

**Master thesis**

**Resistance Exercise Training Induces  
Dissimilar Muscle Strength Adaptations  
Between Sexes in the Upper Body While Lower-  
Body Strength Gains are Similar Between  
Sexes Independent of Training Volume**

Styrketrening fører til ulike tilpassingar i muskelstyrke mellom kjønn i overkroppen medan tilpassingar i underkropp er like mellom kjønn uavhengig av treningsvolum

Master of Science in Exercise Physiology

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## **Preface**

I would like to extend my gratitude to my supervisors Knut Sindre Mølmen and Ingvill Odden for their exceptional guidance, collaboration and constructive feedback throughout the writing process of this thesis. Additionally, I want to thank Tomas Urianstad for letting me be part of the Repeat Study. I greatly appreciate the opportunities, trust and responsibilities I have been given with regards to planning and conducting the study. I also want to thank all the members of the Trainome research group for guidance throughout the whole process and for creating an environment that promotes curiosity, critical thinking and learning. Thank you to all the bachelor and master students for putting in countless hours conducting training sessions and performing tests, and for always being positive and solution oriented.

And finally, thank you to all the participants for your effort, positivity and for sacrificing your valuable time in the name of science!

## **Abstract**

Resistance exercise is associated with a wide range of health benefits. However it is not clear whether sex influence training adaptations. In this study, 30 resistance-untrained but otherwise healthy adults (16 females, 14 males) aged 30 to 65 performed three sets per upper-body exercise as well as one set per exercise for one leg and three sets for the other leg for nine weeks (2-3 sessions per week). Knee extension torque, leg press power and force, isometric bicep curl force and m.vastus lateralis muscle thickness was measured before and after the intervention. Females showed greater increases in bicep curl force than males, while no sex differences were found in lower-body muscle strength gains, in either the one- or three set condition. Lower-body training volume did not influence sex differences in lower-body muscle strength gains. Lower-body muscle strength gains correlated poorly with changes in m. vastus lateralis muscle thickness, and the correlations did not differ between sexes.

## **Samandrag**

Styrketrening er assosiert med ei rekke positive helseeffektar. Det er dog uklårt om kjønn påverkar styrketreningsrespons. I denne studien fullførte 30 friske ikkje-styrketrente vaksne (16 kvinner, 14 menn) i alderen 30 til 65 år tre seriar for kvar overkroppsoving, i tillegg til eitt sett for kvar øving i underkroppen for det eine beinet, og tre sett for kvar øving i det andre beinet i tre veker (2-3 økter i veka). Kne-ekstensjonsmoment, effekt og kraft i beinpress, isometrisk armfleksjonskraft og m. vastus lateralis muskeltjukkuleik vart målt før og etter intervensjonen. Kvinner hadde større auke i armsleksjonskraft enn menn, medan ingen kjønnsskilnadar vart påvist for auke i underkroppsstyrke, verken i det beinet som trente ein serie eller beinet som trente tre seriar. Treningsvolum påverka ikkje kjønnsskilnadar i styrkeauke i underkroppen. Styrkeauke i underkroppen korrelerte dårleg med endring i m. vastus lateralis muskeltjukkuleik, og korrelasjonane var ikkje ulike mellom kvinner og menn.

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## **Theory**

Resistance exercise training (RET) is widely recognized for its role in enhancing muscular strength and increasing muscle size. Beyond these well-established functional benefits, a growing body of evidence highlights the health benefits of RET. For instance, studies have shown that RET may reduce the risk of conditions such as age-related mobility limitations, type 2 diabetes, cardiovascular disease, and certain forms of cancer (Mcleod et al., 2019). Moreover, RET is associated with improvements in body composition, physical function, mental health, bone mineral density, insulin sensitivity, blood pressure regulation, lipid profiles, and cardiovascular health (Abou Sawan et al., 2023; Braith & Stewart, 2006; Colberg et al., 2016; Westcott, 2012).

Males and females exhibit distinct anatomical and physiological traits. On a group level, the sexes differ in cardiorespiratory capacity, muscle mass quantity, muscle fiber type composition, bone mineral density, and hormonal responses to exercise (Diaz-Canestro et al., 2022; Fragala et al., 2012; Nuzzo, 2024; Vislocky et al., 2008). These differences have provided a rationale for the hypothesis that males and females may as well respond differently to RET (Da Boit et al., 2016; Kojić et al., 2021; R. M. Miller et al., 2021). However, existing research on sex-specific responses to RET is limited and presents somewhat unclear and conflicting findings (Jones et al., 2021; Roberts et al., 2020). Thus, the theory section of this thesis aims to discuss important factors for maximal muscle strength, underlying physiological mechanisms contributing to potential sex differences in strength gains, as well as to establish what is known about sex differences in strength-adaptations following RET and identify gaps in our understanding of sex differences in RET adaptation.

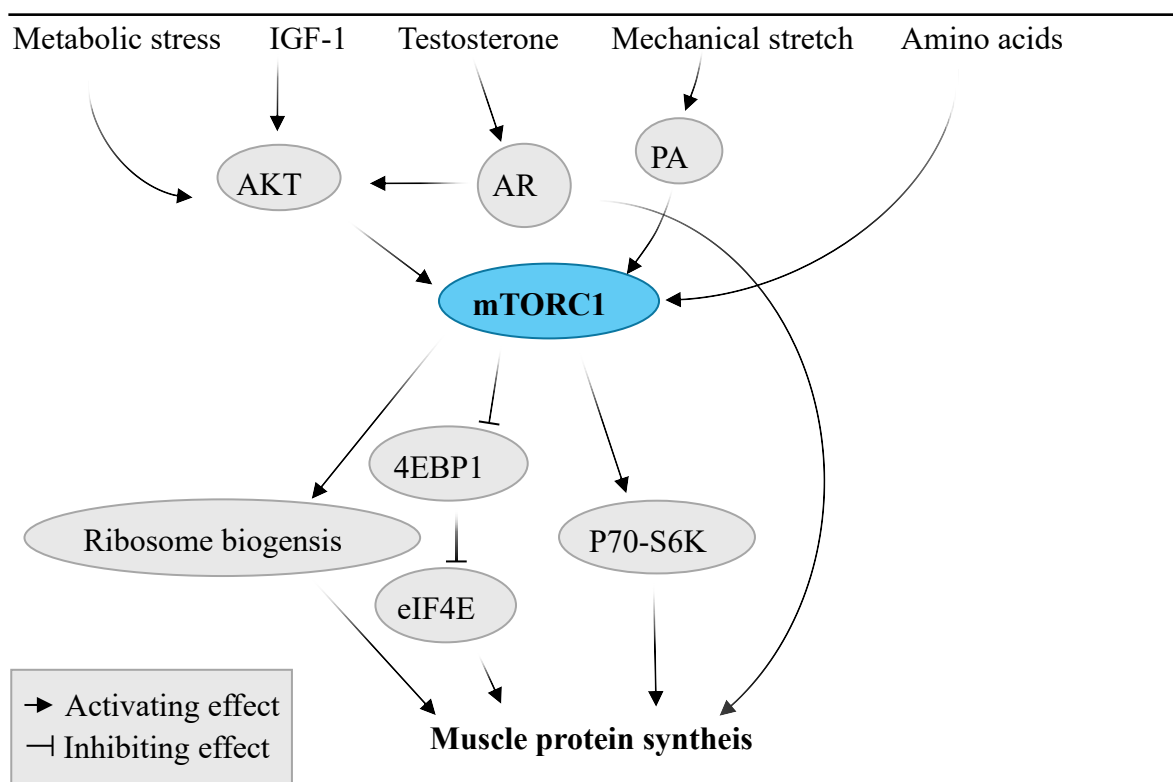
### **Hypertrophic Mechanisms in Skeletal Muscle**

Maximal muscle contractile force is largely determined by the size of the muscle and neuromuscular conditions. There is a positive correlation between muscle mass and maximal muscle strength (Brechue & Abe, 2002; Chen et al., 2013), attributed to an increase in myosin-actin cross-bridges following muscle hypertrophy (Wisdom et al., 2015). There are two possible explanations for how a muscle can grow in size; 1) the number of muscle cells increases, and 2) the volume of each muscle cell increases. The former theory is usually referred to as hyperplasia and has been observed to occur in birds (Alway et al., 1990), cats (Gonyea, 1980; Gonyea et al., 1986) and rodents (Ho et al., 1980; Tamaki et al., 1992). However, assessing the role of hyperplasia in humans implies ethical and technical

challenges, and research on the topic is therefore lacking. A handful of cross-sectional studies conducted on the matter did not rule out the possibility of muscle hyperplasia in humans (Larsson & Tesch, 1986; Tesch & Larsson, 1982). A recent cross-sectional study found that long-term resistance exercise (RE) trained individuals had more muscle fibers than untrained individuals (Maeo et al., 2024). However, because of the cross-sectional study design, these findings are susceptible to selection bias and should therefore be interpreted with caution. On the other hand, the process through which individual muscle cells increase in size has been proven beyond doubt (Currier et al., 2023; LOPEZ et al., 2021; Schoenfeld et al., 2015, 2016) and is usually referred to as muscle hypertrophy. Given that hypertrophy is by far the primary driver of muscle mass increases in response to RET, this thesis will focus on hypertrophic mechanisms rather than the debated phenomenon of hyperplasia in humans.

The rate of muscle hypertrophy or muscle loss (muscle atrophy) is determined by the balance between muscle protein synthesis (MPS) and breakdown (MPB). Muscle growth occurs when MPS is greater than MPB, while muscle loss occurs when MPB is greater than MPS (Kim et al., 2020). There are several cellular pathways through which MPS is stimulated. Some of the most important pathways go through a protein complex called mammalian target of rapamycin complex 1 (mTORC1; ). The effects of activation of mTORC1 on MPS are mediated by its major downstream effectors, ribosomal protein S6 kinase beta-1 (p70-S6K) and eukaryotic translation initiation factor 4E (eIF4E). Activation of eIF4E is mediated by mTORC1's inhibition of its inhibitor, the eukaryotic translation initiation factor 4E-binding protein 1 (4E-BP1). Additionally, mTORC1 stimulates the production of ribosomes (ribosome biogenesis). Ribosomes are organelles where the protein translation takes place. Thus, more ribosomes constitutes a greater capacity for protein translation (Laplane & Sabatini, 2009).





**Figure 1.** Overview of interactions between some of the major up- and downstream effectors of mTORC1.

AR; androgen receptor, PA; phosphatidic acid

mTORC1 activation is determined by several factors, including mechanical stretching of muscles (e.g. through RET), metabolic stress, nutrients (such as amino acids) and hormones (such as testosterone and insulin-like growth factor 1 (IGF-1)). It is widely recognized that mechanical stimuli play an important role in the activation of mTORC1. However, the mechanisms through which this interaction occur are vaguely defined. Evidence suggests stretch-induced activation of ion channels could play a role, though the mechanisms through which this regulates mTORC1 are not well established (Hornberger, 2011). Mechanical stretch could also activate mTORC1 by regulating phosphatidic acid levels, which seems to directly regulate mTORC1 activation (Bond, 2016). Additional potential pathways for the mechanical stretch-induced regulation of mTORC1 are discussed in detail by Hornberger (2011).

Metabolic stress has also been shown to regulate mTORC1. Metabolic stress refers to a physiological environment with insufficient energy availability (caused by insufficient nutrient and/or oxygen availability), leading to metabolite accumulation. Performing RET in

an oxygen-deprived environment has been shown to induce greater muscle hypertrophy compared to RET performed in a normal atmospheric environment (Nishimura et al., 2010). This is likely due to an increase in reactive oxygen species (ROS) in response to hypoxia, which can regulate mTORC1 through IGF-1 and mitogen-activated protein kinase pathways (de Freitas et al., 2017). Intramuscular hypoxia increases the necessity for anaerobic lactic metabolism. Exercise that increases lactate production is therefore associated with hypoxia and metabolic stress. This can be achieved through RE with moderate repetition range and short rest intervals (70% of one repetition maximum (1RM), 10-12 repetitions and one minute rest interval; Gonzalez et al., 2015).

Amino acids upregulate mTORC1 activity by entering the cell through the amino acid transporter, which initiates a cascade of events leading to phosphorylation of mTORC1 (Laplante & Sabatini, 2009). IGF-1 interacts with mTORC1 by binding to its receptor, leading to the activation of protein kinase B (Akt). Akt phosphorylates mTORC1, resulting in increased MPS (Manning & Toker, 2017). Akt can also be activated by a signaling cascade initiated when androgens (e.g. testosterone) binds to androgen receptors (Pungsrinont et al., 2021). Androgens can also increase MPS via androgen receptors in a DNA binding-dependent process, allowing them to regulate target gene transcription (Davey & Grossmann, 2016).

