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Title: Home-based isometric exercise training induced reductions resting blood pressure

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## Abstract

### Purpose:

Isometric exercise training (IET) reduces resting blood pressure (BP). Most previous protocols impose exercise barriers which undermine its effectiveness as a potential physical therapy for altering BP. An inexpensive, home-based programme would promote IET as a valuable tool in the fight against hypertension. The aims of this study were: (a) to investigate whether home-based wall squat training could successfully reduce resting BP, and (b) to explore the physiological variables that might mediate a change in resting BP.

### Methods:

Twenty-eight healthy normotensive males were randomly assigned to a control and a 4 week home-based IET intervention using a crossover design with a 4 week 'washout' period in-between. Wall squat training was completed 3x weekly over 4 weeks with 48 hours between sessions. Each session comprised 4x 2 minute bouts of wall squat exercise performed at a participant-specific knee joint angle relative to a target HR of 95% HR<sub>peak</sub>, with 2 minutes rest between bouts. Resting heart rate, BP, cardiac output, total peripheral resistance and stroke volume were taken at baseline and post each condition.

### Results:

Resting BP (systolic =  $-4 \pm 5$ , diastolic =  $-3 \pm 3$  and mean arterial =  $-3 \pm 3$  mmHg), cardiac output ( $-0.54 \pm 0.66$  L·min<sup>-1</sup>) and heart rate ( $-5 \pm 7$  beats·min<sup>-1</sup>) were all reduced following IET, with no change in total peripheral resistance or stroke volume compared to the control.

### Conclusion:

These findings suggest the wall squat provides an effective method for reducing resting BP in the home resulting primarily from a reduction in resting heart rate.

## Key words

Static exercise, wall squat, randomised controlled trial, normotensive, physiological mechanisms

### Abbreviations:

ANCOVA	Analysis of covariance
BP	Blood pressure
DBP	Diastolic blood pressure
EMG	Electromyography
HR	Heart rate
HR <sub>peak</sub>	Peak heart rate

IET	Isometric exercise training
MAP	Mean arterial blood pressure
MCID	Minimal clinically important difference
MVC	Maximal voluntary contraction
$\dot{Q}$	Cardiac output
SBP	Systolic blood pressure
SV	Stroke volume
THRR	Target heart rate range
TPR	Total peripheral resistance

## Introduction

A growing body of research demonstrates that isometric exercise training (IET), albeit conducted predominantly in a laboratory setting, is capable of lowering resting blood pressure (BP) (Devereux et al. 2010; Wiles et al. 2010; Baross et al. 2012; Badrov et al. 2013; Millar et al. 2013a) equally in both males and females (Badrov et al. 2016). Furthermore, the results of meta-analysis and evidence based review suggest that IET may be the most effective type of exercise to achieve clinically meaningful reductions in this important cardiovascular risk factor (Millar et al. 2013a; Carlson et al. 2014). However, despite the apparent efficacy of IET, previous studies have selected a range of contraction styles (constant force vs. constant electromyography - EMG) and exercise modes (handgrip vs. leg extensions), which may have inadvertently curtailed more widespread application of IET.

Traditionally isometric exercise is performed at a constant force, normally as a percentage of an individual's maximal voluntary contraction (Lind 2011). Recently this method has been implemented using a programmable digital handgrip dynamometer (Stiller-Moldovan et al. 2012; Badrov et al. 2013; Millar et al. 2013a), which guides an individual through a complete IET session (Abe and Bisognano 2011) and can therefore be used without supervision (Millar et al. 2009) in the home. However, it is currently on the market in the United Kingdom from £299 to £449 (Zona Health, 2016), which is arguably a relatively excessive financial investment for a large proportion of the general population. In another study resting BP was successfully lowered using an inexpensive (\$2.00) spring-loaded handgrip device (Millar et al. 2008). However, due to the protocols simplicity the isometric handgrip training was not set at a precise intensity (~30-40% maximum voluntary contraction - MVC) and therefore intensity (as well as calibration) was not rigorously controlled, which is fundamental in the safe and effective prescription of isometric exercise (Wiles et al. 2005).

Some studies have utilised an alternative style in which IET was completed at a participant-specific EMG activity value that equated to a percentage of their peak heart rate (Devereux et al. 2010; Wiles et al. 2010; Baross et al. 2012). However, these protocols required the use of an isokinetic dynamometer and electromyography, which are not only expensive but also require an individual to continually travel to and from a facility to complete their training using the specialist equipment under supervision. It is suggested that the majority of previous IET studies are likely to have imposed exercise barriers, such as cost and time, which could reduce the effectiveness of IET as a potential physical therapy for altering BP (Millar et al. 2009). It is proposed that an inexpensive, home-based IET programme would help to promote the use of IET as a valuable tool in the fight against high blood pressure.

