# EQUIVALENT HYPERTROPHY AND STRENGTH GAINS IN HMB OR LEUCINE SUPPLEMENTED MEN

# EQUIVALENT HYPERTROPHY AND STRENGTH GAINS IN HMB OR LEUCINE SUPPLEMENTED MEN

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## LAY ABSTRACT

Whey protein supplementation following resistance training (RT) is an effective strategy to enhance RT-induced gains in skeletal muscle mass and strength. The anabolic properties of whey protein are attributed, in part, to the branched-chain amino acid leucine. Leucine is a substrate for protein synthesis and a potent signal that turns on the protein synthetic machinery. A metabolite of leucine, β-hydroxy, β-methylbutyrate (HMB) has been claimed to share similar or greater anabolic properties of leucine. Recently, supplementation with HMB during RT has been shown to result in large gains in muscle mass and strength. The purpose of this study was to examine whether HMB, versus leucine, added to whey protein, would result in different muscle hypertrophy and strength gains in young men during RT. Body composition and maximum strength tests were performed before, during and after 12 weeks of RT. Following 12 weeks of RT, both groups experienced similar gains in muscle mass and strength. We observed that HMB is no more effective in stimulating RT-induced hypertrophy and strength gains than its parent amino acid, leucine.

**ABSTRACT**

Ingestion of proteins with high leucine content during resistance training (RT) can augment hypertrophy. There are data suggesting that a leucine metabolite, β-hydroxy, β-methylbutyrate (HMB), may, however, be substantially more anabolic than leucine. **Purpose:** We aimed to test whether supplementation with HMB versus leucine, added to whey protein, would result in different muscle hypertrophy and strength gains in young men performing resistance training (RT). **Methods:** Twenty-six resistance-trained men (23 ± 2 y) performed 12 wk of RT with 3 phases. Phase 1: 8 wk of periodized RT (3 training sessions/wk). Phase 2: 2 wk overreaching period (5 sessions/wk). Phase 3: 2 wk taper (3 sessions/wk). Participants were randomly assigned to twice daily ingestion of: whey protein (25 g) plus HMB (1.5 g) (Whey+HMB; n=13) or whey protein (25 g) plus leucine (1.5 g) (Whey+Leu; n=13). Skeletal muscle biopsies were performed before and after RT. Measures of fat and bone-free mass (FBFM), *vastus lateralis* (VL) muscle thickness and muscle cross-sectional area (CSA – both by ultrasound), muscle fiber CSA, and 1-repetition maximum (1-RM) strength tests were determined. **Results:** We observed increases in FBFM, VL muscle thickness, muscle CSA and fiber type CSA and 1-RM strength, with no differences between HMB and leucine at any phase. Furthermore, no differences were observed in hormone concentrations between groups, or in time-by-group interactions in hormone concentrations at any phase of the RT program. **Conclusion:** HMB did not result in greater increases in any measure of muscle mass, strength, or hormonal concentration compared to leucine during 12 weeks of RT.

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## DECLARATION OF ACADEMIC ACHIEVEMENT

J.S Jakubowski was the principal contributor for the conceptualizing the research question, research hypothesis, experimental design, data collection, data analysis and data interpretation. S.M. Phillips, E. Nunes and C. McGlory assisted with the research question, research hypothesis, experimental design and data interpretation. E. Wong and J. Vanderweerd contributed to the data collection and data interpretation.

**LIST OF TABLES AND FIGURES**

## LIST OF ABBREVIATIONS

| | |
|---|---|
| MPS | Muscle protein synthesis |
| MPB | Muscle protein breakdown |
| RE | Resistance exercise |
| RT | Resistance training |
| mTORC-1 | Mechanistic target of rapamycin complex 1 |
| ACSM | American College of Sports Medicine |
| AA | Amino acids |
| EAA | Essential amino acids |
| Non-EAA | Non-essential amino acids |
| HMB | Beta-hydroxy, beta-methylbutryate |
| HMB-Ca | HMB-Calcium form |
| HMB-FA | HMB-Free acid |
| 1RM | 1 repetition maximum |
| FBFM | Fat and bone-free mass |
| CSA | Cross-sectional area |
| DXA | Dual-energy X-ray absorptiometry |
| LBM | Lean body mass |