### **Neural Adaptations to RET**

Motor neurons' interactions with muscle fibers are organized in motor units. A motor unit is the term for a single motor neuron and all the muscle fiber it innervates. Each muscle fiber is only innervated by one motor neuron. If an action potential from the neuron causes the membrane potential of the innervated muscle fibers to exceed the threshold potential, an action potential will be triggered in all myofibrils in the muscle fiber, initiating a single twitch. The frequency of twitches within a given period of time determines the force output, as higher firing rates result in greater calcium release from the sarcoplasmic reticulum, enhancing cross-bridge formation and force production (Maffiuletti et al., 2016). Collectively, adaptations in motor unit recruitment threshold, frequency of twitches and antagonist muscle coactivation seem to be an important factor for maximal muscle strength gains in the first few weeks after initiating RET (Del Vecchio et al., 2019; Moritani & deVries, 1979).

### ***Motor Unit Recruitment***

According to Henneman's size principle, motor units are recruited in order from smallest to largest. Small units have the lowest threshold force and are recruited first. As the demand for contractile force increases, progressively larger units are recruited (Henneman, 1957). Large motor units are more reluctant to recruit because they require a greater synaptic current to depolarize (Purves et al., 2001). Evidence suggests that untrained individuals are usually not able to recruit all motor units during maximum voluntary contractions (MVC). For instance, Huang and colleagues (2010) found that voluntary motor unit recruitment ranged from 83.30% to 97.24% during MVC in adolescent males. However, as demonstrated in several trials (Del Vecchio et al., 2019; Häkkinen & Komi, 1983, 1986; Moritani & deVries, 1979), motor unit recruitment threshold decreases in response to RET, potentially implying an increase in motor unit recruitment during MVC.

### ***Rate Coding***

Neural factors contributing to force development in skeletal muscle are not limited to the number of motor units producing twitches; it also depends on the rate at which twitches are produced. A single twitch only lasts for a fraction of a second. Thus, a continuous series of twitches are required for continuous calcium release from the sarcoplasmic reticulum and thus sustained force-production. The frequency of action potentials in motor units is referred to as 'rate coding'. The greater the rate coding, the greater the force produced. Findings from past studies indicate that at least 50 pulses per second are required to produce peak motor unit contractile force. Peak discharge rates are, however, usually less than 50 pulses per second during MVC (Enoka & Duchateau, 2017). Evidence suggests that rate coding during MVC increases in response to RET, and thus explains part of the strength gains following RET (Del Vecchio et al., 2019).

### ***Antagonist Muscle Coactivation***

**Net joint torque is determined not only by the contribution of agonist muscles, but also by antagonist muscle coactivation. Antagonist coactivation improves joint stability (Centomo et al., 2008; J. P. Miller et al., 2000; Rao et al., 2009; Stokes & Gardner-Morse, 2003) and movement accuracy (Gribble et al., 2003; Tanaka, 1974). Of course, contracting antagonists translates to lower net joint torque. However, previous studies have demonstrated decreased antagonist muscle activation during isometric contractions following RET (Bru & Amarantini, 2008; Carolan & Cafarelli, 1992; Griffin & Cafarelli, 2005; Häkkinen et al., 1998, 2000), and that these adaptations not only occur on a peripheral level, but also in central structures (Duchateau & Enoka, 2002; Griffin & Cafarelli, 2005). For example, Carolan and Cafarelli (1992) demonstrated that unilateral RET reduced antagonist coactivation in both the trained and untrained limb, suggesting central adaptations. It is worth noting, however, that these adaptations seem to occur primarily within the first couple of weeks after starting a RET program (Carolan & Cafarelli, 1992; Häkkinen et al., 1998).**

**Training Volume**

Training volume plays an important role in adaptations in maximal muscle strength and muscle mass. In the context of RET, training volume is often defined as the number of sets per muscle group per week (Brigatto et al., 2022; Heaselgrave et al., 2019; Ostrowski et al., 1997; Rhea et al., 2002; Schoenfeld et al., 2017, 2019). Several studies have reported a dose-response relationship between training volume and maximal muscle strength gains (Brigatto et al., 2022; Rhea et al., 2002) and hypertrophy (Brigatto et al., 2022; Schoenfeld et al., 2017, 2019). However, significant adaptations can be achieved even at relatively low RET volumes. For example, training volumes of one set and three sets per exercise has both been shown to elicit significant adaptations in maximal strength and thigh muscle cross-sectional area in the lower extremity, though adaptations are greater with three sets (Hammarström et al., 2020; Rønnestad et al., 2007). Conversely, Rønnestad and colleagues (2007) revealed that for the upper body, adaptations in maximal strength and muscle cross-sectional area were similar for both training volumes.

## **Physiological and Anatomical Differences Between Sexes**

It is well documented that the sexes differ on a physiological level. Some of these differences could potentially influence RET adaptations. Possibly one of the most well-known physiological sex differences is the higher circulating testosterone concentration in males (Clark et al., 2019). As previously discussed, testosterone is important in upregulation of mTORC1, thereby increasing MPS. In fact, studies have reported that males produce 20 times more testosterone than females, resulting in 15 times greater circulating testosterone concentrations (Handelsman et al., 2018). Research has also found higher androgen receptor content in males than in females (Nicoll et al., 2019). Since testosterone exerts its effects on mTORC1 through androgen receptors, a higher receptor density could potentially amplify its anabolic impact.

Another physiological difference between sexes is that females typically have a greater proportion of type I muscle fibers than males, while males have a greater proportion of type II muscle fibers (Nuzzo, 2024). Evidence suggests that the relationship between type I and type II muscle fiber hypertrophy is dependent on exercise intensity, with type I fibers favoring low intensity RET and type II fibers favoring high intensity RET (Ogborn & Schoenfeld, 2014). Type I muscle fibers are typically more fatigue resistant, while type II muscle fibers typically produce more force (Nuzzo, 2024). One could hypothesize that this leads to the sexes relying on dissimilar mTORC1 signaling pathways, as females may be able to exercise with more time under tension, while males possibly experience greater mechanical tension.

## **Sex-Specific Acute Responses to RET**

Based on the physiological sex differences discussed above, one could assume that the sexes exhibit dissimilar acute responses to RET, which may, in turn, contribute to differences in muscle strength adaptations. Contrary to this assumption, Dreyer et al. (2010) found that an acute bout of RE increased MPS and Akt-, mTOR-, and S6K1 phosphorylation, measured for two hours after exercise, to the same extent in both sexes. However, males exhibited higher blood lactate levels immediately after exercise. This could imply proportionally greater anaerobic glycolysis reliance in males, greater lactate clearance in females, or simply that males exercised at a higher relative intensity.

In line with this, researchers have observed that females generally show less fatigability in response to RET, resulting in the ability to produce sustained force for longer at the same

relative intensity compared to males (Ansdell et al., 2017; Hunter et al., 2004, 2006; Wüst et al., 2008). This could be due to the greater proportion of type I muscle fibers in females, as these fibers generally have greater mitochondria volume density and capillary-fiber contact length and thus have a greater capacity for aerobic metabolism than type II fibers (Ceaser & Hunter, 2015; Wilson et al., 2012). This female-specific fatigue resistance may enable more time with high mechanical tension during RE, positively affecting mTORC1 activation, ultimately leading to greater hypertrophic adaptations compared to males.

It has been widely reported that in males, circulating testosterone increases following acute bouts of RE (Häkkinen & Pakarinen, 1995; Kraemer et al., 1998; Vingren et al., 2009). Interpreting hormonal responses to acute exercise bouts in females is more complex due to menstrual cycle fluctuations (Cano Sokoloff et al., 2016). Yet, a review by Consitt and colleagues (2002) reported that acute bouts of RE did not elicit a post-exercise increase in testosterone levels in females. As previously discussed, testosterone is an important regulator for MPS. Interestingly, Spiering and colleagues (2009) discovered that testosterone possibly increases androgen receptor content in muscle cells. Androgen receptor content has been associated with muscle hypertrophy (Morton et al., 2018). Additionally, testosterone inhibits MPB (Demling & Orgill, 2000), further potentiating its anabolic effects. Interestingly, despite the lack of RE-induced increases in circulating testosterone in females, post RE acute increases in androgen receptor content seems to be greater in females than in males (Vingren et al., 2009), further suggesting intrinsic sex differences in acute RE response. A recent study found, however, that 48 hours after RE, males exhibited elevated androgen receptor protein content compared to baseline, while no increase was observed in females (Hatt et al., 2024).

### **Current Knowledge on Sex Differences in Muscle Strength Adaptations to RET**

Several studies have demonstrated that males typically achieve greater muscle strength gains in absolute terms than females following RET (Abe et al., 2000; Da Boit et al., 2016; Dorgo et al., 2012; Hubal et al., 2005; Jozsi et al., 1999; Lemmer et al., 2001). However, when expressing muscle strength gains as a percentage increase, greater improvements are often observed in females than in males (Dorgo et al., 2012; Hubal et al., 2005; Lemmer et al., 2001). This coincides with the findings of recent systematic reviews and meta-analysis (Hawley et al., 2023; Jones et al., 2021). In one of the largest trials on the topic to date, Hubal and colleagues (2005) found that females exhibited a 61% greater relative increase in elbow flexor strength than males in response to a 12-week RET intervention. Furthermore, Dias et

al. (2005) reported that, following an eight-week RET intervention, females exhibited nearly double the relative muscle strength increases compared to males. On the contrary, other studies have found no difference in relative strength gains between sexes (Gentil et al., 2016; Kojić et al., 2021; Lexell et al., 1996; R. M. Miller et al., 2021).

Findings are equivocal regarding whether the sex differences in adaptations are dependent on the muscle group being assessed. For example, Lemmer et al. (2001) found a greater increase in absolute upper-body muscle strength in males than in females, while no difference was found between sexes in absolute lower-body strength gains. Conversely, a meta-analysis by Roberts et al. (2020) found greater relative increases in upper-body muscle strength in females than in males, while no sex differences were evident for lower-body muscle strength. Yet, a different meta-analysis (Jones et al., 2021) found that females exhibited greater increases in relative lower-body strength, while no sex difference was demonstrated for upper-body muscle strength gains.

Interestingly, Dorgo et al. (2012) reported that a 12-week RET program resulted in greater absolute increases in knee extension strength in males compared to females, while no sex differences were observed for knee flexion strength gains. These findings suggest that there also may be sex-specific adaptations across different muscle groups within the same limb.

At present, few studies have investigated how RET volume affects muscle strength adaptations between sexes. Yet, Hammarström et al. (2020) demonstrated that training volume (one set vs. three sets per exercise) did not affect lower-body muscle strength gains differently between sexes. Another study conducted on untrained males found that three sets per exercise elicited superior muscle strength adaptations compared to one set in the lower body, while no differences in upper-body muscle strength was observed between one and three sets in untrained males (Rønnestad et al., 2007). Interestingly, a nearly identical study was conducted on female participants a few years later. This time, the authors found that three sets elicited greater muscle strength adaptations in both the lower- and upper-body (Vikmoen et al., 2012). Collectively, these findings suggest that three sets are superior to one set in eliciting lower-body muscle strength adaptations in both sexes. However, for upper-body muscle strength adaptations, three sets seem to be favorable only in females.

### **Gaps in Current Knowledge**

There is still limited understanding regarding the sex-based differences in muscle strength adaptations to RET. Specifically, it remains unclear whether sex influences muscle strength

gains differently between the upper and lower limbs, as well as within different muscle groups of the same limb. Furthermore, to the best of the author's knowledge, little to no research has examined whether different training volumes contribute to sex differences in muscle strength gains. Literature searches also failed in identifying previous studies comparing the extent to which muscle strength gains can be attributed to muscle hypertrophy between sexes. This gap in knowledge limits our ability to fully understand how males and females respond to RET and whether they exhibit distinct adaptation patterns. Gaining a deeper understanding of these distinctions is crucial, as it could shed light on the physiological mechanisms underlying potential sex differences in muscle strength development. Such knowledge would not only improve the precision of future research but also provide valuable insights for developing sex-specific exercise prescriptions that promotes muscle growth, health, and performance for both males and females.

### **Objectives and Hypothesis**

Because of the equivocal findings in the literature and the existing gaps in our understanding, the current study aims to contribute to the body of knowledge by addressing the following questions:

- i. Do Males And Females Exhibit Different Relative Muscle Strength Adaptations In Response To Ret?
- ii. Do Exercise Volume Influence Lower-Body Muscle Strength Gains Differently Between Males And Females?
- iii. Are Changes In Lower-Body Muscle Strength Following Ret Attributable To Muscle Hypertrophy To The Same Extent In Both Sexes?