An alternative exercise mode that may be more suitable for home-based training is the isometric wall squat which utilises a constant position isometric contraction style (Hunter et al. 2002), with participants required to keep their knee joint at a prescribed angle while supporting an inertial load (body mass) using the quadriceps. Measuring the knee joint angle to set the wall squat position requires inexpensive and easy to use equipment, such as a goniometer (Reese and Bandy 2010). Therefore, it is proposed that the wall squat is simple to perform, requires minimal equipment and is therefore both economical and accessible.

Finally, the mechanisms that regulate a reduction in resting BP following IET are not well understood (Millar et al. 2013a). As mean arterial pressure (MAP) is determined by cardiac output ( $\dot{Q}$ ) and total peripheral resistance

(TPR) (Hietanen 1984), any reductions in resting BP are likely to be moderated primarily by either one or both of these variables (Pescatello et al. 2004). As  $\dot{Q}$  does not typically alter following this type of training, it is suggested that a reduction in resting 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 published studies to date have measured both of these parameters pre- and post-IET, although no statistically significant changes in  $\dot{Q}$  or TPR were detected despite the fact that resting BP was reduced (Devereux et al. 2010; Wiles et al. 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 elicit clinically relevant reductions ( $\geq 2$  mmHg) in resting blood pressure**. 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.

## **Methods**

### **Participants**

Twenty-eight healthy, normotensive males ( $30 \pm 7$  years;  $1.78 \pm 0.05$  m;  $78.7 \pm 11.1$  kg; mean  $\pm$  SD) volunteered to participate. Each participant received a written explanation of the procedures and provided written informed consent. Participants completed a health and medical questionnaire and self-reported that they were not suffering from any injury or disease. All participants were physically active, non-smokers and not taking any medication during the investigation. Participants agreed to maintain regular dietary and physical activity habits throughout the testing period, and abstain from food 2 hours, caffeine 4 hours, alcohol 12 hours and strenuous exercise 24 hours pretesting. All participants verbally confirmed adherence to the testing requirements prior to the start of each testing session. The study was approved by the University Ethics Committee and conducted according to the 1964 Declaration of Helsinki.

### **Study design**

All participants were required to complete two conditions in a randomised crossover study design – a control (condition 1) and a 4 week isometric training intervention (condition 2). A four week ‘washout’ period was given between conditions during which time no treatment was appointed. A schematic of the overall design is presented in Figure 1.

### **Figure 1 here**

## Laboratory-based testing

Prior to all data collection, participants were familiarised with the testing protocols and the measurement procedures. Resting measures for heart rate (HR), BP,  $\dot{Q}$ , TPR, and stroke volume (SV) were taken at baseline / pre and post each condition. Post-training resting measures were taken at least 72 hours after the participants' final training session.

Upon arrival to the laboratory, participants rested in a seated position for 15 minutes. After an initial 10 minute period, systolic BP (SBP), diastolic BP (DBP) and  $\dot{Q}$  were measured continuously for 5 minutes with HR measured simultaneously. Heart rate was recorded (both at rest and during exercise testing) 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 ECG electrodes (Ambu® Blue Sensor R, Ambu A/S, Ballerup, Denmark) using a standard three-lead bipolar arrangement. 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 then continuously displayed on a computer using the LabChart Pro software. Mean arterial pressure (MAP) was calculated instantaneously using the formulae:  $MAP = DBP + [1/3(SBP - DBP)]$ . Resting  $\dot{Q}$  was also measured using the Finometer and continuously displayed on a computer using the LabChart Pro software. **The Finometer uses the Modelflow method to provide an estimation of  $\dot{Q}$ , which for absolute values must be calibrated against a 'gold' standard technique (Wesseling et al. 1993). However when comparing  $\dot{Q}$  values obtained from uncalibrated Modelflow and thermodilution the error (CV = 18%) has been shown to be largely systematic, which means that without calibration the Modelflow method can be used to reliably track changes in  $\dot{Q}$  compared to baseline (Shibasaki et al. 2011).** Resting TPR was estimated offline using the MAP and  $\dot{Q}$  data, which was entered into the formulae:  $TPR = MAP / \dot{Q}$ . Resting SV was estimated offline using the  $\dot{Q}$  and HR data, which was input into the formulae:  $SV = \dot{Q} / HR$ . Mean SBP, DBP, MAP,  $\dot{Q}$ , TPR, HR and SV were then calculated for the 5 minute resting period.