# CHAPTER 1: STRATEGIES TO OPTIMIZE RESISTANCE EXERCISE-INDUCED HYPERTROPHY

# Chapter 1. Overview and Aims

Skeletal muscle mass is critical for locomotion, is a substantial contributor to basal metabolic rate and post-prandial glucose disposal (4), and is responsible for the production of mechanical force (5). It was discovered in ~1930 through the use of isotopically labeled tracers that skeletal muscle is in a state of dynamic flux (6). Indeed, skeletal muscle mass is maintained by the dynamic processes of muscle protein synthesis (MPS) and muscle protein breakdown (MPB), which oppose each other and yet occur simultaneously (7). The process of MPS describes the incorporation of amino acids, through the translation of mRNA, into newly synthesized proteins and is stimulated in response to nutritional, hormonal, and/or contractile stimuli (7, 8). MPB describes the release of amino acids via proteolytic action of protein structures into the intracellular muscle pool, which can then be reutilized for the synthesis of new muscle proteins, metabolized, or released into systematic circulation to be metabolized by other tissues (7, 8). In the postabsorptive phases of the day MPB predominates (e.g., during sleep and upon waking prior to eating a meal) (9). An important constituent of the diet that stimulates MPS and promotes net anabolism in skeletal muscle is protein (10). The ingestion of protein and subsequent aminoacidemia induces a transient and dose-saturable increase in MPS and suppression of MPB (7, 11). During the day, some limited postabsorptive liberation of amino acids from muscle protein is balanced by the net incorporation of amino acids into muscle protein during feeding, such that net protein balance (defined as the algebraic difference between the rates of MPS and MPB: MPS – MPB = 0) is achieved (9, 12-14).

Skeletal muscle hypertrophy is defined as the radial growth of skeletal muscle fibres and occurs as a result of successive periods of net positive protein balance (MPS>MPB) (15). Positive net protein balance is achieved through ingestion of protein, and the resultant hyperaminoacidemia, as well as participation in resistance exercise (RE). These two stimuli act through different mechanisms, but share similar canonical signaling pathways (16). Performance of RE in the postabsorptive state results in an increase in MPS and MPB, however, net protein remains negative although less so due to a greater relative stimulation of MPS than MPB (8, 14). However, when RE is followed by the ingestion of protein – either through whole-food or supplemental sources – a positive protein balance ensues (7, 17). A popular strategy to enhance RE-induced muscle anabolism has therefore centered around consumption/supplementation with high quality protein during a RE program (18).

Whey protein is a high-quality protein because it contains a full complement of essential amino acids and is highly digestible (19, 20). The anabolic effects of whey protein are well-known and its potency in stimulating MPS is largely attributable to its high leucine content (21-23). Ingestion of leucine alone can independently stimulate the mechanistic target of rapamycin complex-1 (mTORC1), a key protein kinase central to the stimulation of MPS (24-26). Recently, a metabolite of leucine, β-hydroxy-β-methylbutyrate (HMB), has received much attention because it too can stimulate MPS (1, 27), and has been reported to augment resistance training (RT)-induced muscle mass and strength (28-30). Moreover, research has demonstrated substantial increases in lean body mass (LBM) and strength with HMB supplementation, which is available commercially

in a free-acid (HMB-FA) and calcium form (HMB-Ca), during RT, suggesting a potency of HMB that is equivalent to, or greater than, leucine (28, 30). The purpose of Chapter one of this thesis is to discuss extant strategies to optimize RE-induced hypertrophy. To accomplish this objective, the review focuses on: 1) the manipulation of RE program variables purported to enhance gains in muscle mass and strength; 2) the notable benefits of a high leucine containing protein supplement to augment training-induced hypertrophy; and 3) the anabolic potency of the leucine metabolite HMB, and the use of HMB to enhance RT-induced hypertrophy.

## 1.1 Resistance Exercise

Resistance exercise (RE), defined as the purposeful loaded contractile activity of skeletal muscle (31), is leveraged in athletic and clinical populations to promote muscle hypertrophy and increase strength. The American College of Sports Medicine (ACSM) recommends that healthy adults engage in RE on a minimum of two days per week (32). The mechanisms that underpin the growth of skeletal muscle as a result of RE are now beginning to be understood and are briefly reviewed here.

