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An Acute Crossover Trial of Passive Movement Training with and without Blood Flow Restriction to Determine the Impact on Postprandial Glycaemia

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Contents

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Declaration

I declare that all the data presented is my own work unless stated otherwise and this thesis was constructed by myself. Appropriate referencing has been used to refer to all published literature within this thesis. None of the data presented within this thesis has previously been submitted for assessment towards a higher degree.

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Abstract

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Diabetes is increasingly prevalent whereby glycaemic control is compromised from ineffective physiological glucose homeostasis. Consequences of poor glycaemic control in diabetes can increase the risk of coronary heart disease due to more favourable conditions for atherosclerosis development. While one of the most effective non-pharmacological preventative and treatment strategies for improving insulin sensitivity and lowering postprandial blood glucose is exercise, some populations are unable to exercise. These populations are at a further increased risk of diabetes onset, not only due to directly less physical activity in their daily lives, but also the secondary effects of this inactivity. Effective non-conventional exercise needs to be developed in order to make exercise accessible to those who cannot access conventional exercise modalities. This study assessed the effectiveness of passive movement training, with and without blood flow restriction, on blood glucose (and other metabolic and muscular markers). Eleven healthy males undertook a crossover trial of three treatments (CTRL, PMT, PMT + BFR) on three separate study visits, separated by at least a one-day washout period. Each participant arrived fasted and was administered a standardised meal. The protocol was then undertaken whilst blood samples were taken at pre-determined intervals to measure glucose, lactate and insulin. Muscular thickness changes were measured via ultrasound. Results showed no statistically significant differences between the three treatment groups for glucose, lactate or insulin. A statistically significant difference of muscular thickness ($p = 0.0042$) from pre- to post-treatment was detected in PMT + BFR only. These findings suggest that to increase postprandial glucose disposal versus rest, exercise must be active in nature and based upon voluntary muscular contraction, or include an exaggerated muscular stretch. These findings inform exercise prescription for the prevention of the onset, and management of diabetes.

Background

Diabetes mellitus refers to two different conditions, type one and type two diabetes mellitus (T2DM). Type two diabetes mellitus represents 90% of diabetes cases worldwide (Ahmad *et al*., 2022). In the United Kingdom, prevalence of T2DM is estimated at approximately 7% of the adult population (UK GOV, 2025). Furthermore, poor blood glucose control in this population can lead to macrovascular and microvascular complication, as well as being associated with obesity incidence and increasing mortality (Ahmad *et al*., 2022). Methods to control blood glucose should be investigated due to the large proportion of the population affected by T2DM, as well as the annual cost of T2DM in the United Kingdom being £14 billion as of 2022 (Hex *et al*., 2024).

Type two diabetes mellitus is a common metabolic condition characterised by two main features. The first is insensitivity of the tissues which insulin acts upon to maintain glucose blood homeostasis via glucose uptake. This then causes hyperinsulinemia which secondarily leads to pancreatic beta cells that normally secrete insulin, becoming defective (Galicia-Garcia *et al*., 2020). This study may produce findings with therapeutic potential for T2DM.

Importantly, once an individual has a T2DM diagnosis, this can be reversed in the early stages of the condition by improving tissue insulin sensitivity (Suleiman *et al*., 2022). This can be achieved through exercise alongside dietary changes (Lemieux, 2020). Exercise and diet exert beneficial effects on T2DM management and prevention via several mechanisms, including the ability to induce mobilisation of visceral and hepatic adipose tissue. Further, these two types of adipose tissue are key factors of T2DM onset (Lim *et al*., 2011). Recently, a systematic review suggested exercise interventions may aid in restoring insulin sensitivity, although the studies included presented significant heterogeneity in their exercise programme intensities and modalities (Ribeiro, Carvalho & Bento-Torres, 2023). Unfortunately, many people are unable to exercise such as those with spinal cord injury. Similarly, spinal cord injury as an example presents a

twofold increased prevalence of T2DM compared to the general population (Cragg *et al*., 2013).

Glucose metabolism

Blood glucose concentration is a dynamic equilibrium of glucose entering the bloodstream and glucose being up taken from the bloodstream. There are three ways in which glucose can enter the bloodstream including intestinal absorption from food, glycogenolysis (from the breakdown of glycogen) and gluconeogenesis (the formation of glucose in a fasted state from amino acids and lactate) (Aronoff *et al*., 2004). The process of glucose which is derived from food entering the bloodstream has a significantly variable rate. This is because the rate of glucose availability for absorption in the small intestine is dependent on the rate at which the stomach empties after a meal (gastric emptying) which depends on nutritional composition (Maki *et al*., 2016).

For glucose to be used as energy in the cell, it must be converted into adenosine triphosphate (ATP). Adenosine triphosphate is then used for an array of physiological functions including but not limited to cell division, muscle contraction and active transport (Nakrani *et al*., 2023).

Blood glucose concentration is homeostatically regulated within a tight range (4-7 mmol/L in healthy populations when fasted) (National Institute for Health and Care Excellence, 2023). When glucose concentration increases beyond physiological requirements, a negative feedback homeostatic loop acts to decrease blood glucose concentration via the polypeptide insulin hormone being secreted by beta cells of the pancreas (Rahman *et al*., 2021). Glucose homeostasis is regulated by insulin and glucagon, both of which are polypeptide hormones (Jiang & Zhang, 2003; Rahman *et al*., 2021). Glucagon is derived from proglucagon which is expressed in tissues including the pancreas, brain and intestine. Further, proglucagon is then processed into functional glucagon (Jiang & Zhang, 2003). Glucagon is then released into the bloodstream when circulating

blood glucose is low. On release into the bloodstream, the role of glucagon is to primarily increase hepatic glucose output, which then increases circulating glucose (Jiang & Zhang, 2003). In the opposite case where circulating glucose is high, insulin is released from the beta cells of the pancreas. Then action by insulin elicits a decrease in blood glucose by stimulating glucose uptake by skeletal muscle, the liver and adipose tissue (Rahman *et al*., 2021). Skeletal muscle is a major site of glucose disposal accounting for approximately 70% of glucose uptake, with one study quoting that during exercise over 85% of glucose uptake was accounted for by skeletal muscle (DeFronzo *et al*., 1981). Insulin reduces blood glucose by binding to the insulin receptor on the cell surface, which initiates translocation of the GLUT-4 receptor to allow facilitated diffusion into the cell (Rahman *et al*., 2021). The liver also stores glucose in the form of glycogen, a highly branched carbohydrate polymer (Hantzidiamantis *et al*., 2024). The hormone glucagon acts when blood glucose requires increasing and does so by stimulating glycogenolysis, the breakdown of glycogen into glucose (Hantzidiamantis *et al*., 2024).

Mechanism of normal glucose uptake by skeletal muscle and T2DM impairments

Cell membranes are effectively impermeable to glucose, therefore glucose movement across cell membranes is mediated by protein transporters (Brown, 2000). The main protein concerned with glucose uptake into skeletal muscle is the GLUT-4 transporter. Furthermore, GLUT-4 is an insulin-responsive protein transporter. This means insulin mediates GLUT-4 to uptake glucose from the bloodstream into the cell but is not the only stimulus exclusively responsible for GLUT-4 translocation (Huang & Czech, 2007).

Insulin is stored ready for release in the vesicles of pancreatic β cells (Lang, 1999). Release of insulin into the bloodstream is stimulated by glucose depolarising the cell membrane of the pancreatic β cells which causes a calcium ion (Ca^{2+}) influx through voltage-dependant channels (Lang, 1999).

Interestingly, under non-stimulated insulin conditions the abundance of GLUT-4 receptors on the skeletal myocyte membrane is relatively sparse. This is because the GLUT-4 proteins are located on the membranes of vesicles within the cytoplasm (Brown, 2000). However, by the action of insulin these transporters are translocated to the myocyte membrane, therefore allowing effective glucose uptake from the bloodstream as GLUT-4 is known to be a major mediator of glucose uptake (Huang & Czech, 2007). As a result, blood glucose concentrations are tightly regulated to maintain glucose homeostasis.

A chronic adaptation to exercise which has been demonstrated in humans is increased GLUT-4 expression. Furthermore, this is associated with an enhanced action of insulin and therefore increased effectiveness of blood glucose excursion (Richter & Hargreaves, 2013).

Blood flow has been reported to be a partial determinant of glucose uptake rate (Fugmann *et al*., 2003). Data suggests that insulin directly interacts with the endothelium to elicit secretion of the vasodilatory compound nitric oxide (NO) (Baron & Clark, 1997). Previous findings have shown that hyperinsulinemia increased femoral arterial blood flow to approximately twofold that of hyperinsulinemia combined with a L-n-monomethyl arginine (an NO inhibitor) (Baron & Clark, 1997). These findings imply insulin causes vasodilation via NO release, at least partly.

Interestingly, an increase in blood flow has been shown to promote skeletal muscle glucose uptake, even independently of the vasodilation caused by insulin. Furthermore, one study showed that leg glucose uptake was significantly increased during hyperinsulinemia (Baron *et al*., 1994). This study demonstrated that increasing muscle blood perfusion during hyperinsulinemia did act as an independent determinant of glucose uptake.

Usually in order to elicit GLUT-4 translocation and therefore glucose uptake, insulin is required (Richter & Hargreaves, 2013). However, GLUT-4 translocation can occur during exercise independently of insulin (Kennedy *et al*., 1999). Therefore, exercise represents a key technique of eliciting greater glucose disposal from the blood into skeletal muscle to achieve glycaemic control. However, some individuals cannot exercise due to disability or injury. Thus mimicking molecular signals of exercise, which elicit GLUT-4 translocation and then glucose uptake is a key priority for the reduction of blood glucose and T2DM risk, which may be addressed through passive exercise.

Mechanical deformation caused during PMT includes an element of muscular stretch. It has been demonstrated that muscular stretch may cause greater NO availability (Pearson *et al*., 2015). Greater NO availability has been shown to mediate skeletal muscle glucose uptake via an insulin-independent pathway (Higaki *et al*., 2001). Therefore, mechanical deformation, such as that caused in PMT, may be able to mimic muscular stretch and lead to greater NO abundance which may therefore elicit glucose uptake via an insulin-independent pathway.

In T2DM, the process of glucose disposal is impaired. Several factors contribute to this impaired ability to uptake glucose and therefore maintain glucose homeostasis.

Postprandial glucose response

Postprandially, there is a normal physiological increase in blood glucose levels as the exogenous carbohydrate content ingested is digested and broken down into glucose and other monosaccharides (Mathew *et al*., 2023). Furthermore, this is controlled by a homeostatic negative feedback loop consisting of the pancreatic beta cells secreting insulin which facilitates cellular absorption of the glucose, which then decreases the blood glucose levels (Chandel, 2021). For those living with T2DM, and individuals with increased insulin resistance, there are increased risks of developing other non-communicable diseases including cardiovascular

disease (Martín-Timón *et al*., 2014). Therefore, maintaining blood glucose levels within a normal physiological range (glycaemic control) is essential to decrease risk of developing T2DM and other conditions for which T2DM and insulin insensitivity are risk factors.

An acute postprandial blood glucose concentration increase is unavoidable and is a normal physiological response to feeding. Methods of controlling the postprandial glucose response should be investigated to avert the development of T2DM in those with prediabetes and prevent complications in those with T2DM (Ceriello, 2005). Glycaemic control can be challenging to attain with a Western diet particularly, due to the large proportion of carbohydrates ingested in a short time.

Undertaking exercise has been demonstrated to attenuate the postprandial blood glucose increase (Erickson *et al.*, 2017). This provides a protective effect to the endothelial wall from high glucose concentrations. Persistent exposure of high glucose concentrations to the endothelial wall has been documented to initiate damage to the endothelial wall, leading to atherosclerosis development (Bakker *et al*., 2009). The development of atherosclerosis is the process by which coronary heart disease develops. The ability to blunt the postprandial glucose response has also been shown to be a more accurate predictor of cardiovascular disease than HbA1c and fasting glucose levels (Erickson *et al*., 2017). Therefore, this may suggest undertaking a form of exercise habitually postprandially, may be an effective technique for reduction in the development of T2DM and cardiovascular disease. The acute effect of exercise post-meal is suggested to be effective at blunting the increase in blood glucose levels (Colberg *et al*., 2009). However, the chronic positive effect of habitual postprandial exercise should also not be dismissed.