### Condition 1: control

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.

### Condition 2: isometric exercise training

Prior to starting condition 2, participants completed an initial incremental exercise test to determine the isometric training intensity.

#### Incremental Isometric wall squat test

Goldring et al. (2014) previously demonstrated that constant position isometric wall squat exercise intensity can be reliably adjusted by manipulating knee joint angle and that the inverse relationship between knee joint angle and HR is reproducible ( $r = -0.9940$ ;  $P < 0.05$ ) using an incremental isometric wall squat test (Wiles et al. 2008). The incremental isometric wall squat test required participants to perform continuous isometric wall squat

exercise in stages of increasing intensity, which in this case was adjusted by decreasing knee joint angle measured using a clinical goniometer (MIE Clinical Goniometer, MIE Medical Research Ltd., Leeds, U.K.). Using four 25 mm elastic Velcro straps, the goniometer was carefully attached to the participant's left leg, ensuring that compression of the muscle did not occur (Figure 2). The fulcrum was aligned with the lateral epicondyle of the femur, the moving arm was 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. A spirit level was attached to the stationary arm to ensure that the lower leg was kept vertical during exercise. The internal angle between the femur and fibula was measured. Based upon the work of Goldring et al. (2014), 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°. The exercise intensity was increased every 2 minutes until the participant reached the end of 95° stage, or could no longer maintain the knee joint angle within 5° of the target value (volitional fatigue). Upon cessation, all participants verbally confirmed that the test had been completed to maximum.

### **Figure 2 here**

#### Determining isometric wall squat exercise training intensity

Using the participant's data from the incremental test, knee joint angle was plotted against the mean HR for the last 30 seconds of each incremental stage, this relationship was then used to calculate the specific knee joint angle required to elicit a target HR of 95% heart rate peak -  $HR_{peak}$  (CV =2.8%, 95% CI =2.1-4.1%) as utilised by Devereux et al. (2010), with  $HR_{peak}$  defined as the mean HR of the last 30 seconds achieved during the incremental test. Additionally, each individuals' target heart rate range (THRR) was established using the 95% reference interval (Hopkins 2000).

#### Isometric wall squat training

Condition 2 consisted of 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, T1-T12) with 48 hours between training sessions. Each training session was composed of 4 x 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 relative to their individualised target HR (95%  $HR_{peak}$ ).

The first session (T1) was completed under supervision in the laboratory where participants were assigned their home-based training equipment. A goniometer was not deemed practical for participant measurement of knee joint angle during home-based training, therefore an alternative device was designed and created called the 'Bend and Squat' (made in-house). This simple device aligned a participant's feet and back into the correct position for a given wall squat knee joint angle (Figure 3.) and was based on the principal that lower wall squat exercise positions required participants to move their feet forward and back down the wall - preliminary testing demonstrated that knee joint angle produced linear relationships with both the feet ( $r = -1.00$ ;  $P < 0.05$ ) and back ( $r = 0.99$ ;  $P < 0.05$ ) positions.



The Bend and Squat device (available in small, medium and large) consisted of two adjustable plastic arms for the feet and back positions which were adjusted to the desired lengths for the wall squat angle to be performed. 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 very small rounded lip for the bottom of the participant's coccyx to touch as a physical reference point to inform the correct position.

**Figure 3 here**

Participants received a 'Training Manual', which contained instructions for equipment (Bend and Squat device and heart rate monitor - Polar RS400 Computer and a Polar WearLink V2 transmitter, Polar Electro Oy, Kempele, Finland), a 'breathe' sign to help prevent the Valsalva manoeuvre during training and detailed the training protocol and procedures (isometric wall squat exercise and sending data).

During the first session, participants completed 3 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 (wall to calcaneus) and back positions (floor to coccyx) were recorded using a standard metre rule. The mean of the three feet and back measurements were calculated and the correct size Bend and Squat device was assigned to the participant. 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 subsequently completed.

All training sessions (T2 – T12) thereafter were completed in the home. During the training sessions, the HR value displayed at the end of each 4 x 2-minute wall squat was recorded for subsequent analysis. If the mean HR of the four exercise bouts deviated from the prescribed THRR on two consecutive sessions the knee joint angle was altered based upon further interpolation of their HR / knee joint angle relationship. If the mean HR was still not within the THRR during the next training session, the participant completed an additional incremental test in the laboratory to re-determine their relationship between HR and knee joint angle, from which the knee joint angle was re-prescribed.

