**

Here is a suggested layout for your email:

- This is my heart rate data for training session ?:
  - Rest: ???
  - Exercise 1: ???
  - Exercise 2: ???
  - Exercise 3: ???
  - Exercise 4: ???
- *For example: This is my heart rate data for training session 1:*
  - Rest: 50
  - Exercise 1: 62
  - Exercise 2: 71
  - Exercise 3: 101
  - Exercise 4: 118

SECTION 9: TRAINING SESSION TIMETABLE

	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
5:00 AM							
5:30 AM							
6:00 AM							
6:30 AM							
7:00 AM							
7:30 AM							
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10:00 PM							
10:30 PM							

SECTION 10: BREATHE SIGN

**BREATHIE**

**SECTION 11: DISCLAIMER**

In the unlikely event of an adverse reaction occurring during a home-based exercise session (e.g. severe or unusual shortness of breath, dizziness, chest pain/discomfort, light-headedness, etc.), you should stop exercising immediately and seek advice from a qualified medical practitioner.

Do not continue with the training programme until you have contacted:

**Natalie Goldring**

**Tel:** 01227 767700 ext. 3198

**Email:** [natalie.goldring@canterbury.ac.uk](mailto:natalie.goldring@canterbury.ac.uk)



## APPENDIX 9



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**Journal of Sports Sciences**

Volume 32, Issue 2, 2014

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### The effects of isometric wall squat exercise on heart rate and blood pressure in a normotensive population

**DOI:** 10.1080/02640414.2013.809471

Natalie Goldring<sup>a</sup>, Jonathan D. Wiles<sup>a</sup> & Damian Coleman<sup>a</sup>

pages 129-136

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**Details**

- Citation information: PubMed Web of Science ®
- Accepted: 24 May 2013
- Published online: 24 Jul 2013


>

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Taylor and Francis Online (2013) Available at:  
<http://www.tandfonline.com/doi/abs/10.1080/02640414.2013.809471#.VSToENzF91a>  
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