Techniques for glucose measurement

Glucose may be measured by a variety of methods, each being appropriate in different cases (Wrench *et al*., 2024). Glycosylated haemoglobin (HbA1c) is often

used clinically because haemoglobin has a lifespan of circa 120 days. Furthermore, once haemoglobin becomes glycated (glucose bound to haemoglobin) it is irreversible (Nathan *et al*., 2007). Due to the irreversible nature of this binding coupled with the lifespan of haemoglobin, HbA1c is considered the gold-standard measure of mean blood glucose of the 8-12 weeks prior to testing (Nathan *et al*., 2007). However, due to this nature of HbA1c being a long-term mean blood glucose, it was not appropriate for this acute study. Technological advances have enabled continuous glucose monitors (CGMs) to be developed. Use of CGMs allows blood glucose to be recorded periodically over the lifespan of the sensor (Berganstal, 2018). Use of CGMs and HbA1c both allow an overall measurement of glycaemic control but do not elucidate the underlying physiology of the glycaemic data they provide (Wrench *et al*., 2024).

Alternative methodology for the measurement of glucose is to use stable isotope tracers. Isotopic tracers allow tracking of ingested carbohydrates to examine metabolism and give insight into health and performance (Gonzalez & King, 2022). Since isotopes have the same assumed chemical properties but distinction between the tracers can be made, they are a useful method of metabolic monitoring (Rennie, 1999). Stable isotope tracers allow the tracking and distinction between endogenous and exogenous carbohydrate (Gonzalez & King, 2022).

The most appropriate glucose monitoring for the present study which was used was venous blood sampling via cannulation, the methods of which are presented later. Venous blood sampling can be used instead of the more widely used capillary blood sampling for investigations which require frequent sampling in order to aid in participant comfort. It should be clearly reported which type of blood sampling is used in studies as a statistically significant difference has been found between venous and capillary based measurements of glucose (Topping *et al*., 2019).

Insulin resistance

Insulin acts upon tissues to exert the effect of glucose uptake. Skeletal muscle is the primary tissue upon which insulin acts to initiate glucose uptake (Merz & Thurmond, 2020). In insulin resistance, the response to insulin becomes impaired which is thought to be due to impaired GLUT-4 translocation (Lee, Park & Choi, 2022). The mechanism of insulin resistance is linked to some extent with the impairment of GLUT-4 translocation ability as exercise can increase GLUT-4 expression, which improves glycaemic control (Richter & Hargreaves, 2013). As mentioned previously, secretion of insulin also plays a role in the increase in blood flow which further stimulates glucose uptake (Baron & Clark, 1997).

Acute and chronic effects of exercise on blood glucose regulation

Physical activity, especially exercise, has been documented in the literature to exert a beneficial effect on insulin sensitivity and reduction of long-term health condition risk factors (Melzer, Kayser & Pichard, 2004).

Exercise can independently promote GLUT-4 translocation by skeletal muscle. Furthermore, AMP-activated protein kinase (AMPK) is hypothesised to be a critical signal for GLUT-4 translocation under such conditions (Jessen & Goodyear, 2005). Activation of AMPK has been proposed to act as an energy sensor in mammalian cells. Furthermore, if low ATP is “sensed” AMPK is thought to act to preserve ATP (Grahame *et al*., 1998). Due to exercise including contractile activity, unsurprisingly the energy status of muscle cells becomes depleted, and ATP can become significantly decreased. Therefore, AMPK can become activated under such conditions, thereby potentially signalling GLUT-4 translocation (without insulin involvement) and eliciting glucose uptake (Jessen & Goodyear, 2005). Exercise has been shown to elicit GLUT-4 translocation in people with T2DM also (Kennedy *et al*., 1999).

Passive movement training

Passive movement training (PMT) is a form of physical activity whereby the individual does not voluntarily move their limbs, but an external force is applied to elicit movement of the joint instead. Therefore, no active contraction of skeletal muscle occurs.

Due to the involuntary nature of PMT, it may be implemented in situations where conventional resistance or cardiovascular exercise would not be possible such as paraplegic, comatose and immediately post-operative individuals. It may be pertinent for these populations to perform PMT due to the potential for PMT to attenuate the natural loss of skeletal muscle mass and function through inactivity (muscular atrophy). Unfortunately, muscular atrophy and physical deconditioning is a significant issue in older hospitalised patients also as research suggests these patients spend only 4% of their day out of bed (Pedrinolla *et al*., 2022).

Use of PMT can exert a beneficial effect by eliciting a hyperaemic response (an increase in blood flow to an area of the body in physiological demand). Previously, PMT has been shown to increase femoral peak blood flow velocity significantly in bedbound patients (Pedrinolla *et al*., 2022). Interestingly, increases in femoral peak blood flow velocity have also been observed in spinal cord injury patients, but not consistently (Ballaz *et al*., 2007; Woerds *et al*., 2006). One study concluded that a 10-minute passive movement protocol elicited significant increases in maximal femoral blood flow velocity. It is thought that the mechanism by which PMT increases femoral blood flow velocity is by a marginal increase in stroke volume caused by afferent reflexes response to the stretch of muscle fibres (mechanical deformation) (Ballaz *et al*., 2007). Other studies have suggested that the contributions to the hyperaemic response found with PMT are 35% from central factors and 65% from peripheral mechanisms (Burns *et al*., 2018). This suggestion would be congruent with the inconsistent hyperaemic responses that have been seen in spinal cord injury participants although some studies did measure blood flow after, instead of during their PMT protocol where they may

have missed the hyperaemic response (Burns *et al*., 2018). This may suggest a hyperaemic response is present, and is consistently present in spinal cord injury populations, but these responses may have been missed because the methodology is not suitable to measure the blood flow response. Blood flow increase with PMT only occurs briefly and then returns to baseline within 60 seconds of PMT cessation (Shields *et al*., 2019).

With regards to PMT, blood flow has been seen to increase to approximately 330% of resting values (Trinity & Richardson, 2020). In addition, PMT has been used in previous studies as a method of assessing vascular function by undertaking PMT with ultrasound measurements of vessel flow (Groot *et al*., 2022). This is pertinent to the populations where PMT may be a convenient and effective mode of training to attenuate muscle atrophy and attempt to control blood glucose concentration.

Mechanical deformation of the limb causes the release of NO (Mortensen *et al*., 2012). The release of NO causes an increase in blood flow in PMT, which mimics (to a lesser extent) the increase in blood flow seen in active exercise (Trinity & Richardson, 2020). The hyperaemic effect observed from PMT is thought to be caused by NO, because inhibition of NO has shown to reduce the hyperaemic response to PMT by approximately 90% (Mortensen *et al*., 2012). It has been suggested that skeletal muscle capillaries in vivo are recruited by a NO-dependent action, which may consequently contribute to increased glucose uptake (Vincent *et al*., 2004). Since increases in blood flow has previously been observed with use of passive leg movement protocols (Mortensen *et al*., 2012; Høier *et al*., 2010; Trinity *et al*., 2012), it was hypothesised that PMT could therefore induce greater postprandial glucose uptake through increased in blood flow via NO release. This mechanism has been proposed previously with exogenously administered NO (administered via an NO donor, sodium nitroprusside) stimulating glucose transport by increasing GLUT-4 cells surface expression (Etgen *et al*., 1997).

Previous literature has shown an angiogenic effect of PMT in humans. Angiogenesis is the formation of new blood vessels. One study has shown that undertaking two weeks of PMT was sufficient to induce statistically significant increases in the number of capillaries around a muscle fibre. Furthermore, vascular endothelial growth factor (VEGF) (a key proangiogenic factor) was demonstrated to be no less abundant post-PMT when compared to active exercise (Høier *et al*., 2010). These findings are important to be considered as it may suggest PMT has potential to improve capillarisation chronically. This may have therapeutic potential in rehabilitation settings as both capillaries per fibre and capillary contacts per fibre have been shown to exhibit statistically significant differences between sarcopenic and non-sarcopenic populations (Prior *et al*., 2016). Sarcopenia is the natural age-related decline in muscle mass and function and may be prevalent in rehabilitation populations.

It may be the case that with PMT, those at risk of developing T2DM due to their inability to exercise of perform physical activity (those who are bed bound or have a spinal cord injury) are able to use PMT to elicit glucose uptake after a meal. Potentially this may cause the muscle to uptake glucose and therefore a blood glucose excursion would occur. This method of potentially controlling blood glucose levels, as well as attenuating muscle atrophy may provide a metabolic therapy for those unable to perform conventional exercise. This potential of a metabolic therapy for those who cannot perform conventional exercise may give the ability for those populations to reduce T2DM risk.

Added benefits of blood flow restriction to passive movement training

Blood flow restriction (BFR) is a technique where a cuff is applied proximally to either each of the thighs or each of the upper arms. The cuffs then tighten to cause mechanical pressure and therefore occlusion of the blood flowing between the limb and the rest of the body. Previously seen in the literature, BFR has generally been used to elicit 40-80% arterial occlusion (and therefore complete

venous occlusion) which seems to be an optimal selection to induce benefits of BFR whilst maintaining safety (Lorenz *et al*., 2021). Upon the release of the cuff after BFR, reactive hyperaemia occurs, which is a sudden influx of blood to the distal portion of the limb being occluded. The acute increase in blood flow upon release of BFR may be able to facilitate an increases rate of glucose uptake as blood flow has previously been observed to independently determine glucose uptake in hyper insulinemic conditions (Baron *et al*., 1994).

Mechanisms of BFR in resistance training

Use of BFR is popular within both aerobic training and resistance training. The primary reason for including BFR in this study is to attempt to enhance the hyperaemic effect of PMT. While the benefit of BFR without active contraction as a hypertrophic stimulus is contested (Fuchs *et al*. 2025; Barbalho *et al*. 2019; Clark, Fernhall & Ploutz-Snyder, 2006), we are interested in the effect of PMT+BFR on muscle swelling as a potential indicator of muscle growth as a secondary outcome. For the purposes of this study, the use of BFR in resistance training will be discussed to determine if the mechanisms involved in muscle growth, including those that do not require mechanical tension.

Mechanical tension

Mechanical tension is the strain and stretch exerted on muscle fibres upon activation (Martin *et al*., 2022). As a result of the relatively low loads used during BFR training, mechanical tension produced in the skeletal muscle is relatively low. However, mechanical tension is well known to contribute to muscular protein synthesis and therefore hypertrophy.

It has been suggested that mechanical tension becomes a stimulus for hypertrophy at significantly lower loads of training with the application of BFR (Cognetti *et al*., 2022). It is believed that an increased number of motor units are

recruited at a lower relative load of the muscle under BFR, due to ischaemia and peripheral fatigue (Cognetti *et al*., 2022).

As a result of this relative ischaemia, it is possible there is a shift in metabolism to an increased dependence on anaerobic metabolism, and therefore fast-twitch muscle fibres (Martin *et al*., 2022). It has been shown via a protocol using BFR and surface electromyography (EMG) that an 80% increase in muscle stimulation occurred in BFR, compared with a control whereby equal mechanical tension was produced (Takarada *et al*., 2000). However, this conclusion is not fully supported by some evidence as BFR without voluntary muscular contraction/exercise has been shown to attenuate muscular atrophy, implying mechanical tension may not be the only mediator of BFR's hypertrophic effect (Clark, Fernhall & Ploutz-Snyder, 2006; Barbalho *et al*., 2019). However, another study concluded that BFR alone during immobilisation did not prevent atrophy (Fuchs *et al*., 2025). It is also important to note, the extent to which fast-twitch muscle fibres are recruited in BFR at low loads of exercise will likely still not be to the extent they are recruited during traditional high load resistance training.

Metabolic stress

Generally, in protocols using BFR, the occlusion pressure will be sufficient to cause complete venous occlusion (no venous flow distally beyond the point of the BFR device) but not sufficient to cause complete arterial occlusion (Pearson & Hussain, 2015). It should be noted, this occlusion during exercise often still maintains an increased blood flow relative to that seen at rest.

A hypoxic environment is present during BFR. This may provide a degree of stimulus for increases in muscular hypertrophy and function by facilitating greater recruitment of type II muscle fibres (Scott *et al*., 2014). This BFR causes a build-up of metabolites also. These factors are thought to enhance the training effect

and therefore allows BFR to elicit similar training effects oh hypertrophy at lower loads and training volumes, than conventional training methods.

It is likely that the metabolic stress then initiates other mechanisms which contribute to the training effect of BFR. Such downstream effects are thought to include increased recruitment of fast twitch muscle fibres, elevation of circulating hormones, cell swelling and increased production of reactive oxygen species (Pearson & Hussain, 2015). These effects (to be discussed later) are thought to originate from a combination of metabolic stress and mechanical tension. Metabolic stress resulting from conventional exercise includes the elements of increased lactate, inorganic phosphate and hydrogen ions (H^+) (Schoenfeld, 2013).