## Data analysis

Before analysis, all data were checked for conformity with the parametric assumptions (Field, 2009). Data analysis was performed with IBM SPSS (BM SPSS Statistics for Windows, version 19.0, Armonk, NY: IBM Corporation). 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) 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. For all tests, an alpha level of  $< 0.05$  was set as the threshold for statistical significance. All data are expressed as mean  $\pm$  S.D., unless otherwise indicated.

## Results

### Resting blood pressure

Four weeks of isometric wall squat exercise training resulted in significant reductions in resting SBP ( $-4 \pm 5$  mmHg), DBP ( $-3 \pm 3$  mmHg), and MAP ( $-3 \pm 3$  mmHg) compared to the control condition ( $P < 0.001$  in all cases); data presented in Figure 4 and Table 1. Clinically relevant reductions ( $\geq 2$  mmHg) in SBP and DBP were recorded in 68 and 71% of the participants respectively.

No significant differences were observed for the baseline blood pressure data prior to each phase of the study ( $P > 0.05$ ). To assess the efficacy of the washout period, the data from the participants that engaged with training as their first phase of the study were analysed. The baseline resting values for SBP were  $126 \pm 7$  mmHg prior to the training phase, with post training resting SBP reducing to  $122 \pm 8$  mmHg. Following the washout period, the control phase began with a baseline value of  $125 \pm 7$  mmHg for SBP in these 14 participants. These values compare to the initial baseline of  $129 \pm 7$  mmHg, post control phase  $128 \pm 7$  mmHg, and then post training values  $125 \pm 8$  mmHg for the remaining participants who undertook the control phase first. For the group that undertook training as their first condition, DBP values were initially  $79 \pm 5$  mmHg, reducing to  $75 \pm 5$  mmHg following training, then rising to  $79 \pm 5$  mmHg post washout period. This compared to  $78 \pm 5$  mmHg,  $79 \pm 4$  mmHg, and  $77 \pm 5$  mmHg for these three assessments in the participants that undertook the control phase first.

### Figure 4 here

Table 1. demonstrates mean values for the BP parameters before and after both the control and training experimental conditions.

### Table 1 here

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  $\dot{Q}$  ( $-0.54 \pm 0.66$  L $\cdot$ min $^{-1}$ ) in comparison to the control group ( $-0.04 \pm 0.63$  L $\cdot$ min $^{-1}$ ) ( $P = 0.01$ ) and also a significant reduction in resting HR after training ( $-5 \pm 7$  beats $\cdot$ min $^{-1}$ ) compared to the control group data ( $-1 \pm 4$  beats $\cdot$ min $^{-1}$ ) ( $P = 0.01$ ). However, there was no significant change in resting TPR with training ( $1.10 \pm 2.15$  mmHg $\cdot$ mL $^{-1}\cdot$ min $^{-1}$ ) compared to the control data ( $-0.06 \pm 1.90$  mmHg $\cdot$ mL $^{-1}\cdot$ min $^{-1}$ ) ( $P = 0.06$ ) and also no significant change in resting SV following training ( $-1.58 \pm 9.95$  mL) compared to the control group ( $1.52 \pm 9.96$  mL) ( $P = 0.19$ ); data presented in Figure 5 and Table 2.

### Figure 5 here

Table 2. demonstrates mean values for  $\dot{Q}$ , TPR, HR and SV before and after both experimental conditions.

### Table 2 here

## Discussion

Four weeks of home-based constant position isometric wall squat exercise training successfully lowered resting BP in normotensive males. The resting BP reductions are similar in magnitude to those previously reported following IET that was partly laboratory-based with participants performing constant force contractions (McGowan et al. 2007a; Millar et al. 2013a) and completely laboratory-based using constant EMG contractions (Devereux et al. 2010; Wiles et al. 2010; Gill et al. 2015). Furthermore, the rate of reduction in all resting BP parameters occurred at either a faster (Wiles et al. 2010) or equal rate (Devereux et al. 2010) to that reported previously in normotensive participants following bilateral-leg IET using the same acute programme variables and exercise intensity in a laboratory setting. Therefore, the novel isometric wall squat training protocol utilised within this study appears to provide a viable alternative home-based method for the reduction of resting BP.