Based on the currently available information on the objectives, the following outcomes for the study are hypothesized:

- i. Females Will Display Greater Relative Strength Increases Than Males In The Upper- And Lower Body.
- ii. Training Volume Will Not Influence Lower-Body Muscle Strength Adaptations Differently Between Sexes.
- iii. Lower-Body Strength Gains Will Be Partially Explained By Muscle Hypertrophy In Both Sexes, But Possibly Less So In Females.



## Introduction

RET is well-known for increasing muscular strength and size, but emerging research also highlights its extensive health benefits. RET has been shown to reduce the risk of age-related mobility limitations, type 2 diabetes, cardiovascular disease, and certain cancers (Abou Sawan et al., 2023; Braith & Stewart, 2006; Mcleod et al., 2019; Westcott, 2012). Additionally, it improves body composition, physical function, mental health, and bone mineral density, as well as physiological markers such as insulin sensitivity, blood pressure regulation, and lipid profiles (Abou Sawan et al., 2023; Braith & Stewart, 2006; Colberg et al., 2016; Westcott, 2012).

The magnitude of adaptations to RET varies significantly between individuals (Ahtiainen et al., 2020; Erskine et al., 2010), a concept often referred to as ‘trainability’. Trainability appears to be largely influenced by genetics, with research estimating that genetic factors account for approximately 50% of the interindividual variability in training adaptations (Hecksteden et al., 2015). However, other factors, such as baseline training status, psychological stress, sleep, habitual physical activity, and nutrition may also play important roles in explaining inter-individual differences in trainability (Mann et al., 2014). Furthermore, given the well-documented anatomical and physiological differences between males and females - including disparities in muscle mass (Nuzzo, 2023), fiber-type composition (Nuzzo, 2024), testosterone levels (Handelsman et al., 2018) and androgen receptor content (Nicoll et al., 2019) - it is plausible that the sex itself contributes to the variability in RET adaptations.

Research conducted to date on how the sexes differ with regards to strength gains in response to RET is somewhat inconclusive and dependent on how results are interpreted. Current literature on the matter generally finds males to display a greater increase in absolute muscle strength in response to RET than females (Abe et al., 2000; Da Boit et al., 2016; Dorgo et al., 2012; Hubal et al., 2005; Jozsi et al., 1999; Lemmer et al., 2001). However, several trials have found that when strength gains are interpreted as relative increases from pre to post intervention, females experience greater increases in muscle strength than males (Dorgo et al., 2012; Hubal et al., 2005; Lemmer et al., 2001). This observation is supported by the findings of recent systematic reviews and meta-analyses (Hawley et al., 2023; Jones et al., 2021). Furthermore, in a clinical trial with 585 males and females, Hubal and colleagues (2005) found a 61% greater relative increase in females than in males following a 12 week RET

intervention. In a different trial, Dias et al. (2005) observed that females exhibited nearly twice the relative increase in muscle strength compared to males following an eight-week RET intervention. Conversely, multiple studies have reported similar relative strength gains in males and females (Colliander & Tesch, 1991; Gentil et al., 2016; Kojić et al., 2021; Lexell et al., 1996; R. M. Miller et al., 2021).

The literature is also inconclusive regarding whether the sex differences in adaptations are dependent on the muscle group being assessed. For example, Lemmer and colleagues (2001) reported greater increases in absolute upper-body strength in males, while no sex differences were found in lower body strength gains. Inversely, a recent meta-analysis found greater relative upper-body strength gains in females, while no sex differences were found in lower body strength gains (Roberts et al., 2020). Another recent meta-analysis found greater relative lower-body strength gains in females, while no sex differences were found for upper-body strength gains (Jones et al., 2021).

To the best of the author's knowledge, little research has investigated whether RET volume influence muscle strength adaptation differently across sexes. Furthermore, research on whether muscle strength gains following RET can be attributed to hypertrophy to the same degree in both sexes is lacking. These knowledge gaps hinder our understanding on potentially sex-specific underlying mechanisms responsible for muscle strength gains. Understanding whether and how sex influences RET adaptations is crucial for refining exercise prescriptions to optimize health and performance. As mentioned earlier, males and females exhibit distinct physiological characteristics which could influence their responsiveness to RET. Despite these differences, exercise guidelines are often generalized, assuming similar adaptive potential across sexes. However, if males and females respond differently to RET, sex-specific training recommendations may be necessary to maximize effectiveness and ensure optimal muscle strength development for both sexes.

Because of the equivocal findings in the current literature, there is still a way to go to fully understand how sex affects RET adaptations. Clarification on the subject is therefore essential in identifying sex-specific adaptations pertinent to strength gains. The current study will therefore employ a nine-week whole-body RET intervention with different exercise volumes in the lower body (one set vs. three sets per exercise) with the overall aims to investigate (i) whether sex differences exist in the magnitude of muscle strength adaptations in response to nine weeks of RET, (ii) if exercise volume influence lower-body muscle strength gains differently between males and females, and (iii) whether lower-body muscle strength gains

are attributable to muscle hypertrophy to the same extent in both sexes. It is hypothesized that (i) females will exhibit greater relative strength gains than males in the upper- and lower body, (ii) three sets per exercise will induce greater muscle strength adaptations than one set per exercise in both sexes, though the magnitude of this effect may differ between sexes. Lastly, (iii) lower-body muscle strength gains will be partially explained by muscle hypertrophy in both sexes, but possibly less so in females.

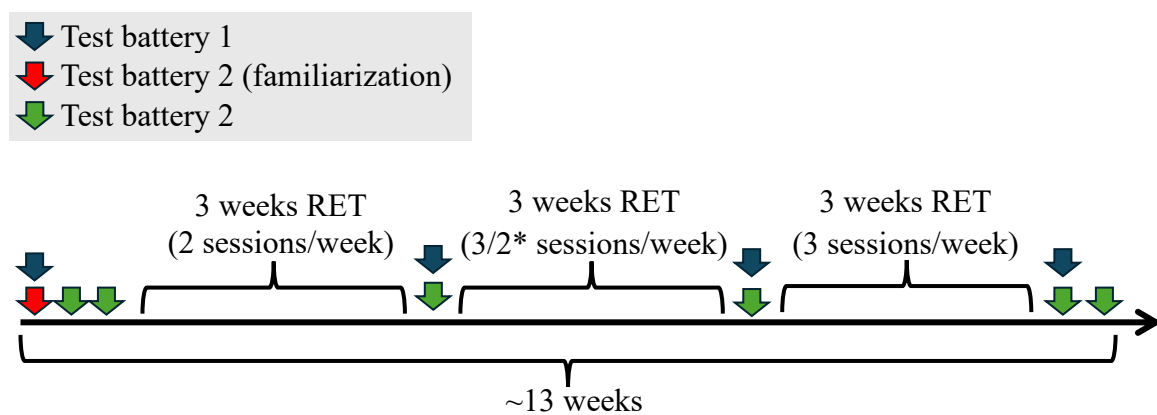
## **Method**

This thesis is part of a larger research project, the Repeat study (study registration: Mølmen et al., 2024), conducted by the Trainome research group at Inland Norway University of Applied Sciences. The research project was conducted in line with ethical standards established in the Declaration of Helsinki and received approval from the Regional Committee for Medical Health Research Ethics – Sout East Norway (REK; reference number 591218). Data processing and storage of personal information were carried out in accordance with guidelines provided by the Norwegian Agency for Shared Services in Education and Research (Sikt; reference number 499593). The main aim of the Repeat study was to investigate the individual variability in exercise training responses following repeated exercise training interventions. The Repeat study consisted of three separate eight-week endurance exercise training interventions over the course of 60 weeks, before concluding with a nine-week RET intervention. The current thesis will focus on the nine-week RET intervention of the Repeat study and is based exclusively on a selection of data relevant to the current thesis from assessments made immediately prior to, during, and immediately after the RET intervention.

### **Experimental Design**

The study employed a quasi-experimental, repeated measures design to investigate sex differences in adaptations to RET. Participants were assigned to experimental groups based on sex. Both groups performed two to three RET sessions a week for nine weeks, in total 24 sessions. To investigate the effect of training volume on sex differences in RET adaptations, participants were randomized to perform three sets per exercise for one leg and one set per exercise for the contralateral leg. The leg assigned to three sets and one set was kept consistent throughout the intervention for each participant.

An overview of the time course of the study is presented in Figure 2. Muscle thickness measurements (test battery 1; see Table 1) were carried out once prior to the intervention, after three and six weeks of RET and after the intervention. Assessments of upper- and lower-body muscle strength (test battery 2; see Table 1) were conducted three times prior to the intervention; one for familiarization, and subsequently two pretests. These tests were then repeated once after week 3 and 6 of RET, and twice immediately after the intervention. However, due to statistical limitations in the present study, only data from pre- and post-testing will be used for analyses. The content and test order in the test batteries are shown in Table 1.



**Figure 2.** Overview of the time course for the study. Arrows indicate the timepoint tests were performed. \*Alternating between three and two sessions per week.

**Table 1.** Content and order of test batteries

Test battery 1
1. Measurement of m. vastus lateralis muscle thickness (measured with ultrasound)
Test battery 2
1. Isometric and isokinetic (60, 180 and 240°/s) knee extension test
2. Test of peak power and force in leg press
3. Isometric test of elbow flexion force

## Participants

36 healthy individuals (16 males, 20 females, age; 30-65 years) who had not performed RET for the past x months were recruited to take part in the RET intervention for the Repeat study. Six participants were excluded due to reasons unrelated to the study ( $n = 4$ ), rib pain during

exercise ( $n = 1$ ) and not complying with inclusion criteria ( $n = 1$ ). The final sample included 30 participants (14 males and 16 females). 22 of these had been participants of the Repeat study since its beginning, of which some were recruited from a previous research project conducted by the same research group, the Alpha & Omega study (REK id: 11959), while the remaining were recruited from the general population using the same inclusion criteria. An additional eight participants who had not taken part in the previous stages of the Repeat study were recruited from the general population. Baseline characteristics of the sample are shown in Table 2. All recruitment from the general population was done through the local newspaper, flyers, and social media. Prior to inclusion, participants were screened for contraindications to RET through a questionnaire. They were also carefully informed on the design of the study, and possible risks and discomfort associated with participation, before giving written consent on their participation.

**Table 2.** *Baseline participant characteristics.*

	Male	Female
<i>N</i>	14	16
Age (years)	52.2 (7.2)	54.8 (9.8)
Body height (cm)	180.1 (9.7)	168.3 (6.7)
Body mass (kg)	93.4 (18.4)	79.3 (11.8)
Body mass index (kg/m <sup>2</sup> )	28.6 (4.0)	28.0 (4.0)

*Data are means and standard deviation (mean (SD)).*

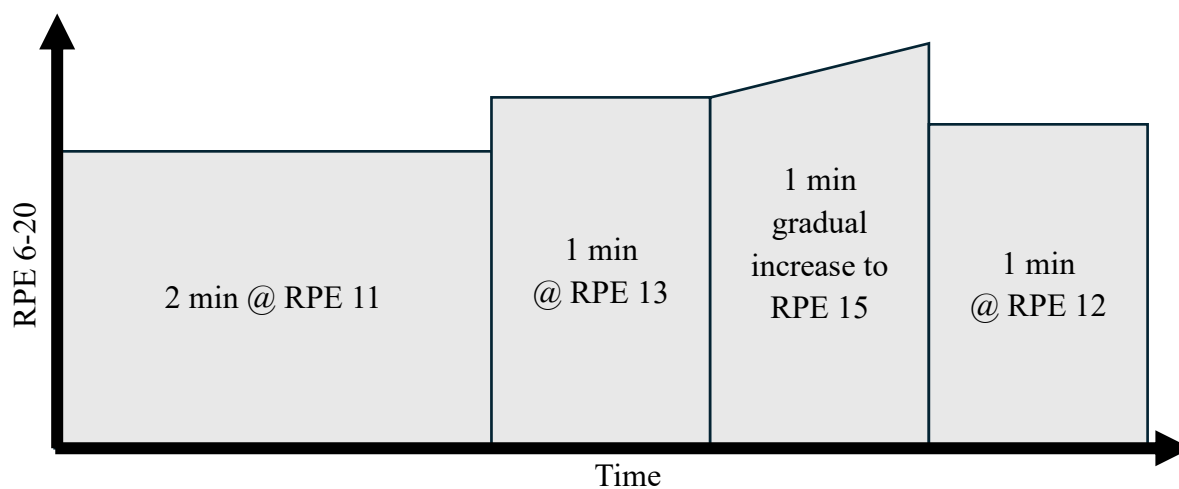
### **Training Intervention**

The intervention lasted for nine weeks and consisted of a total of 24 60-minute RET sessions. Participants performed two RET sessions for the first three weeks, then alternating between three and two sessions for the following three weeks and concluded the RET period with three sessions per week for the final three weeks. All training sessions throughout the nine-week training period included the same exercises, number of sets, and repetition range. Prior to each training session, participants performed a standardized warm-up routine on a Tacx Neo Bike Plus stationary smart bike (Tacx, n.d.; **Figure 3**). Additionally, two warm-up sets of seven repetitions were performed for leg press, at ~40% and ~60% of 1RM, respectively. Only one warm-up set of seven repetitions was performed for preacher curl, at 40% of 1RM. Warm-up sets were separated by at least one minute rest. Henceforth, both experimental groups performed three sets of preacher curls and two sets of unilateral dumbbell rows, in that order.