Cellular swelling

It has been demonstrated that a significant increase in muscle cell swelling, both acutely and over a six-week period is a response to a resistance training programme and is correlated to muscle hypertrophy achieved (Hirono *et al*., 2020). Cellular swelling is thought to occur after conventional resistance training because anabolic signalling processes mean the muscle cell has an osmotic influx of water due to phosphocreatine and hydrogen ion accumulation (Hirono *et al*., 2020).

Interestingly, a proposed mechanism for how BFR elicits a hypertrophic / an atrophy attenuating effect is linked with cell swelling. Use of BFR increases the water content of cells due to an osmotic influx caused by increased metabolite concentration. This is hypothesised to cause activation of an internal volume sensor within the cell (Loenneke *et al*., 2012). Further, the activation of this sensor through intermediaries then activates the mTOR pathway, the master regulator of skeletal muscle growth. Given that acute cellular swelling is correlated with hypertrophy (Hirono *et al*., 2020), PMT+BFR may be beneficial in attenuating muscle atrophy. It has previously been shown that use of BFR on a single leg in

intensive care patients significantly reduced the decrease in muscular thickness during immobilisation compared to the other non-BFR leg (Barbalho *et al*., 2019). We included acute change in muscle thickness as a secondary exploratory measure in the present study.

Study aims

The aim of this study was to examine the impact of PMT, and PMT combined with BFR, on postprandial glycaemic control. In order to examine this effect, we conducted a crossover trial of PMT, PMT + BFR and CTRL visits whilst measuring venous blood glucose levels after a standardised meal. We examined the postprandial glycaemic responses by assessing metrics including area under curve, peak glucose concentration and time to peak glucose concentration. We examined effects on lactate, insulin and muscle thickness as secondary measures.

It was hypothesised that 1) PMT would result in significantly lower postprandial glucose deviations from that at rest when compared with CTRL and 2) PMT + BFR would elicit a greater blunting effect on postprandial blood glucose than PMT alone.

Methods

Subjects and inclusion criteria

Individuals were recruited from Lancaster University's staff and student population between December 2024 and March 2025, as per the inclusion and exclusion criteria. Participant requirements were males, age 18 - 40 inclusive, with no long-term health conditions and medication-free status. Smokers and recent blood donors were excluded. No inclusion range was specified for body

mass index in order to ensure findings represented the general population of the demographic included. If for any reason a participant did not meet the eligibility criteria of the study protocol, they were not eligible for inclusion. It had been identified that further postprandial exercise protocols which represent real-life scenarios (in terms of time of day and meal consumed) are needed to provide further insight into the potential therapeutics of exercise (including PMT) to control blood glucose (Aqeel *et al*., 2020). We aimed to conduct our study in line with this by using timings mirroring that of an average daily routine, coupled with a common everyday meal. The study was undertaken within the boundaries of the 2024 version of the Declaration of Helsinki and all participants provided written informed consent prior to enrolling in the study. The Research Ethics Committee of the Faculty of Health and Medicine of Lancaster University approved the study (identification FHM-2024-4434-SA-2) prior to recruitment commencing. The study was preregistered on ClinicalTrials.gov (NCT06704126) before the recruitment of the first participant.

An *a priori* power calculation was undertaken prior to recruitment. The calculation assumptions were based on data from a previous meta-analysis, upon the effects on blood glucose observed in a passive stretching protocol (Thomas *et al*., 2024). A minimum sample size of eight was determined for a power of 0.8 at an alpha of 0.05 based on the estimated reduction of 2.0 (±1.6) mg/dL post-intervention using data from the meta-analysis. In total 12 participants were screened for inclusion, resulting in 11 being included for session randomisation. One participant who was screened was not eligible for inclusion as they did not meet the inclusion criteria. There were no dropouts post-randomisation, and all participants successfully included from screening completed the trial. Subjects were required to arrive fasted. Participant phenotype is shown in Table 1.

Table 1 Physiological Phenotype of Participants

Parameter	**Mean ± SD**
Age (years)	26.9 ± 8.3

Mass (kg)	81.9 ± 9.0
Height (m)	1.79 ± 0.08
Fat (% of bodyweight)	16.1 ± 4.3
BMI (kg/m^2)	25.7 ± 2.1
Muscle mass (kg)	65.2 ± 7.1
Muscle mass % of bodyweight (%)	79.7 ± 4.1

Study design

This study was a single-centre crossover study with the primary outcome of acute blood glucose change throughout the duration of the treatments (150 minutes). The crossover design consisted of participants completing three protocols (PMT, PMT + BFR and a control protocol). All protocols were of equal duration, and each participant completed all three protocols at approximately the same time of day, on non-consecutive days. Participants completed the three testing visits in a randomly allocated sequence. This was achieved by assigning each treatment type with a number (1-3) and using a random number generator (https://www.calculatorsoup.com/calculators/statistics/random-number-generator.php) to produce a series of randomised numbers, which allocated a treatment to each session.

Screening appointment

Prior to testing, a short separate screening and familiarisation visit was completed by each participant. During this screening, participants were asked if they had any queries regarding participating in the study. Once these were answered, the participant provided written informed consent. Copies of written informed consent will be retained securely as per Lancaster University's policy, for a period of 10 years from the date of study completion.

This screening visit then entailed completion of a screening form (appendix 3) consistent of basic health questions and measurement of anthropometric parameters (height, body mass and blood pressure) (287, Seca, Hamburg, Germany; 287, Seca, Hamburg, Germany; Omron, Kyoto, Japan). Body composition was also measured (DC-430P, Tanita, Tokyo, Japan) after a fast of ≥ 8 hours to obtain an accurate reading as a varying degree of gastric filling is known to impact bioimpedance by a small but significant magnitude (Androutos *et al*., 2015). Blood pressure of the participant's preferred arm was measured with their hand supinated resting on a table to ensure the cuff was positioned on the upper arm at heart level.

Screening for atrial fibrillation was also carried out via a one lead electrocardiogram (KardiaMobile, Alivecor, California, USA). The participant was not eligible for inclusion if a normal sinus rhythm was not detected, or a blood pressure reading ≥140/90 mmHg (either figure) was detected. Any answers of 'yes' in response to the health screening contraindications to exercise (appendix 3) also satisfied grounds for exclusion (ACSM, 2018).

Experimental protocols

Participants attended testing sessions having refrained from eating or drinking (except for water) since 8pm of the day prior to the morning of testing. Avoidance of physical exercise in the 24 hours pre-testing was also required with maintenance of similar activity levels prior to each testing session specified.

Participants were initially fitted with an antegrade cannula positioned in the antecubital fossa of the elbow. The cannula was inserted into a suitable superficial vein as determined by a member of the study team suitably trained in cannulation. Immediately after a cannula was fitted and initial fasting samples were obtained participants were given a standardised high carbohydrate breakfast meal (Table 2). This was consistent across the three testing protocols (PMT, PMT + BFR and control). Between initial fasting blood measures taken to the PMT / PMT + BFR / control protocol commencing, there was a 30-minute window (Figure 1). This timeframe was used to fit an electromyography skin sensor (Delsys, Natick, USA) to the most visually prominent belly of the vastus medialis, measure pre-protocol quadriceps muscle thickness across three sites using ultrasound (Logiq 2, GE Healthcare, Wauwatosa, USA) and set up the isokinetic dynamometer (S3, Biodex, New York, USA).

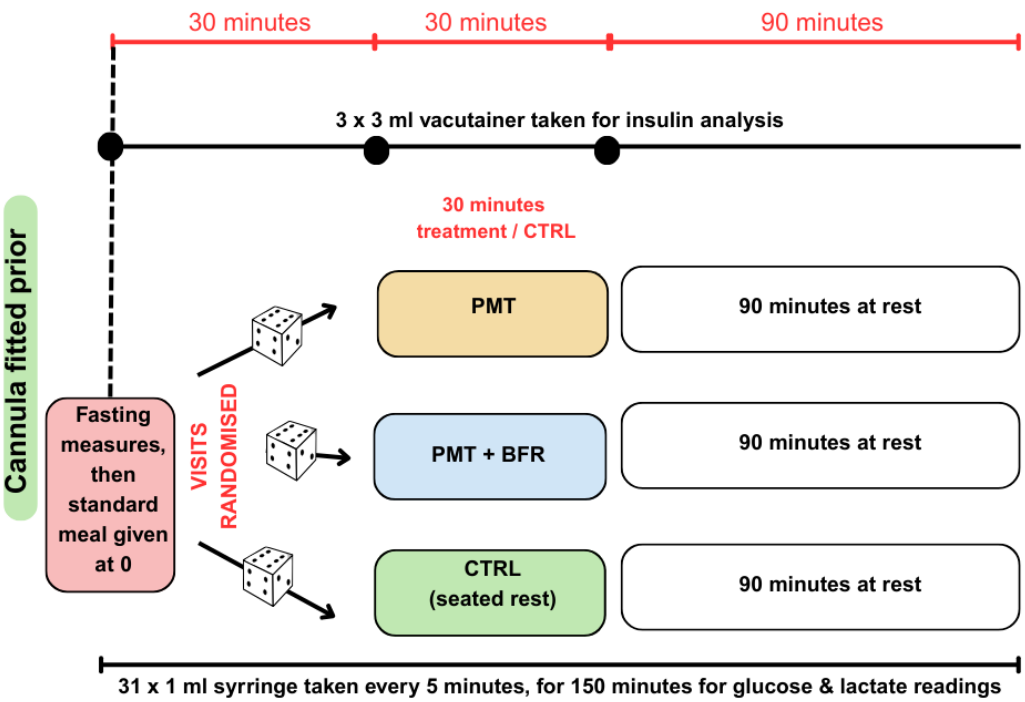

Figure 1 Schematic of Study Design and Timeline. *PMT, passive movement training; PMT + BFR, passive movement training with blood flow restriction; CTRL, control*

The meal given was of nutritional composition (Table 2). This meal was a common breakfast meal in order to represent a glucose response that reflected daily living.

Table 2 Nutritional Composition of Standardised Meal Provided to Participants

Nutrient	Frosties cereal (120 g)	Alpro almond milk (300 ml)	Total
kcal	450	72	**522**
Carbohydrate / g *of which is sugar / g*	104.4 44.4	8.1 7.2	**112.5** **51.6**
Protein / g	5.4	1.5	**6.9**
Fats / g	0.7	3.3	**4.0**
Fibre / g	2.4	0.9	**3.3**

Passive movement training protocol

A PMT protocol was set up on an isokinetic dynamometer (S3, Biodex, New York, USA). The isokinetic dynamometer was set up to ensure the participants knees were directly aligned with the point at which the dynamometer pivots to maintain correct positioning. The extendable arm of the attachment was positioned so that the pads were resting approximately 2cm above the rear of the participants shoes. The participants' ankles were secured using the straps.

The protocol consisted of an 80° range of motion around flexion and extension of both knees simultaneously. Because blood flow returns to almost baseline levels soon in the femoral artery within one minute of PMT, the protocol involved 60 seconds of PMT followed by 60 seconds of rest, repeated for a duration of 30 minutes to maximise the time that femoral blood flow is elevated in response to passive movement (Shields *et al*., 2019). A custom attachment fabricated by the study team was fitted to the isokinetic dynamometer to flex and extend both legs simultaneously. An angular velocity of 180° per second was used as per a

previous PMT protocol with identical range of motion and angular velocity (Burns *et al*., 2018). These setup parameters were input to the isokinetic dynamometer's custom protocol facility to ensure the identical protocol was used across all participants.

Passive movement with blood flow restriction

In addition to the PMT protocol, blood flow restriction cuffs (VALD AirBands, VALD, Brisbane, Australia) were self-fitted as close to the inguinal fold as was accessible to the participant, as the same BFR cuffs were previously fitted similarly (Królikowska *et al*., 2024). The BFR cuffs used were 10cm in width and constructed from sweat-resistant fabric cloth. They were connected to a Bluetooth device and calibration was completed by the manufacturer's mobile application which determined 80% arterial occlusion pressure for each individual participant.

Once calibrated, BFR was applied for five minutes alongside the PMT protocol, with a one-minute interval where BFR was released. This cycle was repeated five times in the duration of the PMT protocol. Unfortunately, BFR protocols used in the literature are often poorly reported such the duration of occlusion is not clearly reported. The occlusion period for the present study was selected as a previous training protocol for RT+BFR prescribed four sets with 60 second interest rest periods, followed by cuff deflation (Centner *et al*., 2019), which we estimate to last around five-minutes. Clark, Fenhall and Ploutz-Snyder (2006) also used five-minute intervals for the BFR only protocol.