The finding that isometric wall squat exercise performed at an intensity of 95% HR<sub>peak</sub> results in significant reductions in all parameters of resting BP after 4 weeks, lends further support to the contention of an intensity dependent rate of resting blood pressure reduction with lower body IET (Wiles et al. 2010). The current findings (in agreement with Devereux et al. 2010) elucidate an intensity dependent continuum of resting blood pressure adaptation whereby Baross et al. (2012) reported no significant differences in any RBP parameters at 4 weeks when bilateral-leg extension was performed at an intensity of 85% HR<sub>peak</sub>, but significant reductions in SBP and MAP at the end of 8 weeks; whereas Gill et al. (2015) showed that all parameters of resting BP were significantly reduced after only 3 weeks of bilateral-leg IET, but only when IET occurred at a higher intensity (~100% HR<sub>peak</sub> or 34%MVC) than previously used.

Theoretically, it could be argued that the isometric wall squat exercise might result in both a greater magnitude (and possibly a greater rate) of resting blood pressure reduction compared to bilateral leg extension exercise.

This is based primarily on the fact that leg extensions isolate the quadriceps (Delavier 2010) and use a smaller muscle mass in comparison to the wall squat exercise, which utilises additional muscle groups (Contreras 2014). It has been hypothesised that isometric contractions of a greater muscle mass require an increased central and peripheral drive (Mitchell et al. 1980; Gálvez et al. 2000). Consequently, the cardiovascular control centres will be stimulated in parallel fashion with the motor cortex (Franke et al. 2000), thus producing a larger increase in cardiovascular response (a likely stimulus for resting BP adaptation) through greater central command (Gálvez et al. 2000). Further to this, evidence suggests that increased motor unit recruitment also enhances the exercise pressor response (Seals 1989) due to either greater physical deformation that stimulates the mechanoreceptors (Gálvez et al., 2000) and/or increased metabolite production activating the metaboreceptors (Iellamo et al. 1999). However, since this study used a unique constant position isometric contraction style, direct comparisons to previous research, such as constant EMG isometric exercise are difficult. This is further exacerbated by the fact that participants performed all training independently in the comfort of their own home as opposed to a highly controlled laboratory environment. Thus further research is required to explore any potential enhancement in blood pressure adaptation using isometric wall squat exercise.

Currently the results obtained following 4 weeks of isometric wall squat training are in agreement with a growing number IET studies using larger muscle mass lower body exercise that have been able to produce reductions in all three BP components (SBP, DBP, MAP) following  $\leq 8$  weeks of isometric leg training (Devereux et al. 2010, Wiles et al. 2010 and Gill et al. 2015). However, all of these previous studies used bilateral-leg extension that required specialised equipment only available in a small number of sport and exercise science laboratories around the country. **Thus the accessible and potentially cost effective training protocol presented for the first time in this study may help to improve isometric exercise's efficacy as a physical therapy for altering resting BP.**

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. Consequently, it is important to consider the data's clinical significance which may be interpreted 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 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 cardiovascular disease (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 which are similar to those presented by Millar et al. (2013b). Another important indicator of clinical significance is effect size, which 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) (Cohen 1988). 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). Therefore it is suggested that isometric wall squat exercise training results in clinically significant reductions in resting BP and has the potential to produce important clinical health benefits, which is the definitive goal of any antihypertensive therapy (Chobanian et al. 2003). **However, it is acknowledged that before this protocol can be**

more widely prescribed, the magnitude of the pressor response would need to be established during this type of isometric exercise in a clinical population.

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 (Pescatello et al. 2004). It was found that significant reduction in  $\dot{Q}$  was produced alongside a reduction in resting BP, with no significant change in TPR. 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 et al. 2010; Wiles et al. 2010).

Further to this, HR also significantly reduced following isometric wall squat training and this was combined with no significant alteration in SV. 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 et al. 2010; Baross et al. 2012) and/or no significant change in SV (-0.2 to 18.52 mL; Devereux et al. 2010; Wiles et al. 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 (Millar et al. 2009a). While some IET research has found autonomic nervous system 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 resting BP (Wiles et al. 2010; Badrov et al. 2013). However, these normotensive studies generally produced relatively modest BP reductions and it has been suggested that the spectral measures of heart rate variability, as used by Wiles et al. (2010), may not be sensitive enough to detect any small changes in neurocardiac modulation (Millar et al. 2013a). As autonomic nervous system 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 both normotensive and hypertensive participants, such as improved endothelial function (McGowan et al. 2007b; Badrov et al. 2016) and improved oxidative stress (Peters et al. 2006), 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 et al. 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 current research suggests that vascular training adaptations occur locally in the muscle rather than systemically (McGowan et al. 2007b; Badrov et al. 2016). Therefore since the calculation of TPR utilised in this study reflects systemic vascular resistance (Boone 2014), localised improvements in vascular function cannot be ruled out.