For the lower body, volume was split between the legs. Participants performed three sets of leg press and leg extension on one leg, and one set for each exercise on the contralateral leg. Leg press was always performed before leg extension. For all unilateral exercises, the order in which the left and right limbs were exercised alternated for each session. All work sets were performed to volitional failure, and aimed for 10 repetitions. If participants managed more than 12 repetitions or reported a score below eight on the Borg CR10 scale, resistance was increased for the subsequent set. Conversely, if participants could not perform 8 or more repetitions, resistance was decreased for the subsequent set. Work sets were separated by at least two minutes rest. All training sessions were separated by at least 48 hours for each participant and conducted with guidance from an instructor at the facilities of University of Inland Norway, campus Lillehammer.

### Isokinetic Joint Torque

Maximal voluntary knee joint extension torque was assessed using the Cybex 6000 isokinetic dynamometer (Cybex International, n.d.) at four different angular velocities; 0°, 60°, 180°, and 240° per second. The test was performed unilaterally in a seated position, as shown in Figure 4. Both legs were tested at each test point. The order in which participant's legs were tested

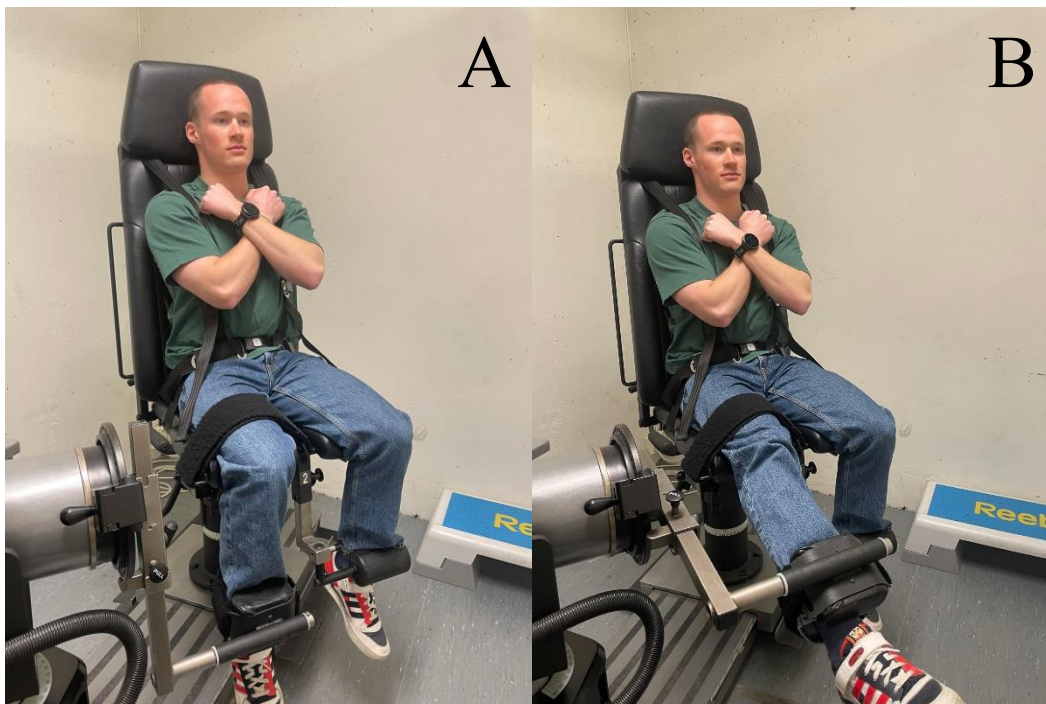


**Figure 3.** Warm-up protocol performed ahead of every RET session. The protocol is performed on an indoor smart bike, and starts off with two minutes at RPE 11, then increasing to RPE 13 for one minute, followed by a one-minute gradual increase to RPE 15, and concluding with one minute at RPE 12. RPE; Rating of perceived exertion; Borg 6-20.

was randomized, and kept consistent throughout the study for each participant. The dynamometer was calibrated according to the dynamometer's user manual no longer than 24

hours prior to each test. Participant's seat adjustments were determined prior to familiarization testing based on the following criteria: 1) the distance between the front end of the seat cushion and the popliteal fossa was equal to two finger widths, 2) the knee's center of rotation was aligned with the center of rotation of the dynamometer arm, and 3) the bottom end of the dynamometer arm's cushion was two finger widths above the malleolus lateralis. Participant's seat and dynamometer adjustments were recorded and kept consistent for all subsequent tests. The tests were carried out by the same test leader for each participant at all test points. Verbal encouragement was given throughout the test.

The test procedure was initiated with the five-minute warm-up routine described earlier (**Figure 3**). Following warm-up, participants were seated in the dynamometer chair and fastened the four-point harness. To allow participants to familiarize themselves with the test, three warm-up repetitions at 60°/s were performed prior to the test, at respectively ~50%, ~75% and 100% of maximal effort. Participants were then given 90 seconds rest. Thereafter, three sets with maximal effort were performed; 4 repetitions at 60°/s, and 5 repetitions at 180°/s and 240°/s, with 90 seconds rest between each increase in angular velocity. The test concluded with two maximal isometric repetitions with a 60° knee joint angle. The isometric repetitions lasted until the participant could no longer increase or maintain knee joint torque, but no longer than 10 seconds. The isometric repetitions were separated by a one-minute rest period. The test procedure was then repeated for the contralateral leg.



**Figure 4.** Illustration of the starting- (A) and end-position (B) in the isokinetic joint torque test.

## Leg Press Test

Peak power and peak force in leg press was assessed using the Keiser AIR300 Leg Press machine (Keiser Corporation, n.d.) which enabled the direct measurement of power output at different resistance levels. The test was performed unilaterally, with the legs being tested in the same order as during the isokinetic knee extension torque test. The test was carried out by the same test leader for each participant at all test points. Verbal encouragement was given throughout the test.

Participants were seated in the Keiser apparatus, and their feet placed horizontally central on the foot pedal with their heel flush with the lower end of the pedal. Their seating position was adjusted so that participants' knee joint angle was at 90 degrees. Participants were then instructed to push the platform as fast as possible until their leg was in an extended position (see Figure 5). The test started with a relatively low resistance, and then gradually increased for each repetition. The test was designed for participants to reach their one repetition maximum at the tenth repetition, however, the test continued until volitional failure. Resistance for the tenth repetition at familiarization testing was based on the participant's body weight; 250 kg for participants with a body mass less than 75 kg, and 280 kg for participants heavier than 75 kg. For all subsequent tests, resistance at the tenth repetition was based on the greatest resistance lifted at familiarization testing.



**Figure 5.** Illustrations of starting- (A) and end-position (B) in the leg press test.

## Maximal Elbow Flexion Force

Maximal isometric elbow flexion force was measured bilaterally using a preacher-curl apparatus and a straight bar in a seated position, as shown in Figure 6. The barbell was



attached to a MUSCLELAB Force Sensor (Ergotest Innovation AS, n.d.-b) using a cargo strap. The force sensor was attached to the base of the preacher-curl apparatus so that the cargo strap was perpendicular to participant's lower arm during the test. The force sensor was linked to a PC running the MUSCLELAB Professional Software (Ergotest Innovation AS, n.d.-d) through the MUSCLELAB Single Data Interface (Ergotest Innovation AS, n.d.-c) and the MUSCLELAB Data Synchronization Unit (Ergotest Innovation AS, n.d.-a). Prior to familiarization testing, the height of the preacher-curl apparatus' arm rest was adjusted so that participant's upper arm rested flat on the cushion. The length of the cargo strap was adjusted so that participant's elbow joint angle was 90 degrees. The same adjustments were used throughout all test points for each participant.



**Figure 6.** *Illustration of the isometric arm flexion test position.*

Participants first performed a warm-up repetition, during which they were instructed to gradually increase force while pulling the straight bar toward themselves, reaching maximal effort after approximately ten seconds. Following the warm-up, they were instructed to complete two attempts, pulling the bar as quickly and forcefully as possible and maintaining maximal effort for up to ten seconds. If they were unable to increase or sustain force output, they were told to stop the attempt. A 30-second rest period was provided between attempts.

### **Muscle Thickness**

Muscle thickness of m. vastus lateralis for both legs was measured using B-mode ultrasonography (Telemed, n.d.-b) and recorded using the Echo Wave II software (Telemed, n.d.-a). Participants fasted for at least 12 hours prior to assessment. A 39 mm 12 MHz linear array probe was used, with dynamic range at 72 dB, image depth of 80 mm, 10 MHz frequency, and 52% gain. Longitudinal sonograms were captured ~50% distally from the trochanter major toward the femoral lateral epicondyle. Three sonograms were captured for each leg at each test point. The location where sonograms were captured was marked on the skin. A soft plastic sheet was then superimposed on the thigh, on which the measuring

location was marked together with landmarks such as moles and scars. The plastic sheet was then used to ensure identical probe location at subsequent tests. At post testing, pre-test sonograms were used as a reference to ensure identical location in relation to anatomical landmarks. Pre- and post-images from each participant were analyzed consecutively using the Fiji software macro tool plug-in “Simple Muscle Architecture Analysis” (Seynnes & Cronin, 2020). The average muscle thickness of the three sonograms was averaged and the average across both legs from each time point was used for further analysis.

### **Statistical Analysis**

All descriptive data are presented as mean and standard deviation (mean (SD)) unless otherwise stated. To compare the effect of volume conditions (one set vs three sets) on muscle strength between sexes, a linear mixed-effects model was used. Relative strength changes from baseline were used as the dependent variable, while sex, volume, and sex  $\times$  volume interaction were used as fixed effects. The model was specified with participant id as random intercept, as participants acted as their own controls for training volumes. Random slopes were not included, as each participant contributed only one observation per volume condition. Simple effects of sex were calculated with volume condition as a moderator to assess whether the sexes differed in training responses within each volume condition. As training volume was consistent at three sets per exercise across both limbs in the upper body, sex differences in maximal elbow flexion force were assessed using an independent samples t-test with pre-to-post percent change in elbow flexion force as the dependent variable and sex as the grouping variable. To assess whether the correlations between relative pre-to-post changes in muscle strength outcomes and relative pre-to-post changes in m. vastus lateralis muscle thickness differed between sexes, Pearson correlation coefficients were first calculated separately for males and females for each strength outcome. Percentage change in muscle thickness (averaged across both legs) was used as the predictor and percentage changes in muscle strength outcomes were used as the dependent variable. Correlation coefficients were then transformed using Fisher z-transformation to normalize their distribution. Z-scores and p-values on the differences between the sexes' correlations were then derived from a z-test on the transformed coefficients. Statistical analyses were carried out in Jamovi version 2.3.28 (The jamovi project, 2024). The alpha level was set to  $p \leq 0.05$ .

## Results

### Adherence

Four participants (three males and one female) were excluded from analyses on bicep curl strength for not completing the upper-body exercises in at least 85% of the prescribed sessions. In the sample included in analyses, average adherence to the intervention was 99.6 (1.3)% for the lower body exercises (range 95.8-100%) and 98.2 (3.6)% for the upper body exercises (range 87.5-100%).