Use of BFR involves applying a cuff to the proximal leg to apply pressure, either via a tourniquet or a pneumatic inflating device (the latter being more commonly used). A pressure is established to conclude what pressure is required for 100% arterial occlusion. Then 40-80% of this pressure is used for the training arterial occlusion pressure (Lorenz *et al*., 2021). This range is considered appropriate to maintain safety, whilst preserving benefits of BFR use. Generally, the wider the

cuff, the less pressure is needed to elicit the occlusion required (Crenshaw *et al*., 1988). A systematic review evaluated the safety of BFR in clinical interventions of musculoskeletal disorders and showed that adverse events were not increased with use of BFR compared with conventional exercise (Minniti *et al*., 2020).

Control protocol

The control protocol consisted of the participant sitting still in the isokinetic dynamometer for 30 minutes with no blood flow restriction applied. Legs remained in their natural sitting position. All measurements were performed at the same time points as the PMT and PMT+BFR visits.

Measures

Cannulation

Venous blood samples were drawn from the cannula from an appropriately selected vein at the antecubital fossa. The samples were drawn and analysed for glucose and lactate concentrations at five-minute intervals for the duration of testing (150 minutes). Each blood sample obtained for these purposes was collected using a 1 ml luer lock syringe connected to one end of the three-way Stopcock (Luer Splitter three-way Single Stopcock, Teqler, Wecker, Luxembourg) attached to the cannula (Versatus Winged and Porter IV Catheter, Terumo, Surrey, United Kingdom).

The 1 ml samples were then immediately expelled onto a non-absorbent pad which allowed a capillary tube to be filled with a blood sample. The capillary tube was then deposited into an aliquot containing haemolysing solution and agitated sufficiently. This solution was analysed via a benchtop blood analyser (Biosen C-Line GP+, EKF, Barleben, Germany). Samples were immediately discarded into appropriate biohazard waste bins after benchtop analysis. The cannula was flushed every 30 minutes in-situ with *quantum satis* saline solution (0.9% sodium chloride) to reduce the likelihood of residual blood clotting within the cannula.

At pre-defined intervals (timepoints 0, 30 and 60 minutes) three additional blood samples were collected via 3 ml gold-top vacutainers for the purposes of insulin analyses to be conducted at a later date. The vacutainers were connected to a stopcock connected to the cannula via a luer adapter with a vacutainer holder.

The samples obtained in vacutainers were left to clot at ambient temperature for 15 minutes. Once 15 minutes had elapsed, the vacutainers were separately spun in a centrifuge (5702R Centrifuge, Eppendorf, Stevenage, UK) at 4°C, 1800 RCF, for 10 minutes. The supernatant was transferred to a microfuge tube via pipette and stored at -80°C until analysis at a future date using an enzyme-linked immunosorbent assay (ELISA). The three samples for insulin analyses were collected immediately prior to meal consumption (fasted), immediately prior to PMT / PMT + BFR / control protocols commencing (30 minutes post-meal), and immediately after the PMT / PMT + BFR / control protocol had finished (60 minutes post-meal).

Insulin measurement

An enzyme-linked immunosorbent assay (ELISA) (Insulin ELISA kit, Crystal Chem, Illinois, USA) was completed to quantify the concentration of insulin in the serum samples obtained. Serum samples were brought to ambient temperature, and the ELISA kit instructions were adhered to (appendix 2).

The assay was then read using an ELISA spectrophotometer (Tecan M200 Pro, Tecan, Austria) using both 450 nm and 630 nm wavelength light. The reading obtained for each well of the assay at 630 nm were then subtracted from the reading obtained at 450 nm. The differences were then used to quantify serum insulin concentrations via interpolation of a standard curve (GraphPad Version 10, Prism, San Diego, USA) from known concentration standards supplied in the ELISA kit.

Ultrasound muscular thickness

Prior to measurements, adequate ultrasound conductive gel (Aquasonic 100, Parker Laboratories Inc, USA) was applied topically to the area to be scanned to promote acoustic coupling whilst promoting minimal compression of the skin. Ultrasound doppler measurements were taken to obtain quadriceps muscular thickness both pre- and post-protocol (Logiq 2, GE Healthcare, Wauwatosa, USA). A linear array L6-12 probe was used. A marker pen was used to mark the point at which the central indicator of the ultrasound transducer was at the three sites for pre-session muscular thickness readings to ensure consistency of probe placement location used for measurements both pre and post. The sites used were located on the participants left leg for consistency and approximately 10cm proximal to the quadriceps tendon on visual inspection. Sites were positioned left, central and right to detect any changes in muscular thickness across the quadriceps.

The transducer was positioned at a 90° insonation angle relative to the skin surface for measurements. Once the transducer was positioned with a satisfactory cross-sectional image present, the freeze function was used alongside the measure function of the ultrasound machine software. The distance measured was from the femur boundary to the epimysium (both defined by distinct grey/white images).

Settings of the ultrasound scanner used were the vascular preset, using the carotid sub-setting. Use of the carotid sub-setting allowed a clearer distinction of the femur surface with good visual clarity. These presets still allowed the scanned depth range to be adjusted to 5cm which was sufficient for this parameter. This protocol for muscular thickness ultrasound measurement was devised for this study to ensure placement of BFR cuffs did not impede measurements.

Coefficients of variance were calculated in preliminary equipment training to verify the repeatability of ultrasound muscular thickness measurements of the investigator. The investigator scored 4.18%, 6.47% and 4.33% across the three

sites from left to right when the coefficient of variation was calculated for five attempts measuring the sites selected.

Electromyography

Surface electromyography (EMG) data was collected at approximately 80% of the distance on the line from between the anterior spina iliaca superior and the joint space in front of the anterior border of the medial ligament on visual inspection (Delsys, Natick, USA). Perpendicular orientation on the EMG sensor was used as per the Seniam guidance, to obtain EMG data for the vastus medialis for five minutes of each of the three protocols (Seniam, 2019). A convenience sample of participants (n = 4) were asked to perform a maximal leg extension contraction with no external load, prior to the protocol commencing for all three visits. The EMG data was obtained to verify that the PMT protocol was passive and active contraction did not occur. The mean EMG signal obtained between 60 and 180 seconds from the protocol beginning was used for analysis. The signal between these timepoints were root mean squared, and the mean signal taken. This mean value was then expressed as a percentage of the maximum signal obtained in the flexion action against no external load obtained prior to the protocol commencing (appendix 1). Software was used to collect the raw EMG signal data (Trigno Discover, Delsys, Natick, USA).

Data management and statistical analysis

This study collected data which the study team regard as personal data, according to Lancaster University's data type classifications. Personal data is of the most sensitive type and therefore was kept confidential by assigning each participant a participant ID at the point of enrolling onto the study (pseudonymised). Data collection was then recorded by using the assigned participant ID and was stored on Lancaster University's OneDrive cloud storage only, in a password protected file via Microsoft Excel, as per Lancaster University's data storage policy.

Imputation of averages

Due to partial missing glucose and lactate data (CTRL = 7.3%, PMT = 1.2%, PMT + BFR = 2.1%) due to the inability to draw blood at that time point, average values for the specific timepoint and treatment were inputted. This was deemed the most appropriate action to take concerning managing missing glucose and lactate data. Due to a small number of missed data points for insulin (CTRL = 12.1%, PMT = 15.2%, PMT + BFR = 18.2%), averages of the timepoint for the treatment concerned were imputed to enable statistical analyses to be completed with a full dataset.

A Monte Carlo imputation was not used as this method assumes missing data are random. This was not the case in this study since missing data were due to samples which were not able to be obtained. The inability to obtain the samples was not random as there was a systematic influence on this. For example, it was more likely that a sample taken later in the protocol timeframe was to be missing, due to the nature of residual blood clotting inside the cannula with further use.

Statistical analysis

GraphPad software was used for statistical analyses (GraphPad Version 10, Prism, San Diego, USA). Shapiro-Wilk tests were undertaken to assess normality of the data. Means are reported ± standard deviation and to two decimal places figures, unless otherwise stated. Where normality was satisfied, one-way ANOVA analysis was carried out for differences between treatments of peak glucose, time to peak glucose, AUC glucose, AUC lactate and peak lactate. Analysis of glucose was done by a two-way ANOVA to analyse time and treatment interactions. Analysis of muscular thickness data was done by way of a two-way ANOVA with Šidák post-hoc analysis. This was a two-way ANOVA with time and intervention factor was to be analysed, whereas all other ANOVAs conducted were analysis of a treatment effect only. An alpha level of significance of 0.05 was set and if a p-value was less than the alpha, the difference observed was deemed statistically significant. P-values are quoted to three significant figures.

Statistical analyses of glucose data were conducted by way of a two-way ANOVA. Normality testing detected a small proportion of timepoints across the conditions, which consisted of non-normally distributed data (7 of 93 (7.53%) datasets). The justification for conducting a parametric test despite containing a small amount of non-normally distributed data was that the vulnerability and downside to using a parametric test with such data is the increased chance of a type I error. However, due to a p-value >0.05 resulting from this test, a type I error does not apply. In addition, parametric methods are recommended when they can be used because they provide a more efficient analysis of the data and provide a higher statistical power for smaller sample sizes (Nahm, 2016).

EMG data processing

Measures of EMG required analysis from the raw data obtained. Analysis software from the sensor manufacturer was used (Trigno, Delsys, Natick, USA). The data were root mean squared to ensure all values were positive to allow analysis as this provides the most insight into the amplitude of the signal (Delsys, 2014). Subsequently the mean value was calculated between 60-180 seconds after the start of the protocol. This mean was then divided by the maximal contraction obtained prior to monitoring and expressed as a percentage (MVC %).

Results

Glucose

Blood glucose concentrations were similar (Figure 2) across all three treatment groups throughout the trials (CTRL, 4.59 ± 0.48 mmol/L; PMT, 4.88 ± 0.82 mmol/L; PMT + BFR, 4.51 ± 0.90 mmol/L). Two-way ANOVA tests of mean glucose concentrations per participant, per treatment also showed no significant time x

treatment interaction (p = 0.887) or treatment interaction (p = 0.498). A significant time effect was detected (p < 0.0001).

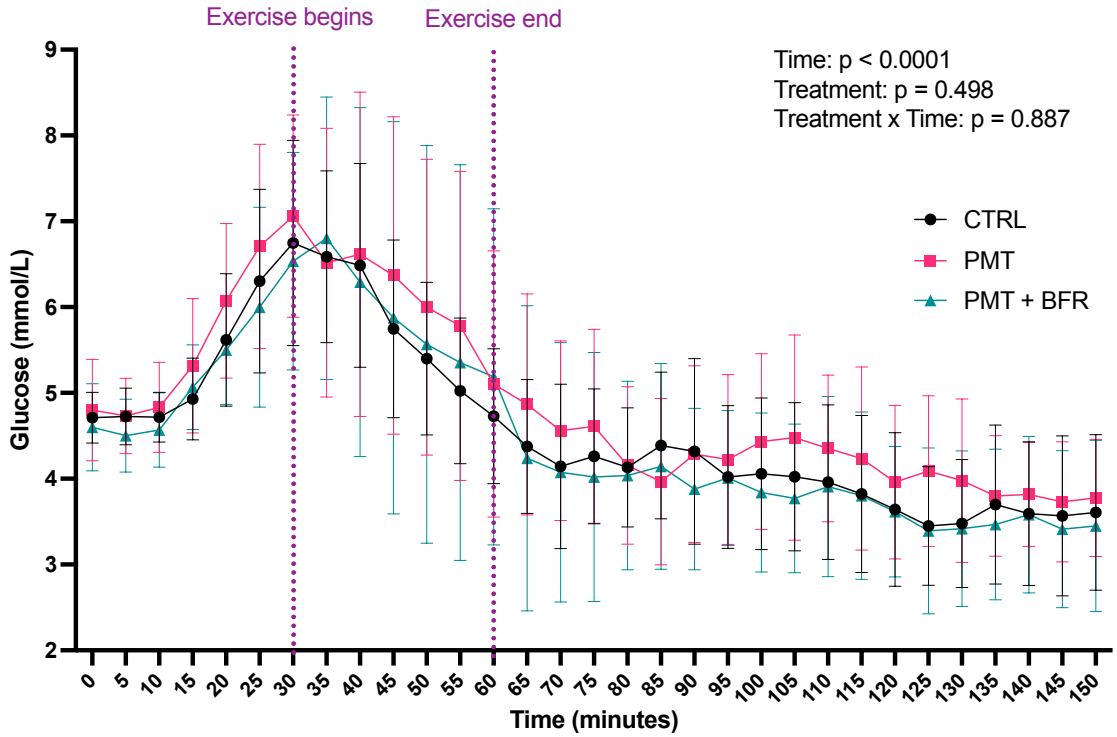

***Figure 2**. Mean glucose concentrations across the three treatment groups with a standardised meal consumed from timepoint zero minutes. Timepoint 30 minutes is where PMT / PMT + BFR protocols commenced in the relevant treatment groups. PMT, passive movement training; PMT + BFR, passive movement training with blood flow restriction; CTRL, control*

An additional representation of the degree of glucose excursion and disposal used was calculation of the area under the curve (AUC) for each participant undergoing each treatment. The AUC was calculated using GraphPad, using the function to calculate AUC which uses the trapezoid rule (GraphPad Version 10, Prism, San Diego, USA) Calculation of AUC was performed for the full 150 minutes and the latter 120 minutes of each protocol. No significant differences were observed via one-way ANOVA in either of these analyses (p = 0.501, p = 0.594) respectively as shown in Figure 3A and 3B.