In conclusion, the current study demonstrates that 4 weeks of home-based isometric wall squat training **can elicit clinically relevant reductions** in 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 after 4 weeks of IET are unlikely to be due to a change in TPR, but are instead mediated by a reduction in  $\dot{Q}$ , which is primarily governed by a decrease in resting HR. However, it must be acknowledged that reductions in resting BP, rather than being reliant upon a single dominant mechanism, are likely to be due to the interaction between multiple physiological mechanisms (Millar et al. 2013b) with their own temporal response rate. Thus future research should consider the possibility that study duration is likely to significantly influence the mechanistic findings linked to reductions in resting blood pressure observed following any given period of isometric exercise training.

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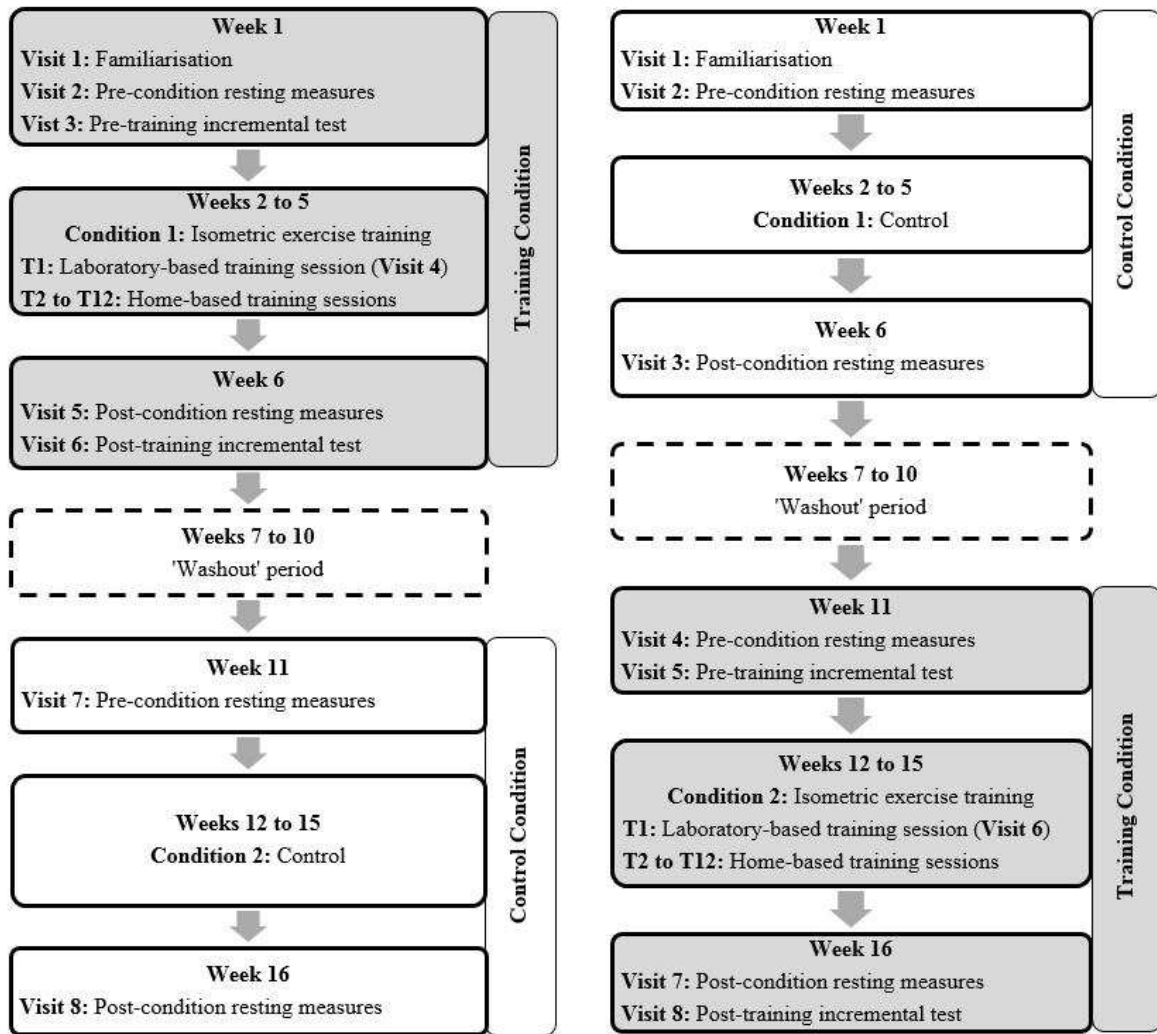