### Sex Differences in Muscle Strength Adaptations

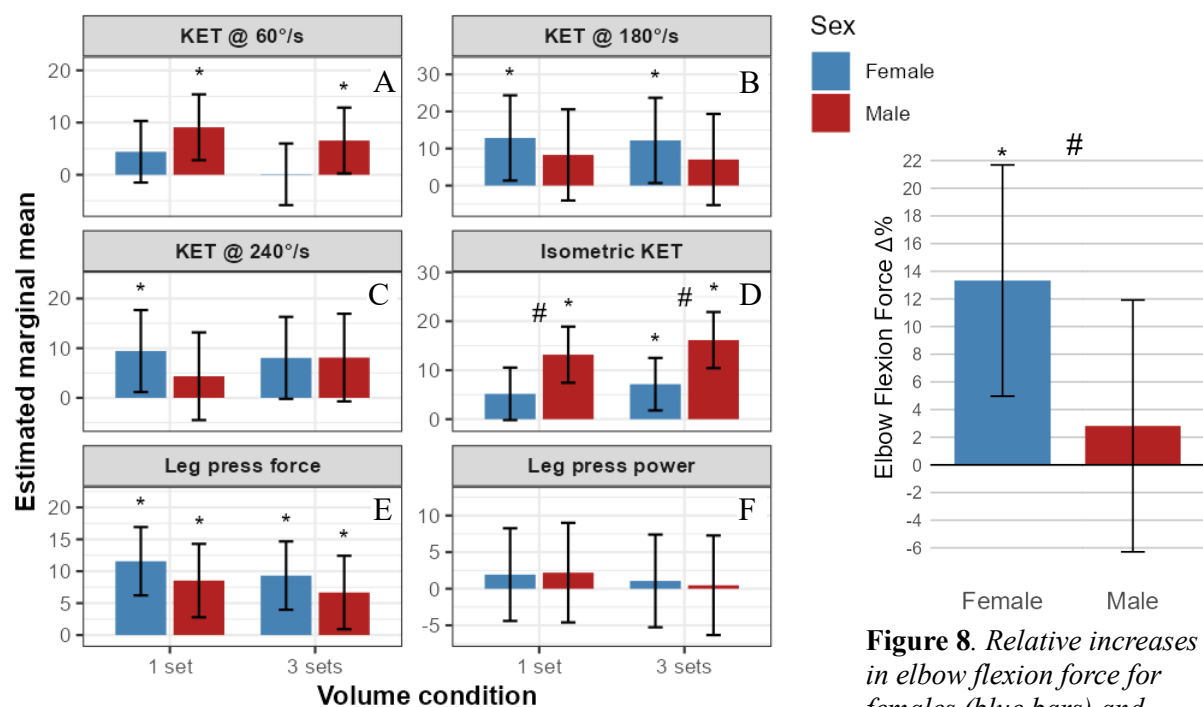
Overall, nine weeks of RET increased lower-body muscle strength by 7.0% (95% confidence interval (CI): [2.7, 11.3],  $p = .002$ ) in females and 7.3% ([5.1, 9.4],  $p < .001$ ) in males (mean values of both volume conditions). Estimated marginal means for relative increases in lower-body muscle strength outcomes, as well as the estimated differences between sexes are shown in Table 3; for visual representation of the data, see Figure 7**Error! Reference source not found.** In females, significant improvements were seen in isokinetic knee extension at 240°/s and isometric knee extension in both volume conditions, as well as in leg press force in the three-set condition. In males, significant improvements were seen across all measures except for in isometric knee extension at 240°/s in the one-set condition and leg press power in both volume conditions. A significant sex-effect was found for relative pre-post change in maximal isometric (0°/s) knee extension torque, with males demonstrating greater improvements compared to females, in both the 1-set condition (13.2 (9.9)% vs. 5.2 (8.4)%,  $p = .046$ ) and the 3-set condition (16.2 (11.7)% vs. 7.1 (12.2)%,  $p = .025$ ). No significant sex differences were observed for knee extension torque at 60°/s, 180°/s, or 240°/s, nor for peak power or peak force in the leg press test, in either the 1-set or 3-sets condition. For the upper body, females demonstrated significantly greater improvements in maximal isometric elbow flexion force compared to males (13.3 (8.4)% vs. 2.8 (9.1)%,  $p = .005$ ; see Figure 8).

**Table 3.** Estimated marginal means and simple effects of sex on relative change in lower-body strength outcomes.

Outcome	Female EMM $\Delta\%$ (SD)	Male EMM $\Delta\%$ (SD)	Sex difference estimate (95% CI)	<i>p</i>
<b>1-set condition</b>				
Leg extension torque				
(60°/s)	4.4 (14.5)	9.1 (8.2)*	4.7 (-4.0, 13.3)	.281
(180°/s)	12.9 (30.8)	8.3 (7.1)**	-4.6 (-21.4, 12.3)	.584
(240°/s)	9.4 (15.5)*	4.4 (16.8)	-5.1 (-17.2, 7.0)	.402
(isometric)	5.2 (8.4)*	13.2 (9.9)**	8.0 (0.2, 15.8)	.046
Leg press force	11.6 (11.0)*	8.5 (10.1)*	-3.0 (-10.9, 4.8)	.438
Leg press power	1.9 (11.1)	2.2 (7.7)	0.3 (-9.0, 9.6)	.953
<b>3-set condition</b>				
Leg extension torque				
(60°/s)	0.1 (13.6)	6.6 (8.4)*	6.5 (-2.2, 15.1)	.139
(180°/s)	12.2 (29.3)	7.0 (8.0)*	-5.2 (-22.0, 11.7)	.537
(240°/s)	8.1 (21.0)	8.1 (9.4)*	0.1 (-12.0, 12.1)	.992
(isometric)	7.1 (12.2)*	16.2 (11.7)**	9.0 (1.2, 16.9)	.025
Leg press force	9.3 (10.7)*	6.7 (8.6)*	-2.6 (-10.5, 5.2)	.499
Leg press power	1.1 (15.7)	0.5 (11.8)	-0.6 (-9.9, 8.7)	.897

Female was used as the reference group; positive sex differences indicate greater improvements in males compared to females. EMM; estimated marginal mean. \*Significant pre-post change ( $p < .05$ ).

\*\*Significant pre-post change ( $p < .001$ ).



**Figure 7.** Estimated marginal means on relative increases in isokinetic knee extension torque at 60°/s (A), 180°/s (B), 240°/s (C), isometric knee extension (D), leg press force (E) and leg press power (F) for females (blue bars) and males (red bars) for each volume condition (1 set and 3 sets). Error bars show 95% CI. KET; knee extension torque. \*Significant increase from pre ( $p < .05$ ). #Significant differences between sexes within volume condition ( $p < .05$ ).

**Figure 8.** Relative increases in elbow flexion force for females (blue bars) and males (red bars). Error bars show SD. \*Significant increase from pre ( $p < .001$ ). #Significant difference between sexes ( $p = .005$ ).

## Sex-Dependent Effects of Volume-Modulation

Results from the mixed-effects model investigating the interaction between sex and volume condition are shown in Table 4. The interaction sex  $\times$  volume was not significant for any of the lower-body muscle strength outcomes.

**Table 4.** Mixed-effects model on the effect of sex, volume condition and sex  $\times$  volume condition interaction on relative pre-post muscle strength change outcomes.

Variable	Predictor	Estimate	SE	95% CI		<i>t</i>	<i>p</i>
				Lower	Upper		
Knee extension torque $\Delta\%$	(60°/s) (Intercept)	5.04	1.57	1.97	8.11	3.22	.003
	Sex (male vs female)	5.58	3.13	-0.56	11.72	1.78	.086
	Volume (3 sets vs 1 set)	-3.43	2.96	-9.23	2.37	-1.16	.257
	Sex $\times$ Volume	1.78	5.92	-9.83	13.39	0.30	.766
	(180°/s) (Intercept)	10.08	4.00	2.25	17.92	2.52	.018
	Sex (male vs female)	-4.87	8.00	-20.54	10.81	-0.61	.548
	Volume (3 sets vs 1 set)	-0.95	2.08	-5.03	3.13	-0.46	.651
	Sex $\times$ Volume	-0.58	4.16	-8.74	7.58	-0.14	.891
	(240°/s) (Intercept)	7.48	2.62	2.34	12.63	2.85	.008
	Sex (male vs female)	-2.51	5.25	-12.80	7.78	-0.48	.636
	Volume (3 sets vs 1 set)	1.20	2.89	-4.48	6.87	0.41	.683
	Sex $\times$ Volume	5.13	5.79	-6.21	16.48	0.89	.383
	(isometric) (Intercept)	10.41	1.69	7.10	13.72	6.16	<.001
	Sex (male vs female)	8.51	3.38	1.88	15.13	2.52	.018
	Volume (3 sets vs 1 set)	2.48	1.94	-1.32	6.28	1.28	.212
	Sex $\times$ Volume	1.01	3.88	-6.59	8.61	0.26	.796
Leg press force $\Delta\%$	(Intercept)	9.02	1.80	5.50	12.54	5.02	<.001
	Sex (male vs female)	-2.84	3.59	-9.88	4.20	-0.79	.437
	Volume (3 sets vs 1 set)	-2.06	1.43	-4.86	0.75	-1.44	.162
	Sex $\times$ Volume	0.39	2.86	-5.22	6.00	0.14	.893
Leg press power $\Delta\%$	(Intercept)	1.42	2.16	-2.82	5.65	0.66	.518
	Sex (male vs female)	-0.16	4.32	-8.63	8.30	-0.04	.970
	Volume (3 sets vs 1 set)	-1.30	1.46	-4.16	1.57	-0.88	.384
	Sex $\times$ Volume	-0.87	2.93	-6.61	4.87	-0.30	.770

*Female was used as the reference group for sex, while the 1-set condition was used as the reference group for volume; 'intercept' describes the mean relative change for females in the 1-set condition.*

## Relationship Between Muscle Hypertrophy and Strength Gains Across Sexes

On average across both volume conditions, m. vastus lateralis muscle thickness increased by 4.9 (9.1)% in females ( $p = .049$ ) and 8.6 (7.0)% in males ( $p = .001$ ; see Figure 10). The difference in muscle thickness increase between sexes was not significant ( $p = .227$ ).

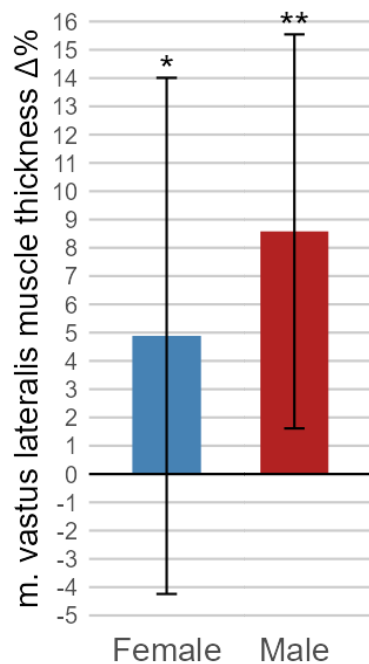
As shown in Table 5, both sexes demonstrated weak to no correlations between changes in m. vastus lateralis thickness and changes in lower-body muscle strength outcomes. Z-tests on

Fisher-transformed correlation coefficients revealed no significant differences in correlation between sexes for any of the lower body muscle strength outcomes (all  $p > 0.05$ ; for visual representation see Figure 9).

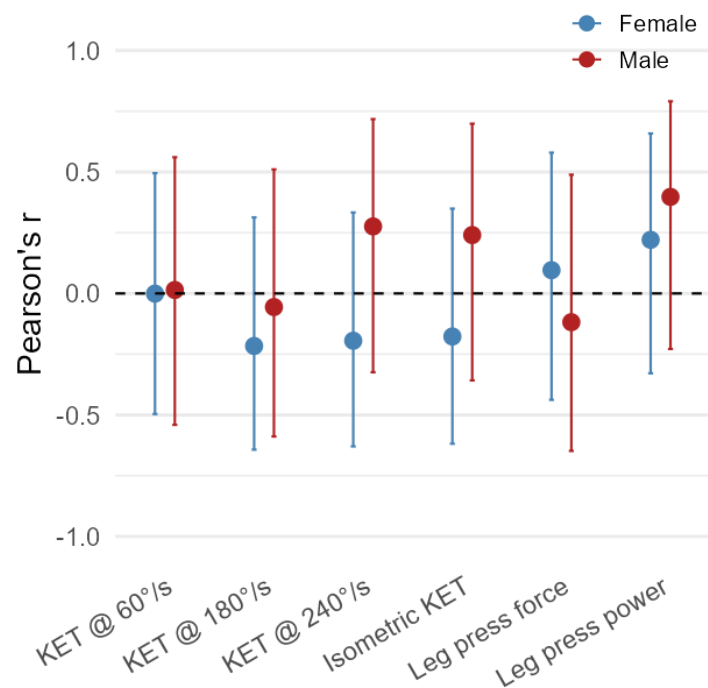
**Table 5.** Pearson correlation coefficients between relative changes in *m. vastus lateralis* muscle thickness and relative pre-to-post changes in lower-body muscle strength outcomes for females and males, respectively, with corresponding *z*-scores and *p*-values on differences in correlation between sexes.