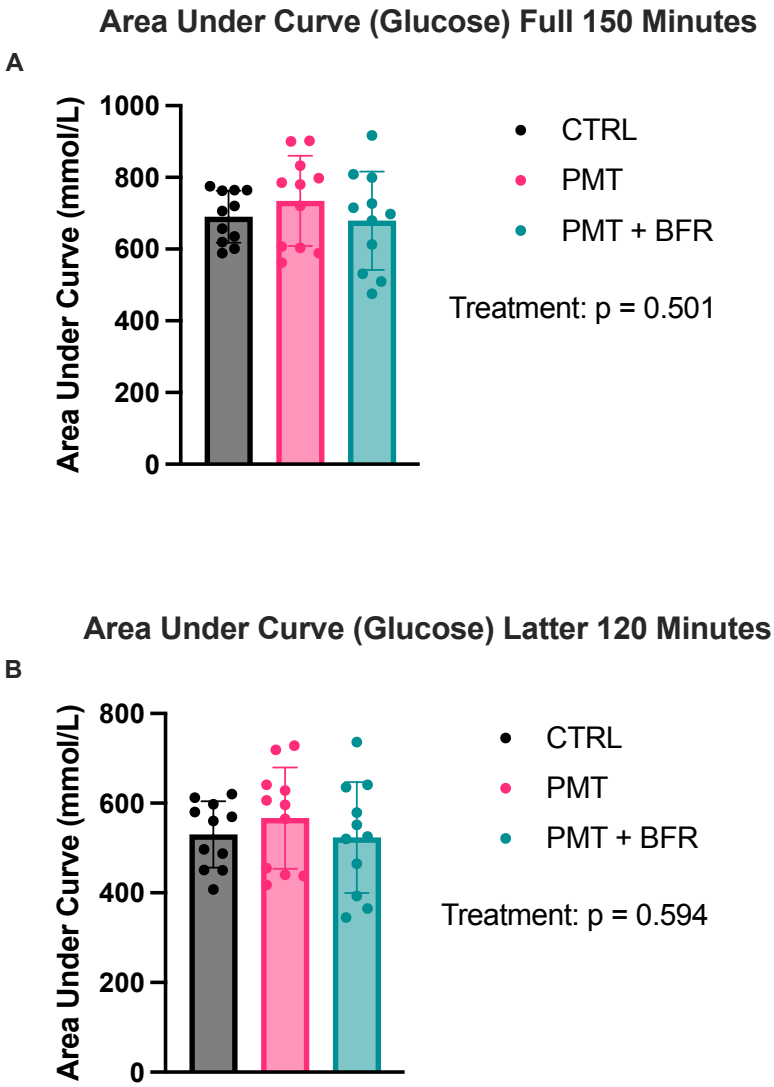

Figure 3*. Area under curve of glucose data, representative of the entire 150 minutes for which samples were taken (A) and the latter 120 minutes (B)*

PMT, passive movement training; PMT + BFR, passive movement training with blood flow restriction; CTRL, control

Peak glucose concentration was also compared via one way ANOVA test, with no statistical difference detected between the three treatment groups (p = 0.793).

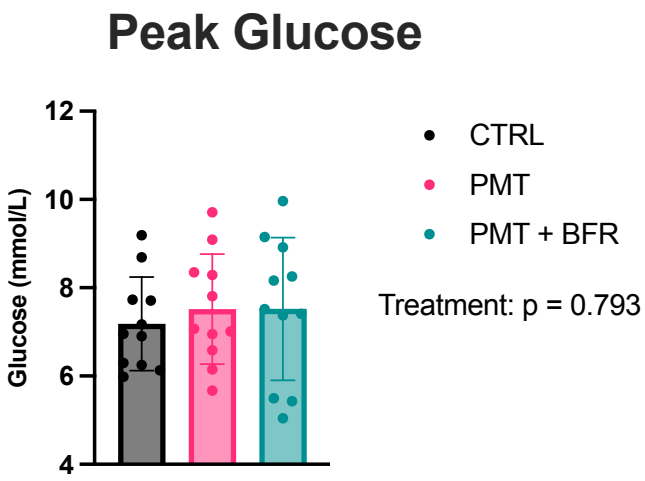

Figure 4*. Peak glucose concentrations, calculated as at the timepoint of individual participant peak glucose concentration (CTRL 7.18 ± 1.06 mmol/L; PMT 7.52 ± 1.25 mmol/L; PMT + BFR 7.52 ± 1.62 mmol/L)*
PMT, passive movement training; PMT + BFR, passive movement training with blood flow restriction; CTRL, control

Time taken to reach peak glucose concentration was analysed. No significant differences were detected via one way ANOVA analysis (p = 0.936).

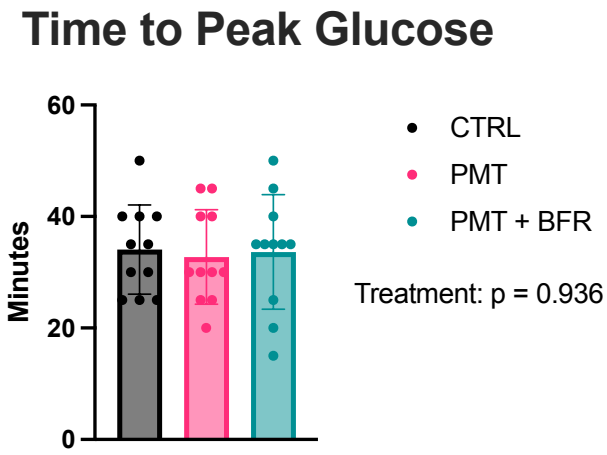

Figure 5. *Time to peak glucose concentration (CTRL 34.09 ± 8.01 minutes; PMT 32.73 ± 8.47 minutes; PMT + BFR 33.64 ± 10.27 minutes)*

PMT, passive movement training; PMT + BFR, passive movement training with blood flow restriction; CTRL, control

Glucose levels at the start of exercise were analysed for statistically significant differences between treatment groups. No statistical difference was detected ($p = 0.601$, figure 6A). Glucose levels were analysed midway into exercise and the end of exercise (45 minutes post-feeding, and 60 minutes post-feeding respectively). Statistically significant differences were not detected at either timepoint via one way ANOVA analyses ($p = 0.696$; $p = 0.753$) (figures 6B and 6C, respectively).

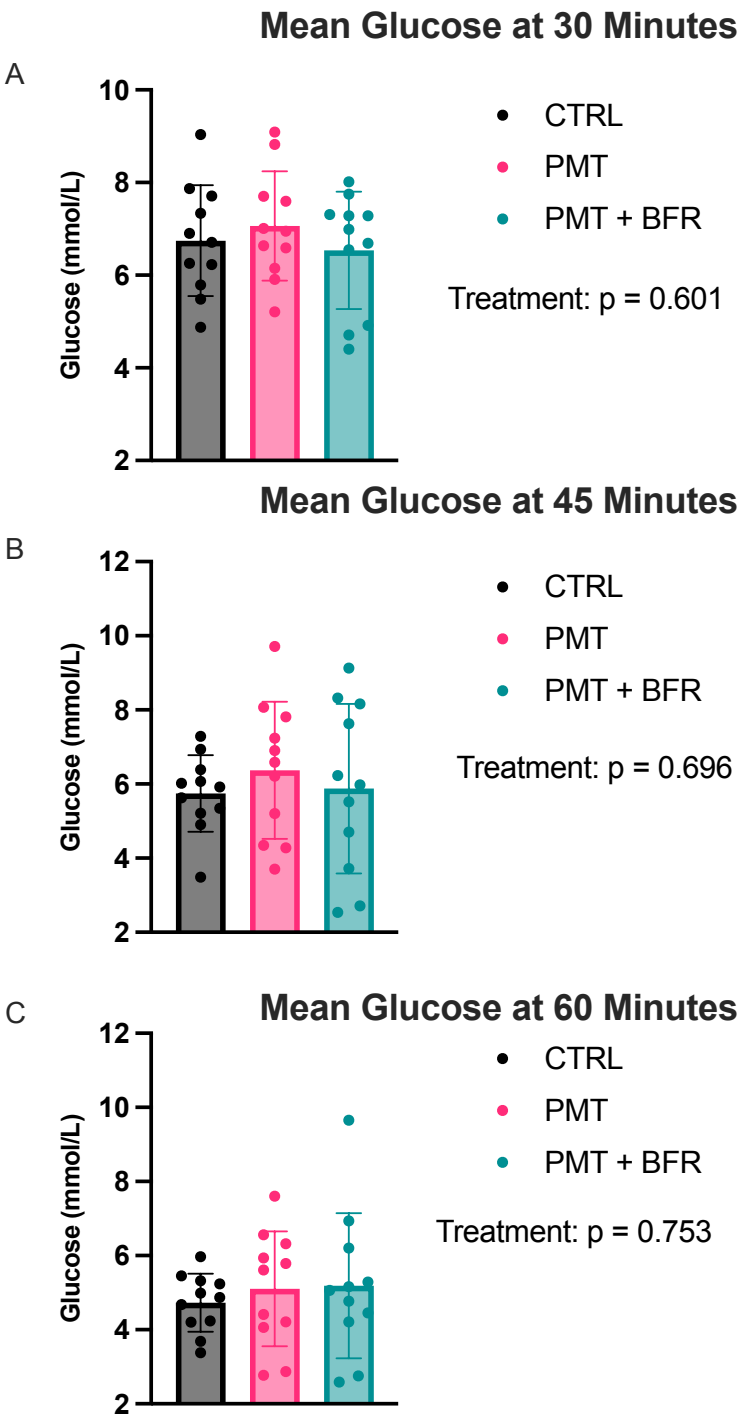

Figure 6. *Glucose levels at the start of exercise (A), midway into exercise (B) and end of exercise (C)*

PMT, passive movement training; PMT + BFR, passive movement training with blood flow restriction; CTRL, control

Due to visual inspection of the glucose data suggesting a larger spread of data in the PMT and PMT + BFR groups than CTRL, glucose range indices were calculated and analysed via a one-way ANOVA. No significant difference was detected in glucose range indices (p = 0.685) (Figure 7).