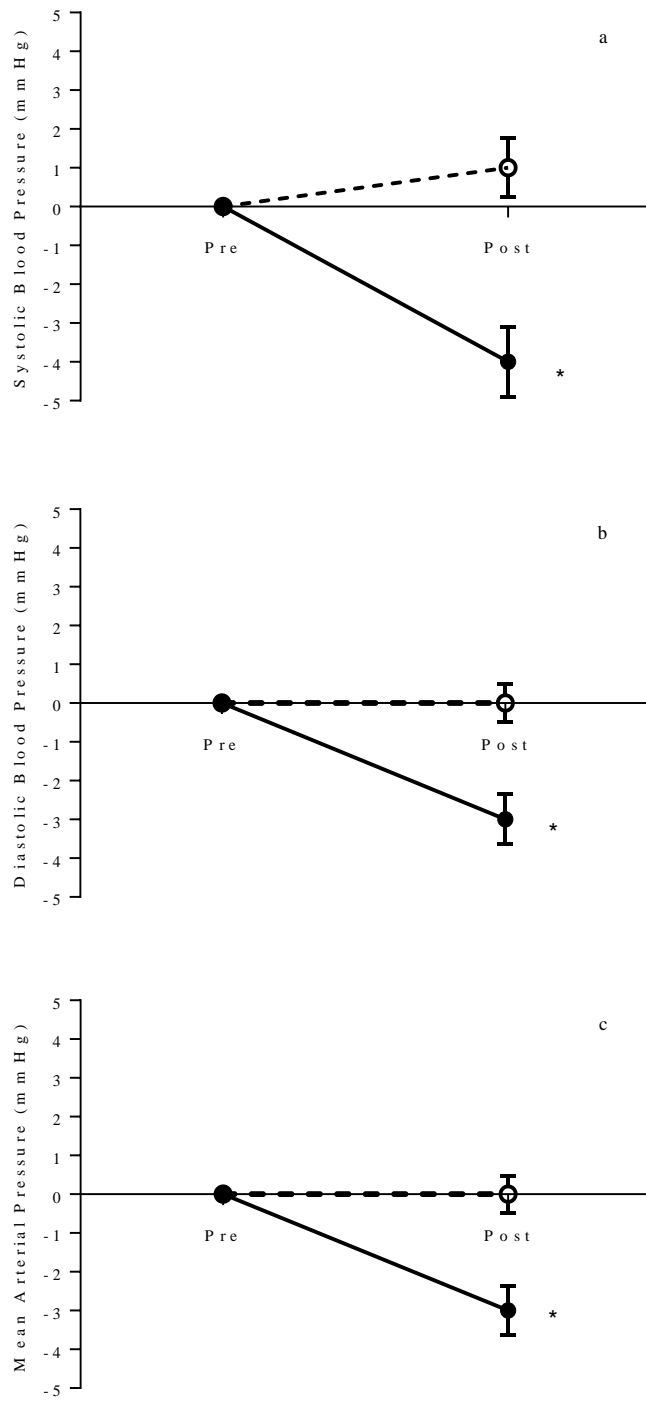
Figure 1. Schematic illustration of overall study design showing the training or control condition as randomly selected first.



**Figure 2.** Goniometry of the knee joint.



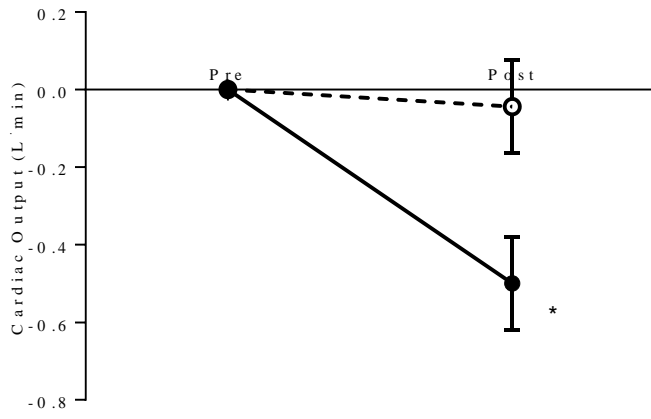
**Figure 3.** The Bend and Squat device for setting knee joint angle during isometric wall squat exercise.