Variable	VL MT $\Delta\%$				<i>z</i>	<i>p</i>
	Female		Male			
	Pearson's r	95% CI	Pearson's r	95% CI		
Knee extension torque $\Delta\%$						
(60°/s)	.00	[-.50, .50]	.01	[-.54, .56]	-0.04	.972
(180°/s)	-.22	[-.64, .31]	-.06	[-.59, .51]	-0.39	.697
(240°/s)	-.19	[-.63, .33]	.28	[-.32, .72]	-1.14	.253
(isometric)	-.18	[-.62, .35]	.24	[-.36, .70]	-1.01	.313
Leg press force $\Delta\%$	.10	[-.44, .58]	-.12	[-.65, .49]	0.49	.626
Leg press power $\Delta\%$	.22	[-.33, .66]	.40	[-.23, .79]	-0.45	.656

VL MT; *Vastus lateralis* muscle thickness, CI; confidence interval



**Figure 10.** Mean relative (%) increase in *m. vastus lateralis* muscle thickness (averaged across both legs) for females (blue bars) and males (red bars). Error bars show SD. \*Significant increase from pre ( $p = .049$ ). \*\*Significant increase from pre ( $p = .001$ ).



**Figure 9.** Visual representation of Pearson's *r* for the correlation between relative *m. vastus lateralis* hypertrophy and relative changes in lower-body muscle strength outcomes. Error bars show 95% confidence intervals. KET; knee extension torque.

## Discussion

The present study examined i) sex-based differences in maximal muscle strength adaptations to RET, ii) the extent to which such differences may be influenced by training volume, and iii) whether the relationship between maximal muscle strength gains and muscle hypertrophy differs between males and females. The results indicate i) largely similar lower-body muscle strength adaptations between sexes in both the one- and three set condition, while improvements in maximal elbow flexor muscle strength were greater in females compared to males. Furthermore, the results indicate that ii) training volume did not influence sex differences in muscle strength adaptations, and iii) the relationship between maximal muscle strength gains and muscle hypertrophy did not differ between sexes.

### Muscle Strength Adaptations

With regards to lower-body strength gains, the present study observed a significant sex difference only in isometric knee extension torque, where males improved more than females in both the one- and three set condition. No other strength outcomes showed significant sex differences, leading to the overall conclusion that males and females exhibit largely similar strength training adaptations. These findings align with a body of evidence suggesting comparable lower-body relative gains in strength between sexes (Dorgo et al., 2012; Kojić et al., 2021; Lemmer et al., 2001; Lexell et al., 1996), which is further corroborated in a recent meta-analysis by Roberts et al. (2020). However, other studies contradict our findings and report that females experience greater relative lower-body strength gains than males (Dias et al., 2005). Similar findings were reported in two recent meta-analyses (Hawley et al., 2023; Jones et al., 2021). It should be noted that both of these meta-analyses specifically looked at older adults ( $\geq 60$  and  $> 50$  years, respectively), while the sample in the meta-analysis of Roberts et al. (2020) was between 18 and 50 years old. The sample in the present study falls somewhat between these polarities, with participants between 30 and 65 years old. One may postulate that differences in sample age explain the conflicting findings. However, a recent study reported that age does to influence muscle strength gains in the lower body (Kittilsen et al., 2021).

Interestingly, Da Boit and colleagues (2016) reported, similarly to the present study, greater increases in isometric knee extension torque in males compared to females. Furthermore, the present study showed a tendency toward a significant sex-effect in isokinetic knee extension torque at  $60^\circ/\text{s}$  ( $p = .086$ ) in favor of males, while sex-effects for higher velocities ( $180^\circ/\text{s}$  and

240°/s) were not significant ( $p = .548$  and  $p = .636$ , respectively). Collectively, these observations suggest that sex differences in lower-body muscle strength gains may be dependent on contraction velocity, with males potentially experiencing greater strength improvements at isometric and low-velocity contractions. The observation that sex differences in muscle strength gain seems to disappear at higher contraction velocities may seem counterintuitive, considering males usually have a greater proportion of type II muscle fibers than females (Nuzzo, 2024). As type II fibers are shown to develop greater force at high contractile velocities than type I fibers (Bottinelli et al., 1999), one may argue that a greater proportion of type II muscle fibers should translate to a greater potential for increasing maximal contractile force at high contraction velocities, especially since both sexes seem to experience type II muscle fiber hypertrophy at similar rates in response to RET (Refalo et al., 2025). A possible counterargument to this assumption could lie in potential sex differences in rate of force development adaptations, possibly due to dissimilar neural adaptations between sexes, as rate of force development is arguably more important in high velocity contractions compared to isometric and low velocity contractions. However, as investigated by Blazevich et al. (2008), the magnitude of adaptations in rate of force development following RET do not seem to differ between sexes.

Overall, the lack of sex differences in strength gains across most of the lower-body strength outcomes does not align with the initial hypothesis, which stated that greater increases were expected in females. Meanwhile, it should be noted that 22 out of the 30 participants had completed a 53-week endurance cycling intervention immediately prior to the initiation of the RET intervention, which potentially influenced their adaptations to RET. Vikmoen et al. (2020) reported that untrained and endurance trained females displayed similar increases in 1RM leg press and maximal isometric knee extension torque following eleven weeks of lower-body RET. However, the initially untrained females showed superior gains in isokinetic knee extension torque at 240°/s. It should be noted that the endurance trained participants in Vikmoen and colleagues' study continued with their normal endurance training for the duration of the RET intervention. As this was not the case in the present study, we cannot be certain their findings apply to the present study. To the author's knowledge, no similar comparisons have been conducted on male participants. In the present study, the proportion of males and females was different between the participants who had taken part in the endurance intervention and those who had not (13 males and 9 females vs. 1 male and 7 females, respectively). Because of this disproportionality, if the endurance intervention influenced



participants' trainability to RET, it would have skewed the results differently between sexes, potentially influencing the outcomes of the study.

The present study found greater increases in elbow flexor muscle strength in females compared to males, which is in line with what was initially hypothesized. This observation has also been made in previous trials (Dias et al., 2005; Hubal et al., 2005). Furthermore, when assessing changes in upper-body muscle strength categorically, not elbow flexor strength specifically, some meta-analyses have reached similar conclusions (Hawley et al., 2023; Roberts et al., 2020), while others have reported no sex differences (Jones et al., 2021). Because of the categorical approach to upper-body muscle strength gains in these meta-analyses, their comparability with the present study is somewhat limited.

There are several potential reasons for the greater increase in elbow flexion force observed in females. Firstly, it could be due to the lower initial strength level in females. In fact, Hubal et al. (2005) reported a moderate negative correlation ( $r = -0.55$ ) between initial 1RM and 1RM percent increase for bicep curl, though the correlation was weaker for maximal isometric elbow flexion force ( $r = -0.27$ ). This could potentially explain why females showed greater changes than males in upper body muscle strength, but not lower-body muscle strength, as sex differences in initial muscle strength levels are shown to be greater in the upper body than in the lower body (Nuzzo, 2023).

Secondly, findings from a selection of studies on the effects of training volume on upper- and lower-body muscle strength may give valuable insight into the differential findings between upper- and lower-body muscle strength changes in the present study. Paulsen et al. (2003) and Rønnestad et al. (2007) utilized two similar protocols investigating the effects of one- vs. three sets per exercise on upper- and lower-body muscle strength in males. In both studies, participants were randomized to perform either three sets for upper-body exercises and three sets for lower-body exercises, or one set for upper-body exercises and three sets for lower-body exercises. The two studies unanimously reported significantly greater muscle strength gains with higher training volume in the lower body. However, training volume did not seem to influence muscle strength gains in the upper body in either study. Interestingly, a similar protocol was conducted on female participants a few years later (Vikmoen et al., 2012). This time, three sets per exercise elicited superior gains compared to one set per exercise in both the upper- and lower body. Collectively, these findings suggest that three sets per exercise elicits greater muscle strength gains in the lower body for both sexes, however, for upper-body muscle strength gains, three sets seem to be favorable only in females. It therefore seems

possible that, for the upper-body, muscle strength adaptations plateau at a lower training volume for males than for females, and that this explains at least in part the muscle strength gain discrepancy between sexes in the upper body observed in the present study.

Unfortunately, the design of the present study did not enable us to address this hypothesis, as all participants performed three sets per exercise bilaterally for the upper-body exercises.

### **Training Volume and Muscle Strength Adaptations**

In the present study, training volume had no significant effect on sex differences in lower-body muscle strength adaptations following RET. In other words, the difference between males and females in lower-body muscle strength adaptations when performing three sets per exercise was not significantly different from the sex difference when performing one set per exercise. To the author's knowledge, Hammarström et al. (2020) is the only previous study to date to have made a direct comparison on the effects of one set vs. three sets per exercise between sexes in lower-body muscle strength gains. Similarly to the findings in the present study, Hammarström et al. (2020) reported no sex differences in muscle strength gains, and volume condition did not influence sex differences in lower-body muscle strength gains. Notably, Hammarström and colleagues did demonstrate significantly greater muscle strength gains in the three-set condition compared to the one-set condition, which was not the case in the present study.

Interestingly, Hammarström et al. (2020) demonstrated a strong correlation within participants between muscle strength adaptations to one-set vs. three-set RET. This correlation highlights the strength of the within-participant modulation of volume conditions utilized in the present study, as this design eliminates the influence of the extensive interindividual variations in RET responses reported by Ahtianinen et al. (2016). However, this design makes adaptations prone to cross-influence between volume conditions from systemic neural adaptations. For example, Carolan and Cafarelli (1992) demonstrated that unilateral RET reduced antagonist coactivation in both the trained and untrained limb, suggesting the presence of systemic neural adaptations influencing net joint torque in the absence of local mechanical stimuli, which has since been repeatedly confirmed (Duchateau & Enoka, 2002; Griffin & Cafarelli, 2005). It is therefore possible that the muscle strength gains observed in the one-set condition in the present study are hyperinflated by the three-set condition due to systemic neural adaptations.

## **Relationship Between Muscle Hypertrophy and Muscle Strength Adaptations**

To the author's knowledge, the present study is the first to demonstrate that m. vastus lateralis hypertrophy and lower-body muscle strength gains do not correlate differently between sexes in the early stages of RET. Despite significant increases in lower-body muscle thickness and -strength being observed in both sexes, the correlations between the two were weak to non-existent in both males and females, suggesting large individual variation in the relationship between increases in muscle thickness and -strength. This lack of correlation between muscle hypertrophy and muscle strength gains is in line with previous observations (Ahtiainen et al., 2016; Erskine et al., 2014), indicating pivotal physiological adaptations beyond muscle hypertrophy responsible for strength gains following the onset of RET. As reported by Moritani and deVries (1979), who investigated the relationship between hypertrophic and neural contributions to muscle strength gains in response to an eight-week RET intervention, neural adaptations seem to account for the majority of muscle strength gains for the first three to five weeks after RET onset. In line with this, it has been reported that rate coding during MVC increases during the first weeks of RET (Del Vecchio et al., 2019), while motor unit recruitment threshold decreases (Del Vecchio et al., 2019; Häkkinen & Komi, 1983; Moritani & deVries, 1979). As discussed earlier, antagonist coactivation during muscle contractions decreases in response to RET, further underscoring the role of neural adaptations in increasing muscle strength. It seems plausible that the extent of neural adaptations in the first few weeks of RET explains why muscle hypertrophy and muscle strength gains showed weak-to-no correlations in the present study. As neural adaptations seem to subside gradually and become negligible after ~eight weeks (Moritani & deVries, 1979), it seems likely that a longer intervention than the one in the present study would increase the degree to which muscle hypertrophy correlates with muscle strength gains, which in turn would enable a more robust assessment of whether the correlation differs between sexes.

## **Considerations**

This study may have limitations with regards to its design. First, and as previously mentioned, not all participants were similar in terms of training status at the time of recruitment. Some participants were completely untrained, while others had taken part in an endurance training intervention just weeks before initiation of the study. As the proportion of males and females differed quite substantially between these two groups, adaptations gained from the endurance training intervention may have skewed the RET adaptations differently between the sexes.

Second, muscle thickness was only assessed at a single location. As the extent of muscle hypertrophy can vary longitudinally in the muscle (Earp et al., 2015), it is possible that alternative hypertrophic adaptations occurred elsewhere in the muscle. Third, due to the nature of studies on training volume and sex differences, participants, training session instructors and test leaders were not blinded. We therefore cannot rule out the influence of bias or placebo effects. Fourth, although participants were requested to refrain from extensive physical activity not related to the intervention, however, this was not systematically monitored. Fifth, menstrual cycle in female participants was not monitored. However, ovulation period does not seem to affect muscle strength (Romero-Moraleda et al., 2019). Finally, although significant m. vastus lateralis hypertrophy was observed at the group level for both sexes, the intervention period may have been too short to elicit significant hypertrophic adaptations in lower body muscles for many of the participants, possibly explaining the weak correlations between muscle hypertrophy and muscle strength gains. This may have, in turn, influenced how the correlations differed between sexes.