### 1.1.1 Resistance Exercise and Muscle Protein Turnover

Skeletal muscle adaptations are specific to the modality of training (33). Briefly, aerobic stimuli, such as moderate-continuous endurance exercise, preferentially stimulates the synthesis of sarcoplasmic and mitochondrial proteins (i.e. those involved in energy flux) that enhance, in part, aerobic capacity (33). Additional adaptations resulting from aerobic exercise training include an increase in skeletal muscle capillary density, which results in a greater capacity to deliver oxygen and nutrients to skeletal muscle (33).

In contrast, mechanical loading of skeletal muscle results in a stimulation of synthesis and the subsequent disposition of primarily contractile proteins (i.e. actin and myosin) that in turn result in radial growth of muscle fibres and an increase muscle strength (34). In response to mechanical loading of skeletal muscle, there is an increase in muscle protein turnover because of a stimulation of MPS and MPB (8, 14). Phillips et al (8) observed that following a bout of RE in untrained (UT) men, MPS was significantly elevated by 112% at 3 hours, 65% at 24 hours, and 34% at 48 hours (8). Whereas MPB was elevated by 31% at 3 hours and 18% at 24 hours but returned to baseline levels by 48 hours (8). Thus, a bout of RE in UT persons induces a sustained increase in MPS (8). To assess protein turnover in response to RE in trained (TR) persons, Phillips et al (35) examined MPS and MPB 4 hours following RE in UT and TR men. The results showed that RE induced a significant increase in MPS in both UT and TR participants, whereas a significant increase in MPB was observed only in UT participants (35). This work was followed by a longitudinal study wherein UT participants trained a single leg for 8 weeks (6 x/week) while the non-exercised leg served as an internal control (36). It was observed that prior RT attenuated the RE-induced increase in MPS and increased muscle protein turnover at rest (36). These investigations did not differentiate between the myofibrillar, sarcoplasmic, and mitochondrial compartments (35, 36). Kim et al (37) examined mixed MPS and myofibrillar protein synthesis following RE in the UT and TR state. Eight UT men engaged in 8 weeks of unilateral RT and following RE, mixed MPS was stimulated in the UT leg, whereas myofibrillar protein synthesis was stimulated to a similar magnitude in the UT and TR leg (37). These data suggest that in the UT state RE induces

a global increase in all protein fractions (37). However, prior RT refines this response such that following a bout of RE there is an increased synthesis of contractile proteins (37). A RT program can be designed based on several variables including training intensity, load, and inter-set rest period (32). The influence of each of these variables on skeletal muscle adaptation is detailed below.

### 1.1.2 Lifting Intensity

A 1-repetition maximum (1-RM) strength test represents the maximum load an individual can lift in a single repetition (32). Training intensity can be defined as the percentage of 1-RM lifted during each set of an acute bout of RE, in which higher intensities correspond with heavier loads (38). In 1945, Delorme utilized a progressive RT program to increase muscle mass and strength in injured soldiers (39). He observed that heavier loads lifted for a smaller number of repetitions increased muscular strength, whereas he stated that lighter loads lifted for a higher number of repetitions would enhance muscular endurance (39). Since this time, few groups have questioned the notion that high-load, low repetition, training is the most effective strategy to enhance muscle size and strength.

A recent meta-analysis reported on the role of higher-load, lower repetition training vs. lower-load, higher repetition training on muscle strength and hypertrophy (40). Schoenfeld et al (40) concluded that low-load training is sufficient to increase mass and strength in UT persons. However, a trend was observed for greater hypertrophy and strength gains with high loads compared to low loads in TR persons (40). Findings from our laboratory have, however, challenged the view that performing RE at a high