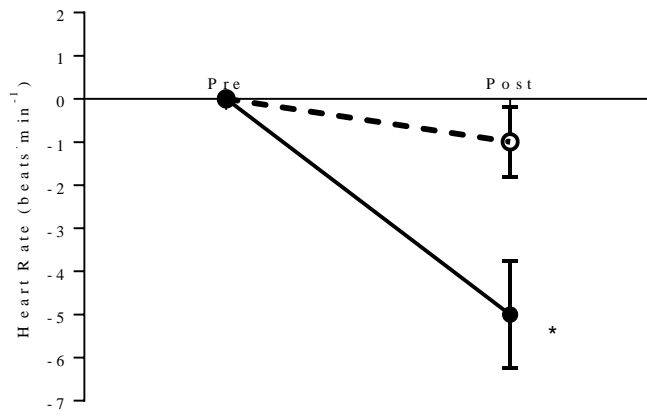
**Figure 4.** The mean systolic (a), diastolic (b) and mean arterial (c) pressure change values at rest for the control (○) and training (●) conditions. Error bars indicate standard error of the mean.

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

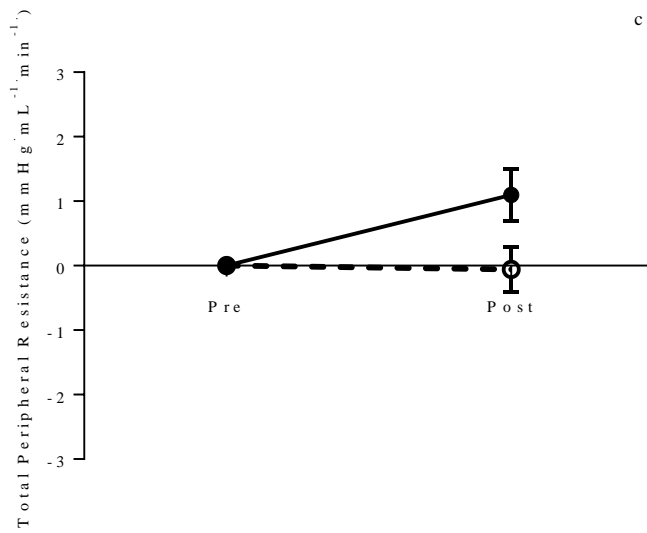
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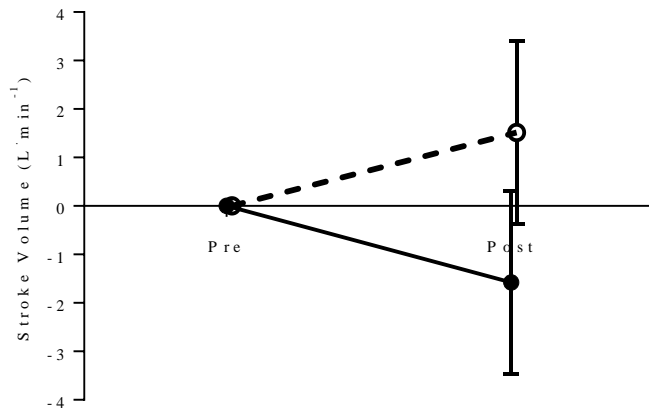
b



c



d



**Figure 5.** The mean cardiac output (a), heart rate (b), total peripheral resistance (c) and stroke volume changes 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 1.** Mean values for resting systolic (SBP), diastolic (DBP) and mean arterial (MAP) pressure before and after the control and training conditions.

<b>BP Parameter</b>	<b>Control</b>		<b>Training</b>	
	<b>Pre</b>	<b>Post</b>	<b>Pre</b>	<b>Post</b>
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.



**Table 2.** 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
$\dot{Q}$ (L·min <sup>-1</sup> )	5.7 ± 1.1	5.6 ± 0.9	5.8 ± 1.0	5.3 ± 0.9 *
TPR (mmHg·mL <sup>-1</sup> ·min <sup>-1</sup> )	17.2 ± 3.7	17.2 ± 2.8	16.8 ± 2.9	17.9 ± 3.0
HR (beats·min <sup>-1</sup> )	64 ± 9	63 ± 9	65 ± 9	60 ± 9 *
SV (mL)	88.5 ± 12.0	90 ± 14.2	90.4 ± 13.6	88.8 ± 9.6

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