### **Practical Implications and Perspectives**

Based on the findings of this study, similar-volume resistance training protocols should be prescribed to males and females with regards to increasing lower-body muscle strength. However, sex differences were apparent in upper-body muscle strength gains. This raises the need for future research to investigate the mechanisms behind dissimilar upper-body adaptations between sexes. Furthermore, future research should implement longer resistance exercise interventions to potentially better assess whether the degree to which muscle strength gains are attributable to muscle hypertrophy between sexes.

### **Conclusions**

In conclusion, nine weeks of resistance exercise training led to greater relative increases in upper-body muscle strength in females than in males, while lower-body gains were similar between sexes. Performing one vs. three sets per lower-body exercise did not alter muscle strength gains differently between sexes. M. vastus lateralis hypertrophy correlated poorly with lower-body muscle strength gains for both sexes, and no significant difference in correlation between sexes was observed.

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## Appendices

### Appendix A: Written Consent Form

#### VIL DU DELTA I FORSKNINGSPROSJEKTET:

#### «**REPEAT**» – HVORFOR HAR UTRENTE PERSONER ULIK EFFEKT AV FYSISK TRENING?

##### FORMÅLET MED PROSJEKTET OG HVORFOR DU BLIR SPURT

Dette er et spørsmål til deg om å delta i et forskningsprosjekt som har som formål å undersøke individuell variasjon i respons på to år med ulik trening. Når vi trener utholdenhets- og styrketrening forbedrer vi kroppens evne til energiomsetning og kraftutvikling, hvorav begge faktorene er avgjørende for opprettholdelse av god helse og normal kroppslig funksjon. Imidlertid ser man at hvor stor effekt man oppnår varierer mellom personer, til tross for at man utsetter kroppen for det samme arbeidet. Dersom du blir med som deltager i denne studien, vil du være med i en studie som ønsker å besvare spørsmål om 1) i hvilken grad samme person responderer likt på trening når treningen repeteres flere ganger, og når treningen gjennomføres over lang tid? 2) Hvordan treningseffektene utvikler seg over tid, og hva som bestemmer størrelsen på effektene? 3) Om det er en sammenheng mellom de som responderer godt på utholdenhetstrening og de som responderer godt på styrketrening? 4) Til slutt tar studien sikte på å identifisere hva som kjennetegner de som lykkes med å fullføre treningen i prosjektet og som fortsetter å trene etter at prosjektet er ferdig.

For å være med i studien kan du ikke ha trent mer enn én utholdenhetstreningsøkt per uke det siste året, du må være frisk og i alderen 30-65 år. Vi ønsker å rekruttere totalt 65 personer til dette prosjektet.

Om du etter å ha lest denne informasjonen ønsker å delta i studien ber vi deg skrive under og returnere den siste siden til oss. Du kan når som helst i etterkant trekke deg fra studien uten å oppgi grunn.

Ansvarlig for studien er Høgskolen i Innlandet og prosjektleder for studien er førsteamanuensis Knut Sindre Mølmen. Ph.d.-student Tomas Urianstad vil ha det praktiske ansvaret for den daglige driften underveis i studien. Studien vil inngå i hans doktorgradsavhandling, samt i flere master- og bacheloroppgaver.

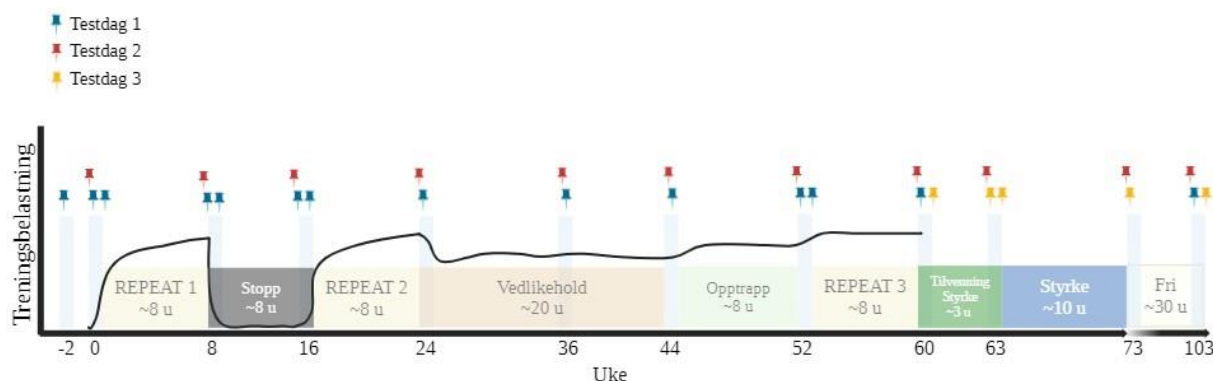
##### HVA INNEBÆRER PROSJEKTET FOR DEG?

Prosjektet har en varighet på to år (103 uker). Som deltager skal du i løpet av den tiden gjennomføre en lengre periode med utholdenhetstrening før en periode med



styrketrening. Treningen deles opp i mindre treningsperioder med ulikt innhold, og det gjennomføres et betydelig antall tester og målinger tilknyttet hver periode. Se figur 1 og tabell 1 for en oversikt over de ulike treningsperiodene og testene og målingene som skal gjennomføres.

De blå (Testdag 1), røde (Testdag 2) og gule (Testdag 3) knappenålene i Figur 1 markerer når de ulike testdagene skal gjennomføres.



**Figur 1.** Oversikt over studiens tidslinje, inkludert trening og testprosedyrer. Totalt vil det bli gjennomført 54-uker med utholdenhetstrening, etterfulgt av 13-uker med styrketrening, før 30-uker fri livsstil. Blå, rød og gul knappenål symboliserer henholdsvis Testdag 1, 2 og 3. Svart heltrukken linje symboliserer tiltenkt treningsbelastning under utholdenhetstreningen.

**Tabell 1:** Oversikt over innhold og rekkefølge på de forskjellige testdagene.

<b>Testdag 1 – ca. 2 timer.</b> Gjennomføres totalt <b>14</b> ganger og består av måling av maksimal fysisk kapasitet og livskvalitet.	
1.	Styrketest
2.	Laktatprofil (4-5 5-min arbeidsperioder med stigende arbeidsintensitet med måling av bl.a. hjerterefrekvens og melkesyre)
3.	Maksimal aerob kapasitetstest ( $VO_{2maks}$ -test)
4.	20 minutters sykkelprestasjonstest
5.	Spørreundersøkelse om helserelatert livskvalitet (SF-36)
<b>Testdag 2 – ca. 2 til 3 timer.</b> Gjennomføres totalt <b>11</b> ganger og inneholder ulike målinger og prøver som må gjøres fastende	

1.	Fastende test av kroppssammensetning (målt med DXA)
2.	Fastende test av muskeltykkelse (målt med ultralyd) og arteriell stivhet (kun før og etter «REPEAT»-periodene og «Styrke»-perioden)
3.	Fastende mikrobiopsi av lårene på begge bein (m. Vastus lateralis) (kun før og etter «REPEAT»-periodene og «Styrke»-perioden)
4.	Fastende blodprøve
5.	Fastende glukosetoleranse-test (kun før og etter «REPEAT»-periodene)
6.	Fastende bestemmelse av blodvariabler (målt med karbonmonoksidgjenpustingstest)
<b>Testdag 3 – ca. 2 timer.</b> Gjennomføres totalt <b>5</b> ganger og består av styrketester.	
1. Styrketester i beinpress og kneekstensjon	

Det vil være forskjeller i innhold og hvor mye tid prosjektet krever i de ulike periodene:

### **REPEAT 1 (de første 8 ukene i prosjektet, se figur 1.)**

I denne perioden gjennomføres:

- Høyintensiv utholdenhetstrening på spinningsykkel
- Treningsfrekvens: 2-4 ganger ukentlig, totalt 24 ganger
  - Hvert oppmøte varer 1 time
- Testdag 1: Gjennomføres tre ganger før og to ganger etter treningsperioden
  - På den siste Testdag 1 dagen etter treningsperioden skal sertifisert helsepersonell tappe ut den eksakte mengden blod du tilegnet deg gjennom treningsperioden før du gjennomfører utholdenhetstestene. Det er antatt at det vil være mellom 1-4 dl (til sammenligning tappes ca. 5 dl blod ved bloddonasjon i blodbanken). Testdag 2: Gjennomføres før og etter treningsperioden **Stopp (den 9. til den 16. uka i prosjektet)**

I denne perioden gjennomføres:

- Ingen aktivitet
  - Du skal stoppe med treningen og gå tilbake til det aktivitetsnivået som du hadde før REPEAT 1

### **REPEAT 2 (den 17. til den 24. uka i prosjektet)**

I denne perioden skal det gjennomføres:

- Høyintensiv utholdenhetstrening på spinningsykkel

- Treningsfrekvens: 2-4 ganger ukentlig, totalt 24 ganger
- Hvert oppmøte varer 1 time
- Testdag 1: Gjennomføres to ganger før og én gang etter treningsperioden
- Testdag 2: Gjennomføres før og etter treningsperioden **Vedlikehold (den**

### **25. til den 44. uka i prosjektet)**

I denne perioden skal det gjennomføres:

- Høyintensiv utholdenhetstrening på spinningsykkel og moderat intensiv egentrening, totalt 45 treningsøkter, hvorav:
- Høyintensiv utholdenhetstrening på spinningsykkel 1-2 ganger ukentlig,
  - Hvert oppmøte varer 1 time
- Moderat intensiv egentrening i valgfri aktivitetsform 0-1 ganger ukentlig
  - Hver økt varer 45 minutter (disse øktene kan gjøres hjemme)
- Testdag 1: Gjennomføres én gang etter 12 uker
- Testdag 2: Gjennomføres én gang etter 12 uker, men uten muskelbiopsi, og det vil heller ikke bli målt muskeltykkelse, arteriell stivhet eller glukosetoleranse

**Opptropp (den 45. til 52. uka i prosjektet)** I denne perioden skal det gjennomføres:

- Høyintensiv utholdenhetstrening på spinningsykkel
- Treningsfrekvens: 2-3 ganger ukentlig, totalt 20 ganger - Hvert oppmøte varer 1 time
- Testdag 1: Gjennomføres én gang før treningsperioden
- Testdag 2: Gjennomføres én gang før treningsperioden, men uten muskelbiopsi, og det vil heller ikke bli målt muskeltykkelse, arteriell stivhet eller glukosetoleranse **REPEAT 3 (den 53. til 60. uka i prosjektet)**

I denne perioden skal det gjennomføres:

- Høyintensiv utholdenhetstrening på spinningsykkel
- Treningsfrekvens: 2-4 ganger ukentlig, totalt 24 ganger
- Hvert oppmøte varer 1 time
- Testdag 1: Gjennomføres to ganger før og én gang etter treningsperioden
- Testdag 2: Gjennomføres før og etter treningsperioden **Tilvenning Styrke**

### **(den 61. til den 63. uka i prosjektet)**

I denne perioden skal det gjennomføres:

- Tilvenning til tung styrketrening
- Treningsfrekvens: 1 gang ukentlig, totalt 3 ganger
- Hvert oppmøte varer 1 time

- Testdag 3: Gjennomføres før treningsperioden **Styrke (den 64. til den 73.**

#### **uka i prosjektet)**

I denne perioden skal det gjennomføres:

- Tung styrketrening
- Treningsfrekvens: 2 ganger ukentlig, totalt 20 ganger
  - Hvert oppmøte varer 1 time
- Testdag 2: Gjennomføres før og etter treningsperioden, men uten mål av glukosetoleranse • Testdag 3: Gjennomføres før og etter treningsperioden

#### **Fri (den 74. til den 103. uka i prosjektet)**

I denne perioden skal det gjennomføres:

- Fri aktivitet
  - Du vil få tilbud om treningsveiledning, men all trening gjennomføres på egenhånd
- Testdag 1: Gjennomføres etter perioden
- Testdag 2: Gjennomføres etter perioden, men uten muskelbiopsi, og det vil heller ikke bli målt muskeltykkelse, arteriell stivhet eller glukosetoleranse
- Testdag 3: Gjennomføres etter perioden

I tillegg til testene og målingene som gjennomføres vil vi innhente og registrere ulike personopplysninger om deg som er direkte relevante for formålet med studien. Dette vil være informasjon som alder, kroppshøyde og -vekt, samt opplysninger om treningen du gjør. I tillegg vil det bli gjennomført kvalitative dybdeintervjuer med formål å kartlegge opplevelser av prosjektgjennomføringen, identifisere faktorer som kan ha påvirket treningstilpasningene som ikke er relatert til treningen i prosjektet (for eksempel livsstil og livshendelser).