percentage of 1-RM using higher loads is required to induce muscle hypertrophy and improvements in strength in TR participants (41). Morton et al (42) compared high-load, low repetition (75-90% 1-RM, 8-12 reps 3 sets) with low-load, high repetition (30-50% 1-RM, 20-25 reps, 3 sets) training during 12 weeks of whole body RT in young trained men. Both training schemes resulted in muscle hypertrophy with no difference between the loading schemes (42). Although, the strength gains increased in both groups, there was a significant difference between groups for bench press 1-RM. In line with these results, Ogasawara et al (43) observed comparable gains in upper body muscle hypertrophy, but differing gains in strength, following 6 weeks of high-versus low-load resistance training. Thus, there appears to be an influence of training intensity on muscle strength, such that the habitual practice of lifting heavier loads is necessary to stimulate greater strength gains, but this would appear to be a neurological- not a muscle size-based phenomenon (42, 43). The phenotypic changes observed at the whole muscle level with lower load RE are supported at a molecular level as well. Burd et al (44) examined the effect of RE intensity (90% 1-RM vs. 30% 1-RM) on MPS, and observed a similar increase in mixed and myoMPS 4 hrs following training in both groups (44). Interestingly, myofibrillar protein synthesis remained elevated at 24 hrs post-RE only in the 30% 1-RM group (44). Collectively, the extant literature does not support a superior role for higher intensity, higher load training compared to lower intensity, lower load training, at least in regard to muscle hypertrophy; however, there does appear to be an influence of higher loads on muscle strength (40, 42, 43). Thus, many strength coaches

encourage high-load, low repetition training to maximize strength gains (32), which also stimulates muscle growth.

### 1.1.3 Training volume

Training volume (usually expressed in total kg lifted/training session) is defined as the product of load (kg/rep), number of repetitions (rep/set), and number of sets (set/ training session) performed in a single RE session (32). A similar magnitude of training volume can be achieved with a high-load, low repetition or low-load, high repetition schema (45). It follows that weekly training volume increases in proportion to the number of training sessions completed per week, which usually differs based on the training history of the individual. The ACSM position stand recommends at least two days of recovery in UT persons and one day of rest in TR persons (32), who appear to experience comparably less muscle damage in response to each bout of RE (46). Muscle damage is a result of increased stress on each muscle fibre and is sustained for a longer period of time after a bout of unaccustomed RE (47, 48). A proxy marker of muscle damage is raised levels of creatine kinase (CK). This enzyme normally resides within the muscle cell but is released following RE as a result of a loss of membrane integrity (49). Muscle damage manifests as decreased force production, increased muscle soreness, and reduced range of motion (50).

In addition to rest duration *between* bouts of RE, sufficient recovery *within* a training session is important to limit fatigue and allow sustained performance on subsequent exercise sets (32, 51). To maintain muscular performance between sets, approximately 2-4 minutes of rest is recommended (32, 52). Insufficient rest (≤45

seconds) results in a failure to maintain the target repetitions per set when lifting heavy loads, and is thus thought to influence the progression of strength gains (32). If the trainee's goal is to increase muscle size, some have claimed that shorter rest periods are anabolic because they enhance muscle damage and result in increased concentration of purported anabolic hormones (53, 54). Despite data from a recent meta-analysis suggesting that longer rest periods are more advantageous in trained participants (52), the ACSM recommends moderate intensity loads (60-80% 1-RM) with shorter rest periods (1-2 min) for athletes with hypertrophy-centric training goals (32).

A common mode by which athletes manipulate training volume and work:rest ratios during training is to incorporate a period of 'overreaching' into their training programs (55). Overreaching describes a period of increased training volume combined with a planned reduction in rest and recovery and an accepted accompanying decline in performance (55). Overreaching requires significant monitoring because it temporarily blunts strength gains, can result in reduced performance, and is associated with an increased risk of injury (56). However, when followed by a period of adequate recovery and reduced training volume (i.e. a taper phase), an overreaching phase can elicit 'rebound supercompensated' gains in strength (55-57). Despite risks, periodic overreaching is a strategy frequently used by various athletes to allow peak performance for a competition (28, 55).