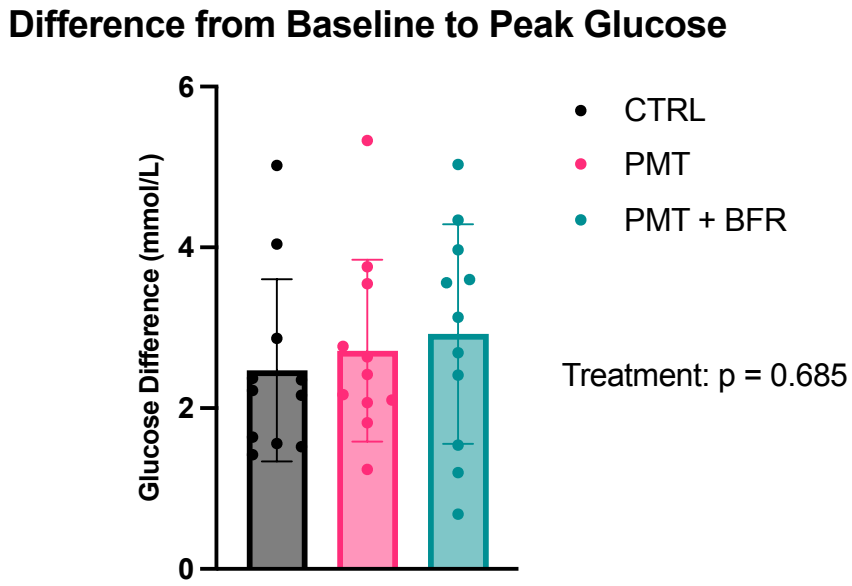

Figure 7. *Differences between peak glucose and baseline glucose*

PMT, passive movement training; PMT + BFR, passive movement training with blood flow restriction; CTRL, control

Insulin

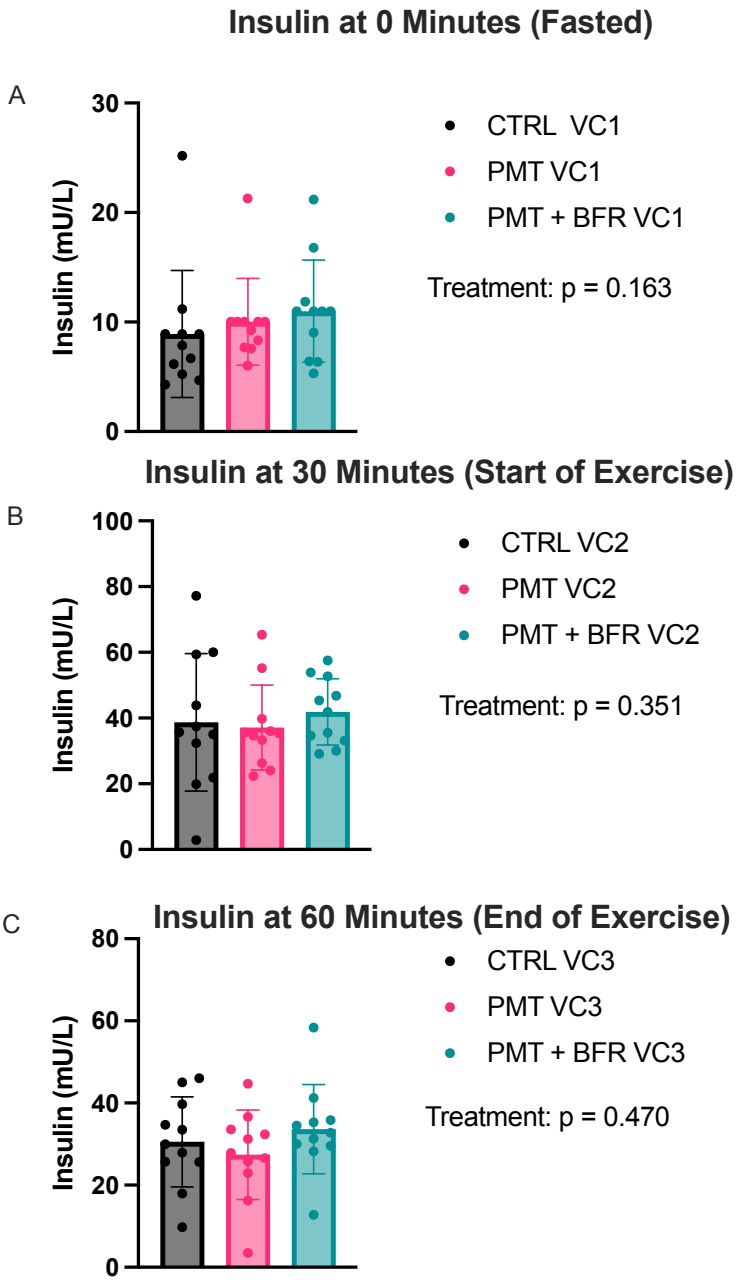

***Figure 8**. Insulin concentrations at 0 minutes (fasted) (vacutainer 1; VC1) (A); at the commencement of* exercise (30 minutes) *(vacutainer 2; VC2* (B) and end of exercise (60 minutes) *(vacutainer 3; VC3)* (C).

PMT, passive movement training; PMT + BFR, passive movement training with blood flow restriction; CTRL, control.

Normality testing determined that insulin measurements were non-normally distributed. A Friedman test was carried out to assess for differences between the treatments. No significant differences (Figure 8) were detected for any timepoints (0 minutes, p = 0.163; 30 minutes, p = 0.351; 60 minutes, p = 0.470).

Lactate

Peak lactate concentrations were examined for differences across the three treatment groups via one way ANOVA analysis. No statistically significant differences were detected (p = 0.893).

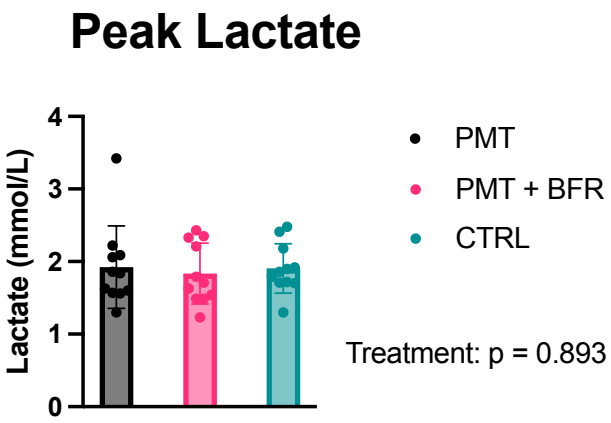

***Figure 9**. Peak lactate concentrations across three treatment groups*
PMT, passive movement training; PMT + BFR, passive movement training with blood flow restriction; CTRL, control

In the interest of a comprehensive examination of lactate concentrations throughout the protocols, area under curve analyses were also conducted. Calculations were carried out for the full 150 minutes of the protocol as well as the latter 120 minutes (from exercise commencing onwards). No significant differences were observed between the three treatment groups in either timeframe (p = 0.841; p = 0.895 respectively).

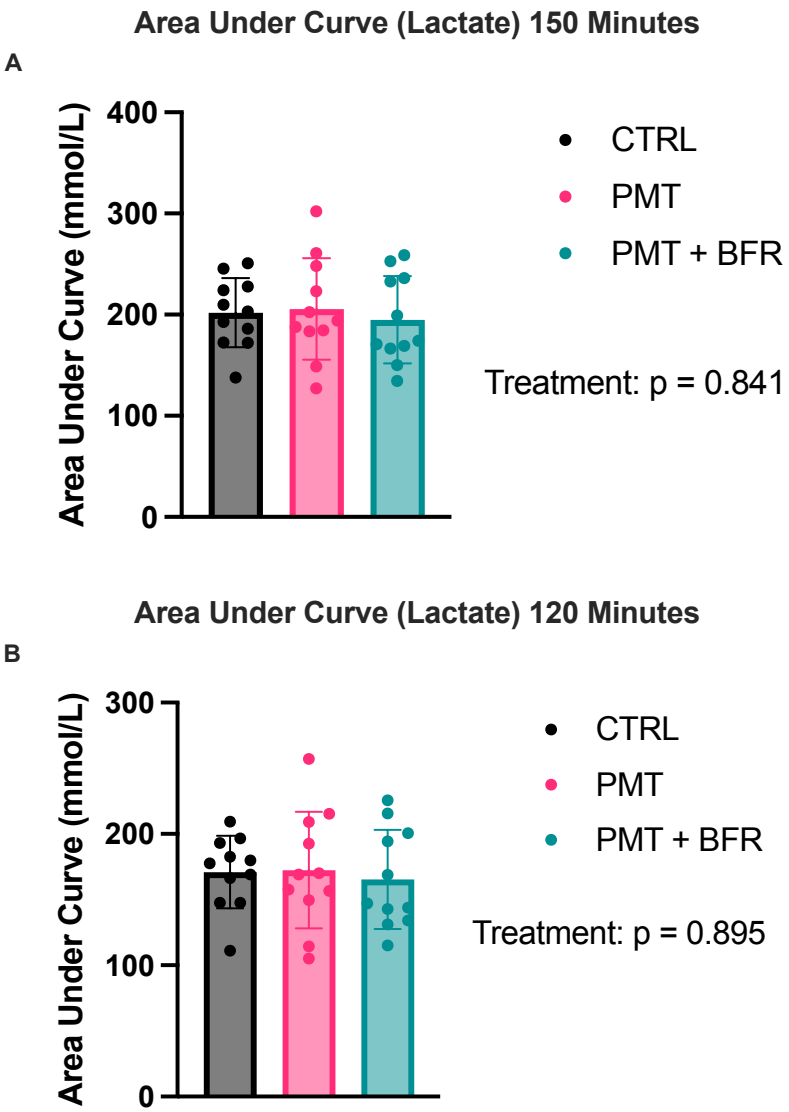

***Figure 10**. Area under curve of lactate data, representative of the entire 150 minutes for which samples were taken (A) and the latter 120 minutes (B)*
PMT, passive movement training; PMT + BFR, passive movement training with blood flow restriction; CTRL, control

Muscular thickness

A two-way ANOVA for muscular thickness between the three treatments revealed a statistically significant time x treatment interaction (p = 0.00420) in the PMT + BFR protocol only. Post-hoc analyses revealed the difference lied between mean PRE and mean POST in the PMT + BFR treatment (p = 0.0016). Cohen's D was used to evaluate effect size of pre to post muscular swelling in PMT + BFR and was calculated as 1.05.

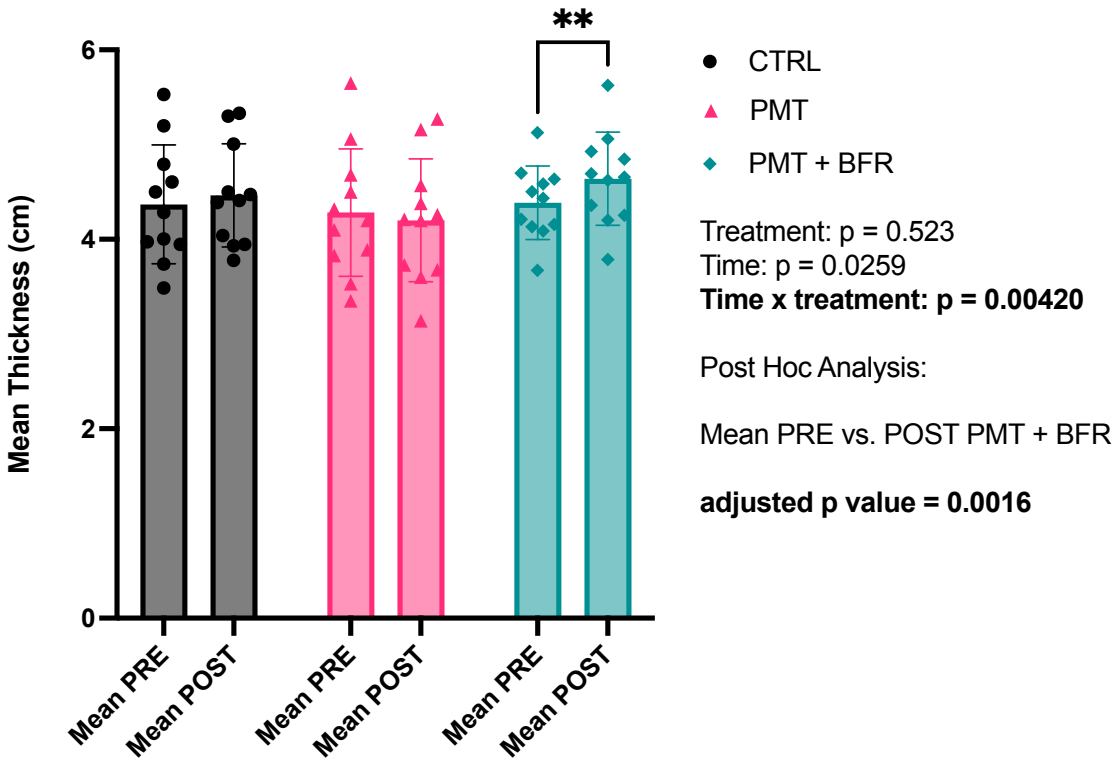

Figure 11*. Muscular thickness changed over time between treatments. Undertaking PMT + BFR displayed significant acute increases from pre- to post-protocol in muscle thickness (p = 0.00420).* ****p < 0.01.***

PMT, passive movement training; PMT + BFR, passive movement training with blood flow restriction; CTRL, control

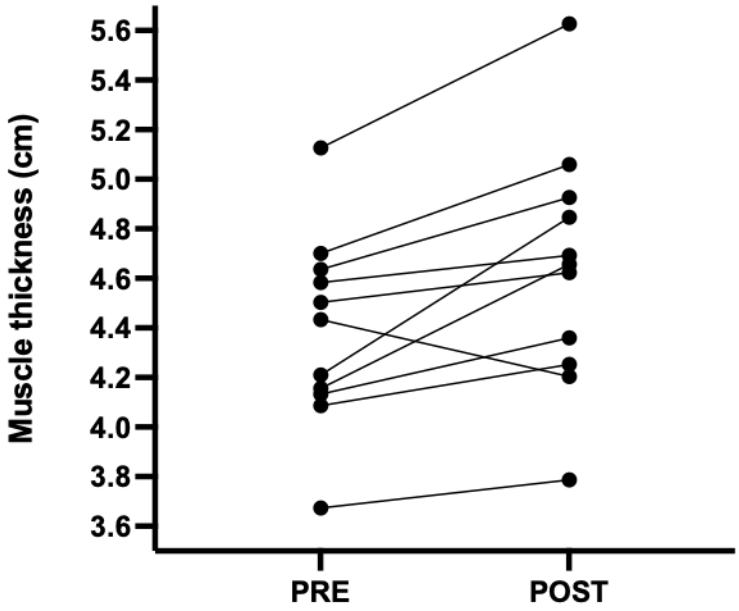

Figure 12. *Passive Movement Training + Blood Flow Restriction treatment only, individual participant pre- and post-treatment muscular thickness measurements (mean PRE 4.39cm ± 0.39; mean POST 4.64cm ± 0.49)*

Discussion

There were no significant differences in the rate of glucose disposal across the three treatment groups as measured by area under curve, peak glucose and average glucose. These results did not align with the initial hypotheses which predicted 1) undertaking PMT would elicit a blunted elevation in postprandial blood glucose and 2) that this effect would be exaggerated further with the addition of BFR. However, our findings revealed a significant muscular thickness time x treatment interaction elicited by undergoing PMT + BFR . This may suggest promise of using BFR as a method of attenuating atrophy through a cellular swelling-mediated mechanism.