### **MULIGE FORDELER OG ULEMPER**

**Fordeler ved deltagelse i studien:** Som deltager i denne studien vil du få god innsikt i din egen helse, samt kunnskap om hva slags effekter utholdenhet- og styrketrening vil gi deg. Du vil få veiledet trening og oppfølging gjennom et helt år og vil gjennomgå flere avanserte tester som man vanligvis ikke får mulighet til, bl.a. ulike tester med måling av oksygenopptak på sykkel,

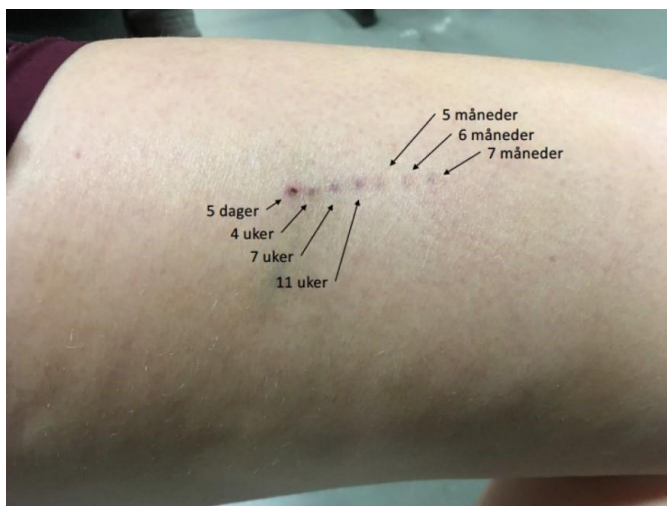
kroppssammensetning, måling av blodvolum, samt inngående analyser av hva som karakteriserer muskulaturen din. Du vil få kunnskap om hvordan du skal trene på en effektiv måte, samt få nøyaktige svar på hvordan din fysiske form er. Du vil også få et

innblikk i hvordan forskning foregår og tilegne deg kunnskap om hvordan blod og muskulatur endrer seg med trening.

**Potensielle ulemper ved deltagelse i studien:** Deltagelse i prosjektet vil kreve mye tid og oppmerksomhet da du må møte opp til treningsøkter opptil fire ganger i uken gjennom året, i tillegg til oppmøtene for tilvenning og testing.

Enkelte av sykkeløktene og de fysiske testene skal gjennomføres på en relativt høy intensitet. Dette kan oppleves som anstrengende, og du bør regne med at du kan bli litt støl/sår i muskulaturen etter de første testene og treningene.

Muskelprøvene tas med den svært skånsomme mikrobiopsimetoden. Noen synes likevel biopsier er ubehagelig. Du vil typisk bli litt støl i muskelen en til to dager i etterkant, først og fremst på grunn av små blødninger i muskulaturen. Inngrepet vil etterlate små arr, men disse vil forsvinne hos de fleste med tiden (se Figur 2). I svært få tilfeller vil biopsitaking føre til at følelsen i huden rundt biopsien forsvinner over en lengre periode. Biopsitaking er også forbundet med en viss infeksjonsfare. Risikoen for disse komplikasjonene er imidlertid svært liten ved bruk av prosedyrene som benyttes i dette prosjektet. Du vil få klare instruksjoner om hvordan du skal behandle såret i etterkant av prøvetagningen. Blodprøvene som skal tas er ikke forbundet med noen risiko. Hvis det skulle oppstå noen uforutsette hendelser kan du kontakte medisinsk ansvarlig i prosjektet Inger Johanne Løkkevik på telefon: 45151929.



**Figur 2.** Typisk arrdannelse etter mikrobiopsitaking. De angitte tidspunktene indikerer tid siden biopsitaking.

Enkelte kan i ettertid av blodtapping (som gjennomføres etter «Repeat 1») oppleve noe slapphet, trøtthet og/eller svimmelhet, men dette er forbigående. I tillegg kan det tenkes at noe av treningseffekten som du fikk gjennom den første treningsperioden forsvinner etter blodtappingen, men at denne treningseffekten vil komme tilbake når du går i gang med den andre treningsperioden.

Karbonmonoksid-gjenpusting som benyttes for å måle blodvariabler, kan oppleves som ubehagelig for noen. Under disse målingene skal du puste inn en liten mengde karbonmonoksid (tilsvarende mengden karbonmonoksid en får i seg ved å røyke en håndfull sigaretter), men denne mengden er så liten at den ikke anses som helseskadelig. Karbonmonoksid forsvinner ut av kroppen innen 12-14 timer.

#### FRIVILLIG DELTAKELSE OG MULIGHET FOR Å TREKKE DITT SAMTYKKE

Det er frivillig å delta i prosjektet. Dersom du ønsker å delta, undertegner du samtykkeerklæringen på siste side. Du kan når som helst og uten å oppgi noen grunn trekke ditt samtykke. Det vil ikke ha noen negative konsekvenser for deg hvis du ikke vil delta eller senere velger å trekke deg. Du kan også kreve dataene dine slettet så lenge de er identifiserbare i datamaterialet. Dersom du ønsker å trekke deg eller har spørsmål til prosjektet, kan du kontakte prosjektleder (se kontaktinformasjon på siste side).

#### HVA SKJER MED OPPLYSNINGENE OM DEG?

Opplysningene som registreres om deg skal kun brukes slik som beskrevet under formålet med prosjektet, og planlegges brukt til og med prosjektslutt 31.12.2030. Etter prosjektslutt skal opplysningene oppbevares i fem år for dokumentasjonshensyn. Eventuelle utvidelser i bruk og oppbevaringstid kan kun skje etter godkjenning fra Regional Komité for Medisinsk og Helsefaglig Forskningsetikk og andre relevante myndigheter.

Du har rett til innsyn i hvilke opplysninger som er registrert om deg og rett til å få korrigeret eventuelle feil i de opplysningene som er registrert. Du har også rett til å få innsyn i sikkerhetstiltakene ved behandling av opplysningene. Alle data skal oppbevares på sikker server, Tjenester for sensitive data (TSD), ved Universitetet i Oslo som Høgskolen i Innlandet har databehandleravtale med. Du kan klage på behandlingen av dine opplysninger til Datatilsynet og institusjonen sitt personvernombud. Vi behandler opplysningene konfidensielt og i samsvar med personvernregelverket. Det er bare medlemmer i prosjektgruppa som får tilgang på disse dataene. Navnet og kontaktopplysningene dine vil erstattes med en kode som lagres på egen navneliste adskilt fra øvrige data. Det er kun anonyme testresultater som publiseres, slik at du ikke vil kunne gjenkjennes i publikasjoner.

## HVA SKJER MED PRØVER SOM BLIR TATT AV DEG?

Opplysningene vi samler inn om deg i prosjektet vil bli behandlet uten navn og aidentifisert (se avsnittet «Hva skjer med opplysningene om deg?»). Daglig leder i prosjektet (Tomas Urianstad) vil være den eneste som er involvert i innsamlingen og behandlingen av spørreskjemaene.

Vi leter i utgangspunktet ikke etter helseutfordringer. Skulle vi likevel oppdage noe som avviker fra det vi forventer og/eller gir oss mistanke om helseutfordringer vil det bli tatt initiativ til videre medisinsk oppfølging. Du vil da bli kontaktet av medisinsk ansvarlig i prosjektet eller autorisert helsepersonell ved Seksjon for Helse og Treningsfysiologi. Denne personen vil veilede deg videre om hvordan du bør håndtere situasjonen.

Muskelvevet og blodprøven som tas av deg skal oppbevares i en forskningsbiobank tilknyttet prosjektet ved Høgskolen i Innlandet campus Lillehammer. Ansvarlig for denne biobanken er Knut Sindre Mølmen.

## FORSIKRING

Som deltager i studien er du forsikret gjennom Høgskolen i Innlandets forsikring hos Gjensidige.

## GODKJENNINGER

Etter ny personopplysningslov har behandlingsansvarlig Høgskolen i Innlandet og prosjektleder Knut Sindre Mølmen et selvstendig ansvar for å sikre at behandlingen av dine opplysninger har et lovlig grunnlag. Dette prosjektet har rettslige grunnlag i EUs personvernforordning artikkel 6 nr. 1a og artikkel 9 nr. 2a og ditt samtykke. Du har rett til å klage på behandlingen av dine opplysninger til Datatilsynet.

Vi behandler opplysningene basert på ditt samtykke.

## KONTAKTOPPLYSNINGER

Dersom du har spørsmål til prosjektet eller ønsker å trekke deg fra deltagelse, kan du kontakte:

Prosjektleder: Knut Sindre Mølmen, telefon: 94860805, e-post:  
[knut.sindre.molmen@inn.no](mailto:knut.sindre.molmen@inn.no)

Daglig leder i prosjektet: Tomas Urianstad, telefon: 98091190, e-post:  
[tomas.urianstad@inn.no](mailto:tomas.urianstad@inn.no)

Dersom det skulle dukke opp uheldige opplevelser i prosjektet som du ikke ønsker å dele med prosjektleder eller andre i prosjektgruppen kan du kontakte autorisert helsepersonell ved Seksjon for Helse- og Treningsfysiologi: Anne Mette Rustaden, telefon: 61288023, e-post: [anne.rustaden@inn.no](mailto:anne.rustaden@inn.no).

Dersom du har spørsmål om personvernet i prosjektet, kan du kontakte personvernombudet ved institusjonen:

<https://www.inn.no/om-hogskolen/personvern/>



JEG SAMTYKKER TIL Å DELTA I PROSJEKTET OG TIL AT MINE PERSONOPPLYSNINGER  
OG MINE DATA BRUKES SLIK DET ER BESKREVET

-----  
Sted og dato

-----  
Deltagers signatur

-----  
Deltagers navn med trykte bokstaver

For deg som tidligere har deltatt i styrketreningsprosjekt i regi av Høgskolen i  
Innlandet: Jeg samtykker til at data som omhandler treningsrespons i det  
prosjektet kan overføres til dette prosjektet (det innebærer informasjon om  
endringer fra før til etter styrketreningsperioden på variabler som glukosetoleranse,  
samt muskelstyrke, -funksjon, -kvalitet og -masse)

-----  
Sted og dato

-----  
Deltagers signatur

-----  
Deltagers navn med trykte bokstaver

## Appendix B: Self-Declaration Of Health

Studie-ID:

Opplysninger til prosjekt

Alder: \_\_\_\_\_

Har du følgende:

Ustabil kardiovaskulær sykdom?

Blitt behandlet for kreft <5år?:

Fysisk begrensende muskel-skjelettsykdom?

Har du eller har du hatt astma?

Alvorlig (behandlingskrevende) psykisk sykdom?

Har du blitt anbefalt av lege å unngå fysisk anstrengelse?

Tar du noen medisiner som kan påvirke fysisk prestasjon (eks. hormoner eller steroider)?

Hvis ja, hvilke?: \_\_\_\_\_

Tar du blodfortynnende medisin?

Hvis ja, hvilke?: \_\_\_\_\_

Er du blodgiver?

Hvis ja, når ga du sist blod? \_\_\_\_\_

Andre sykdommer eller informasjon, som kan være relevant for prosjektet?

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Opplysninger før testing på Fysiologisk Testlaboratorium på HINN

	JA	NEI
Har du fått målt forhøyet blodtrykk noen gang?	<input type="checkbox"/>	<input type="checkbox"/>
Hvis ja - hvor høyt var det? _____		
Bruker du noen medisiner daglig?	<input type="checkbox"/>	<input type="checkbox"/>
Hvis ja: hvilke?: _____		
Får du smerter i brystet ved fysisk aktivitet?	<input type="checkbox"/>	<input type="checkbox"/>
Er du kortpustet i hvile ved lett aktivitet?	<input type="checkbox"/>	<input type="checkbox"/>
Har du de siste måneder hatt bryst smerter i hvile?	<input type="checkbox"/>	<input type="checkbox"/>
Plages du av svimmelhet eller balanseproblemer?	<input type="checkbox"/>	<input type="checkbox"/>
Opplever du deg som uvanlig slapp eller kortpusten ved daglig aktivitet?	<input type="checkbox"/>	<input type="checkbox"/>
Har du hevelse rundt ankene?	<input type="checkbox"/>	<input type="checkbox"/>
Har du en kjent bilyd over hjertet?	<input type="checkbox"/>	<input type="checkbox"/>
Har du pusteproblemer om natten?	<input type="checkbox"/>	<input type="checkbox"/>
Har du plager fra armer, ben eller ledd som blir verre under fysisk aktivitet?	<input type="checkbox"/>	<input type="checkbox"/>
Har du andre plager som hindrer deg i å være fysisk aktiv?	<input type="checkbox"/>	<input type="checkbox"/>

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### EGENERKLÆRING

Jeg, ..... er klar over at jeg gjennomfører maksimalt belastende styrke og utholdenhetstester på Høgskolen og har gitt alt av relevant informasjon som kan argumentere imot å gjennomføre dette.

Sted og dato: \_\_\_\_\_ Underskrift \_\_\_\_\_