Glucose disposal and possible mechanistic explanations

Across all metrics used to evaluate the impact of PMT or PMT + BFR on the rate of glucose disposal, no significant differences were found between PMT, PMT + BFR and CTRL groups. These findings suggest that exercise must be active and not passive, to elicit a greater rate of glucose disposal than at rest, as is shown with conventional exercise (Richter & Hargreaves, 2013). To ensure a thorough examination of the rate of glucose disposal was conducted, several metrics were analysed. These included differences between the three treatment groups at each of the 31 sampled timepoints, AUC of the full 150 minutes and AUC of the latter 120 minutes. Both AUC timeframes were evaluated because the initial 30 minutes of each treatment were identical.

The rationale for undertaking this study was multifaceted. Previously PMT has been shown to increase blood flow to approximately 330% of that at rest (a hyperaemic effect) (Trinity & Richardson, 2020). The hyperaemic effect observed from PMT is thought to be caused by NO, because inhibition of NO has shown to reduce the hyperaemic response to PMT by approximately 90% (Mortensen *et al*., 2012). It has been suggested that skeletal muscle capillaries in vivo are recruited by a NO-dependent action, which may consequently contribute to increased glucose uptake (Vincent *et al*., 2004). We attempted to investigate if PMT be used to postprandially to increase blood flow from resting levels, to then elicit an increased rate of glucose disposal.

In addition, a further study has shown that a mechanism which results in the hyperaemic responses caused by PMT is nitric oxide dependant (Mortensen *et al*., 2012). In the aforementioned study, nitric oxide inhibited participants displayed lower blood flow increases in response to PMT, compared to uninhibited controls. This suggests that the hyperaemic response to PMT is nitric oxide dependant. However, Mortensen *et al*. (2012) do state that healthy elderly participants who underwent the treatment showed lower increases in blood flow than younger, healthy participants. This would imply that the participants recruited for the present study (healthy males 18-40 years-old) should have

experienced a relatively high magnitude of increase in blood flow under PMT. This however did not result in significant glucose response differences. It should be noted that although blood flow is increased to approximately 3 times that seen at rest, conventional exercise increases blood flow to approximately 17-fold (Morensen *et al*., 2012; Boushel *et al*., 2000).

Other mechanisms may elucidate why glucose uptake was not increased significantly with PMT compared with controls. One such mechanism is a lack of metabolic substrate requirement in skeletal muscle with PMT, compared to conventional active contraction. Active contraction requires cross-bridges (from myosin heads to actin binding sites) to be formed and broken to facilitate contraction via the sliding filament theory (Lemaire *et al*., 2019). This active contraction is an energy intensive process due to the active calcium ion transport required. With PMT, it is likely that the metabolic cost is significantly less than that of active contraction due to the mechanical work and kinetic energy being delivered from the external force applied, rather than the muscle itself. Due to the contraction being passive and not active in the present study, it is likely that glucose disposal rate was not increased because no active contraction occurred which is known to drive glucose uptake in exercise (Richter & Hargreaves, 2013).

Another aspect of PMT which may aid in elucidating as to why glucose disposal was not significantly increased compared to CTRL is the lack of stretch exhibited in PMT. As per a previous published protocol, this study utilised a range of motion for leg flexion/extension of 80° (Burns *et al*., 2018). This range of motion ensured all participants could achieve the full range without excessive discomfort when manipulated through the range by a force exerted by the isokinetic dynamometer. This programme of PMT may not have resulted in the same extent of muscular stretch as active exercise. A meta-analysis from 2024 showed that an 8.85% reduction in acute glucose measures was shown in stretching groups compared to controls (Thomas *et al*., 2024). The meta-analysis included studies consisting of stretching protocols including active, passive and proprioceptive

neuromuscular facilitation. Interestingly, a greater effect in glucose reduction was observed in participants with T2DM than healthy controls (Thomas *et al*., 2024). Mechanistically, stretching may play a role in the reduction in acute glucose metrics by a sequence of events whereby stretching exercise would increase Ca^{2+} release from vascular endothelium, then causing nitric oxide release (Hotta & Muller-Delp, 2022). A small range of motion was used in the present study to enable accessibility to all participants. However, had a larger range of motion been used which would have elicited a more exaggerated stretch, this could have mediated NO release and glucose uptake (Thomas *et al*., 2024). The release of nitric oxide would elicit vasodilation and increased blood flow, which is known to play an important role in glucose uptake as this effect is also exerted by insulin secretion (Baron & Clark, 1997). Increased blood flow (hyperaemia) has also been suggested to play an important role post-exercise in facilitating glucose delivery to previously active muscle (Pellinger & Emhoff, 2022).

A separate but similar mechanism which may be pertinent to consider given this study's BFR aspect, is the hemodynamic fluctuations seen in stretching. Furthermore, it has previously been observed that in the stretch phase a decrease in blood flow occurs and therefore relative ischaemia which does decrease glucose uptake. However, upon release of the stretch an influx of blood (hyperaemia) occurs and therefore an increase in overall glucose uptake (Pellinger & Emhoff, 2022). This may suggest the use of BFR should in theory increase glucose uptake overall due to ischaemia being caused during BFR application, but reactive hyperaemia following BFR release. Reactive hyperaemia could then cause an increase in overall glucose uptake. Potential methodological flaws of the application of BFR in this study are discussed later in this text and may elucidate reasons as to why this was not observed in this study.

No effect of passive movement with or without blood flow restriction on blood lactate

No significant differences in lactate were observed between treatments. It was predicted that an increased AUC of lactate would be detected in the PMT + BFR treatment group compared with CTRL and PMT groups. This hypothesis of the physiological basis that the use of BFR would cause an 80% arterial occlusion, and 100% venous occlusion of the vasculature distal to the BFR cuff. It was predicted that this may have increased lactate due to the ischaemic environment created. Therefore, the ability for oxidative metabolism to function would have decreased and led to increased reliance on anaerobic metabolism with lactate as a byproduct (Goodwin *et al*., 2007).

The parameters of BFR used were so as they are the upper limit of BFR pressures used previously (Patterson *et al*., 2019). The upper limit was used to enhance efficacy to maximise probability of an effect being observed if BFR was to add a compound effect to PMT. The rationale of using BFR in addition to PMT was to examine if an exaggerated glucose disposal was observed. The basis for this was that the release of the BFR would have caused a greater hyperaemic response than PMT alone. Furthermore, it has been reported that reactive hyperaemia follows the release/deflation of BFR (Gundermann *et al*., 2012).

Due to no significant differences detected in lactate across the three treatment groups, the effectiveness of the BFR occlusion should be considered. This contrasts previous findings where resistance exercise combined with intermittent and continuous BFR was examined for lactate changes. The continuous BFR showed greater percentage change than intermittent BFR indicating a positive dose-response relationship to BFR application time and lactate increase (Neto *et al*., 2017). However, due to the lack of autoregulation of pressure during the passive movement exercise, it may be the case that the movement of the limb

resulted in fluctuations of limb circumference and therefore pressure applied. This may have resulted in unintended blood flow during leg movement.

An implication for practice in the use of BFR, whether that may be coupled with PMT or active exercise, is that autoregulation of BFR should be used to ensure consistency of the pressure applied. This may prove an effective strategy to ensure the correct relative arterial occlusion pressure is maintained.

Insulin responses did not differ between study visits

A key aspect of this study was to examine insulin responses in synergy with glucose responses. No significant differences were detected in insulin responses across treatments.

All three treatment groups (CTRL, PMT, PMT + BFR) showed similar insulin response profiles at the timepoints at which measurements were taken (0 minutes (fasted), 30 minutes (immediately pre-exercise) and 60 minutes (immediately post-exercise). These findings, particularly for those taken at 60 minutes, suggest that passive exercise, with or without BFR, has no statistically significant effect on the postprandial insulin response to the meal given. It could be speculated that a difference in insulin was not observed in treatment groups compared to CTRL due to no increase in metabolic demand being present in passive exercise.

Muscle thickness was increased acutely with passive movement and blood flow restriction

In comparison to CTRL and PMT without BFR, it was found that BFR application elicited a significant increase in acute muscular swelling from pre- to post-PMT protocol. Several mechanisms could contribute to acute swelling observed.

One such mechanism is that by applying BFR, the venous outflow from the limb (leg) is completely occluded, however only 80% arterial occlusion is applied. The

net result is there is still blood flow into the limb and therefore the quadriceps and so oedema may occur. An additive effect to the magnitude of oedema may be caused by preventing venous outflow and therefore causing intracellular metabolite accumulation and consequently an osmotic influx into the cells. The osmotic influx would then result in cellular swelling and acute muscular swelling. Previous literature has shown similar effects of BFR with an acute muscular thickness increase observed (Cleary *et al*., 2022). The acute muscular swelling findings observed may suggest potential therapeutic applications of BFR, however further research is required.

Interestingly, a proposed mechanism for how BFR elicits a hypertrophic / atrophy attenuating effect is linked with cell swelling. Use of BFR increases the water content of cells due to an osmotic influx, possibly caused by increased metabolite concentration. Previous findings have shown load-matched BFR exercise caused significantly more acute muscular swelling than free flowing exercise (Haddock *et al*., 2020). The muscle cell has an osmotic influx of water also due to phosphocreatine and hydrogen ion accumulation (Hirono *et al*., 2020). This is hypothesised to cause activation of an internal volume sensor within the cell (Loenneke *et al*., 2012). Further, the activation of this sensor through intermediaries then activates the mTOR pathway, the master regulator of skeletal muscle growth. It must be stated that this mechanism has been observed in low-intensity exercise, however, this cellular swelling does not seem to have been studied in PMT literature. The mechanism between cell swelling and hypertrophy is not fully elucidated. However, if cellular swelling is potentially able to cause activation of the mTOR pathway, this may be a potent method of attenuating atrophy and sarcopenia is inactive populations. The rationale behind this is skeletal muscle is a plastic organ with constant turnover and is maintained by multiple signalling pathways (Bonaldo & Sandri, 2013). Therefore, activation of mTOR may shift this turnover away from overall degradation (atrophy), towards a maintenance state (Bonaldo & Sandri, 2013). This may have the beneficial metabolic effect of maintaining a higher proportion of skeletal muscle mass in inactive populations, which has been concluded to be inversely associated with

blood glucose level (Taha *et al*., 2021). This suggests preservation of muscle mass may be an effective preventative measure for T2DM incidence. Further research is required to elucidate the effectiveness of using BFR for the purpose of mitigating muscular atrophy. Previous studies have provided inconsistent findings regarding the use of BFR in bed rest for the purpose of mitigating atrophy (Fuchs *et al*., 2025; Barbalho *et al*., 2019). Interestingly, Barbalho *et al*. (2019) used PMT + BFR whereas Fuchs *et al*. (2025) used BFR alone. This difference warrants further research to elucidate the effectiveness of PMT + BFR for mitigation of muscular atrophy.

In summary, the findings of this study suggest that passive exercise is not an effective method of reducing postprandial glucose increases, whilst also highlighting the significant acute muscular swelling effect of BFR. These findings indicate that the use of exercise to reduce the postprandial glucose rise must include active exercise or potentially exercise with an increased muscular stretch than was conducted in this study. These findings lay the groundwork for future studies to examine postprandial glucose responses with an increased muscular stretch than was performed in this study. Further, investigation of the effect of standalone BFR on acute muscular swelling with biopsy analysis of muscle which has undergone BFR. Such studies may elucidate potential mechanisms of action of BFR.

Limitations and future research

Multiple limitations of this study should be recognised. One such limitation was that it was not possible to measure femoral arterial pulse speed via ultrasound. This was due to the location and cuff width of the BFR cuffs used. The width of the cuffs meant that on application to the thighs, the area where ultrasound femoral arterial speed measurement should take place was obstructed. The only area of the thigh which could have theoretically been used to measure arterial pulse speed, was excessively distal and therefore in close proximity to the femoral

artery bifurcation. Accurate velocity measurements cannot be obtained from this location due to turbulent blood flow and therefore inaccurate doppler readings. Confirmation of a definitive hyperaemic response is only possible via doppler ultrasound arterial pulse speed measurement. This effect has been observed in previous literature using the same protocol, hence it is assumed that the same hyperaemic response occurred in this investigation (Burns *et al*., 2018).

It is pertinent to consider this in the protocol used due to the passive movement of the limb, and therefore limb circumference fluctuations as the leg moves through an 80° range of motion. As circumference fluctuates, without the BFR cuff autoregulating pressure to maintain a constant pressure on the limb, it cannot be guaranteed that BFR is being maintained, therefore a key limitation of this study was the inability to autoregulate BFR pressure (Hughes *et al*., 2024). It would also be valuable to investigate in the future if use of BFR alone for an extended period is effective at increasing glycolytic metabolism and therefore glucose uptake upon release of the BFR, in addition to its effects on muscle thickness.

Final methodological limitations of this study refer to the indirect measurement of glucose uptake. Blood glucose was measured but this was only a proxy for muscular glucose disposal. Although the independent variable we manipulated was presence or absence of movement of the leg muscles, it is possible that hepatic glucose uptake could have differed between treatments due to factors such as the extent of the fast the participant had undertaken and other extraneous factors. Unfortunately, this study did not examine the mechanistic changes via muscle biopsies, such as GLUT-4 translocation which may have provided further confidence one the extent of postprandial glucose uptake per treatment. Lastly, it was not possible in this trial to blind the participant to the treatment due to the sensation of the treatments being used.

Appendices

Appendix 1 – EMG Monitoring of PMT

(n = 4, to 2 decimal places)

Table 3 Mean Voluntary Contraction During EMG Monitoring Phase, Relative to Maximal Contraction Performed with no External Load

	CTRL	PMT	PMT + BFR
Mean Voluntary Contraction %	4.03 ± 5.08	2.32 ± 2.51	5.00 ± 8.82

Appendix 2 – ELISA Protocol

I. Assay Procedure
All reagents, unless otherwise noted, are stable for a minimum of 2 months at 2-8°C once opened.

I.1. Preparation of reagents

1. Antibody-coated microplate
Provided as ready to use. Protect from moisture.

2. Standards 1-6
Standards are provided in lyophilized form with concentrations ranging from 0 mU/L to 220 mU/L. Dilute each standard with 1 mL of deionized water. After reconstitution, it is recommended that standards be allowed to sit for 5 mins at room temperature and then mixed gently to ensure all solids are dissolved.
Reconstituted standards are stable for two weeks at 2-8°C. For longer term storage, reconstituted standards should be frozen. Standards should be not be repeatedly thawed, so standards should be appropriately aliquoted in appropriate volumes prior to being frozen. Standards are approximately provided in the following concentrations: 0, 3, 10, 30, 110 and 220 mU/L. For exact values, please see calibrator labels on each bottle as values may vary slightly from lot to lot.

3. Controls 1-2
Controls are provided in lyophilized form with target value and ranges included on their labels. Dilute each control with 1 mL of deionized water. After reconstitution, it is recommended that controls be allowed to sit for 5 mins at room temperature and then mixed gently to ensure all solids are dissolved.

Reconstituted controls are stable for two weeks at 2-8°C. For longer term storage, reconstituted controls should be frozen. Controls should be not be repeatedly thawed, so controls should be appropriately aliquoted in appropriate volumes prior to being frozen.

4. HRP Labeled Antibody

The HRP labeled antibody must be diluted 1:12 with diluent prior to use. Please prepare only as needed. For example, mix 0.1 mL of HRP labeled antibody with 1.1 mL of Diluent and mix thoroughly. The stability of the working HRP labeled antibody is two weeks when stored at 2-8°C.

5. Diluent

Provided as ready to use.

6. Wash Buffer (30X Concentrated)

The wash buffer has to be diluted 1:30 with distilled or deionized water prior to use. For example, 50 mL of wash buffer must be diluted with 1,450 mL of deionized water. Wash buffer is stable for 4 weeks at 2-8°C after dilution, so dilute only as needed.

7. Substrate Solution

Provided as ready to use.

8. Stop Solution

Provided as ready to use.

I.2. Assay procedure

Prior to running the assay, all reagents should be brought to room temperature for at least 30 minutes. Reagents should be stored at 2-8°C immediately after use. Before use, mix the reagents thoroughly by gentle agitation or swirling.

1.In each well, add 100 µL of working HRP labeled antibody into each well.
2. In each well, add 25 µL of sample, standard, or control and mix well by repeated pipetting.
3. Cover the wells with a plate sealer and incubate the plate for 2 hours at 37°C.
4. Aspirate well contents and wash three times using 300 µL of Wash Buffer per well. After each wash, remove any remaining solution by inverting and tapping the plate firmly on a clean paper towel.
5. Add 100 µL of Substrate Solution in each well.
6. Incubate the plate for 15 mins in dark room at room temperature.
7. Stop the reaction by adding 100 µL of Stop Solution.
8. Measure absorbance within 30 minutes using a plate reader (measure A450 values and subtract A630 values).

I.3. Determining the insulin concentration

1. Using computer software, construct the insulin calibration curve by plotting the mean change in absorbance value for each calibrator (incl. blank) on the Y axis

versus the corresponding insulin concentration on the X axis. A four parameter or cubic spline curve fit are suitable for the evaluation.
Note: A calibration curve should be plotted every time the assay is performed.

2. Insulin concentrations in the samples are interpolated using the calibration curve and mean absorbance values for each sample. For diluted samples, the values obtained must be multiplied by the dilution factor to obtain the final insulin concentration. The insulin concentration is expressed in mU/L.
Note: Samples with high insulin concentrations (ie. fall above the range of the assay) should be further diluted with the Standard 1 and rerun.

J. Performance characteristics

J.1. Assay range
The Insulin ELISA Kit has an assay range from 0 – 220 mU/L. The analytical sensitivity of the assay is 0.9 mU/L.

J.2. Precision
The assay has a within-run and total precision of CV < 10%.

Appendix 3 - Health Screening Form

Risk Factors	**Risk Factor**	**No Risk Factor**
Q1. **Age** _____years Male. Female	**≥45** **≥55**	**<45** **<55**
Q2. Are you a current **smoker**? *If yes, how many cigarettes do you smoker per day?* ----------_____ If no, have you ever smoked? *If yes, how long has it been since you quit?* _____ *Are you exposed to environmental tobacco smoke?*	**Yes** Yes† *Yes*†	**No** No *No*
Q3. **Family history:** Have any parents or siblings had a heart attack, bypass surgery, angioplasty or **sudden death*** prior to 55 years (male relatives) or 65 years (female relatives)?	**Yes**	**No**

Q4. **Physical inactivity:** In the past 3 months, have you performed at least 30 minutes of activity on at least 3 days per week	**No**	**Yes**
Q5. **Resting blood pressure:** Systolic BP _____mmHg Diastolic BP _____ mmHg *Do you take blood pressure medication?*	**≥140**** **≥90**** **Yes**	**<140** **<90** **No**
Q6. **Anthropometry:** Body mass _____ kg Height _____ cm **Body mass index** _____kg/m^2 **Waist** _____ cm Male Female *Waist-to-Height ratio* _____ Body Composition:	**<18.5 or** **≥30** **>102** **>88** ≥0.5	**≥18.5 and** **<30** **≤102** **≤88** <0.5
Q7. **Blood analysis:** **Fasting blood glucose** _____ mmol/L Non-fasting blood glucose _____ mmol/L **Total cholesterol** _____ mmol/ **LDL cholesterol** _____ mmol/L **HDL cholesterol** _____ mmol/L	**≥5.55^** ≥7.77^ **≥5.18** **≥3.37** **<1.04**	**<5.55** <7.77 **<5.18** **<3.37** **≥1.04^^**
TOTAL NUMBER OF RISK FACTORS (Bold only) † Include as a risk factor if ≤6 months *If YES to **early sudden death** in family history advise pre-participation screening for SCD with GP **If BP ≥140/90mmHg after 2 measurements advise GP visit ^ If ≥5.55 – ≤6.94 (NF ≥7.77 – ≤11.04) class as risk factor, if >6.94 (NF >11.04) class it is a RF and HoD ^^ If HDL ≥1.55mmol/L, subtract 1 from the total risk factors		

NOTE: Risk factors are collected for pre-examination evaluation of CVD risk assessment and not for decision making related to medical referrals

Signs or Symptoms

Q7. Do you ever have pain or discomfort in your chest or surrounding areas (neck, jaw, arms or other areas)?	Yes	No
Q8. Are you ever short of breath at rest or with mild exertion?	Yes	No
Q9. Have you ever experienced dizziness, fainting or loss of consciousness during or shortly after exercise?	Yes	No
Q10. Have you ever been short of breath at rest in the recumbent position or had an attack of breathlessness in the middle of the night which was relieved by sitting up?	Yes	No
Q11. Do your ankles ever become swollen (other than as a result of an injury)?	Yes	No
Q12. Do you ever have palpitations (=the unpleasant awareness of the heart beating in your chest) or an unusual period of rapid heart rate?	Yes	No
Q13. Do you ever suffer from burning or cramping sensations in your legs, brought on by exertion and relieved after 1-2 minutes of rest?	Yes	No
Q14. Has a doctor ever said you have a heart murmur?	Yes	No
Q15. Do you feel unusually fatigued or find it difficult to breathe with usual activities?	Yes	No
SIGNS/SYMPTOMS OF DISEASE	**YES**	**NO**

Personal History of Disease		
Q16. Heart disease	Yes	No
Q17. Peripheral vascular disease	Yes	No
Q18. Cerebrovascular disease (e.g. stroke)	Yes	No
Q19. Asthma (if controlled no further action)	Yes	No
Q20. Chronic obstructive pulmonary disease	Yes	No
Q21. Diabetes mellitus Type 1 Type 2	Yes Yes	No No
Q22. Renal (kidney) disease	Yes	No
Q23. Liver disease	Yes	No
HISTORY OF DISEASE	**YES**	**NO**

Kardia Check for Atrial Fibrillation	
Resting heart rate	
Brief overview of result and any action taken: **Remember to take screenshot of result and store securely for future reference**	

Other Conditions/Additional questions		
Q27. Do you have any bone or joint problems that might get worse with exercise? *If Yes, does this include any of the following conditions?* *Osteoarthritis* *Rheumatoid arthritis* *Osteoporosis*	**Yes** Yes Yes Yes	**No** No No No
Q28. Do you have a current/past injury that may be worsened with exercise? Details: _____ _____	Yes	No
Q29. Do you have any other condition/problem that might make it difficult for you to do strenuous exercise? Details: _____ _____	Yes	No
Q30. Are you or have you recently been pregnant?	Yes	No
Q31. Are you taking any prescription medications? List: _____	Yes	No
Q32. Have you had any **alcohol** to drink in the last 24 hours? *If yes,* how many units? _____ units how long ago? _____ hours	Yes	No
Q33. Are there any other factors that may affect your results today? E.g. viral infection, injury, smoking, exercise, recreational drugs. Details: _____	Yes	No

RISK ANALYSIS		
RISK FACTORS	YES	NO
PARTICIPATES IN REGULAR EXERCISE	YES	NO
SIGNS/SYMPTOMS *Asymptomatic* *Symptomatic*	YES YES	NO NO
HISTORY OF DISEASE (CV, Metabolic or Renal)	YES	NO

ACSM RECOMMENDATION	Action/Medical Clearance: Recommended Intensity: Progression:

Declaration	
I confirm that the above information which I have provided to Lancaster Medical School (Lancaster University) is true and accurate to the best of my knowledge and belief and I understand that I must notify promptly of any changes to the information.	
Student/Participant signature: **Date:**	
Assessor signature: **Date:**	

This screening form has been developed in collaboration with Costas Tsakirides (Leeds Beckett University) and in line with the 2018 ACSM Guidelines for Exercise Testing and Prescription.

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