### 1.1.4 Periodization

In light of all the RT variables discussed, there is little agreement on the 'optimal' program to elicit muscle hypertrophy and strength development. The ACSM encourages

implementing periodized versus non-periodized RT training programs (32). Periodized training is the planned variation of training intensity, volume and rest with the goal of maximizing performance and minimizing injury (58, 59). During periodized training, manipulation of program variables can occur on a multi-monthly or Macro-cycle (6-9 months), a monthly or Meso-cycle (3-4 weeks) or a Micro-cycle (weekly/daily basis) (60). Non-periodized training, however, is not concerned with program variation and is performed in the absence of such rigorous planning. With regards to eliciting gains in muscle mass and strength, periodized training has been proposed as being superior to non-periodized RT (32, 59).

There are two forms of periodization: linear periodization and undulating periodization. Linear periodization begins with low-intensity, high volume training (60). In 3-4 week cycles, training intensity and volume are manipulated by increasing intensity (% 1-RM) and decreasing volume. In contrast, undulating periodized RT has no baseline requirement of low-intensity, high volume training (61). Rather, undulating periodized RT is characterized by frequent alterations in intensity and volume within a micro cycle (58). The frequent manipulation of training variables is thought to facilitate progressive adaptations in muscle mass and strength (62). In addition to variations on a weekly basis, daily undulating periodized training results in the greatest alterations in volume and intensity between successive training sessions within the same week (60, 61). At present, there is little consensus as to which type of training - linear periodization, undulating periodization or daily undulating periodization - elicits the greatest hypertrophy and strength gains (63).

### 1.1.5 Hormonal milieu

Hormones, such as testosterone and growth hormone, are regulatory signalling molecules secreted from organs distinct from their target and requiring transport via the blood to target tissues. Hormones play a role in the development of secondary sex characteristics (i.e., estrogen and testosterone) during adolescence or mediate growth during developmental years (i.e., growth hormone). An intense bout of RE elicits increases in serum growth hormone (GH), insulin-like growth hormone (IGF1) and testosterone concentrations (53, 54). The increased hormone concentration following RE has led some to theorize that hormones contribute to RE-induced skeletal muscle hypertrophy (53, 54, 64). Evidence to support the claim that hormones are stimulatory for muscle growth primarily comes, however, from clinical scenarios examining the anabolic effects of exogenous administration of testosterone in healthy and hypogonadal individuals (65). For instance, supraphysiological doses of testosterone have been shown to increase skeletal muscle mass, fibre cross-sectional area and strength (65, 66). At present, the ACSM position stand states that training programs that maximize anabolic hormone secretion enhance muscle hypertrophy (32). As such, the ACSM encourages performance of compound, multi-joint lifts, performed at moderate intensity (~60% 1-RM) with short rest interspersed between sets (32). While anabolism and growth induced by supraphysiological doses of testosterone (65) and growth hormone (66) are not

contested, the role played by 'anabolic hormones' in the adaptations to RE have been challenged (67, 68).

Our laboratory has performed a series of studies that collectively cast substantial doubt on any significant role of exercise-induced hormone secretion in muscle hypertrophy and strength improvement (42, 67, 69). To investigate the role of RE-induced hormones on MPS, West et al (67) had UT participants perform bicep curls in the presence or absence of elevated anabolic hormones. The hormonal milieu was manipulated by performing lower limb exercises prior to upper body training. West et al (67) observed that RE-induced hormones did not enhance fed-state anabolic signaling or myofibrillar protein synthesis. The same group utilized a similar protocol to examine whether anabolic hormones resulted in differential hypertrophy following 15 weeks of RT (68). Despite an increase in hormone availability during RE, there was no difference in strength gains or muscle mass accretion between groups. More recently, Morton et al (42) observed no significant relationships between the acute post-exercise rise in purported anabolic hormones and gains in muscle mass and strength after 12 weeks of RT in TR men. Collectively, these data suggest that there is little effect of anabolic hormones on muscle hypertrophy in either UT or TR participants. Given these data (42, 67, 68), skeletal muscle adaptation is thought to be due to factors intrinsic to the muscle (i.e. signaling induced by contraction and loading) rather than extrinsic variables, such as anabolic hormones (70).

1.1.6 Resistance training program variables to optimize RE-induced hypertrophy

Regardless of a subjects' training status, program variables manipulated, and concentration of anabolic hormones, RE is a potent stimulus to skeletal MPS and ultimately leads to hypertrophy. RE leads to increased MPS and the intracellular utilization of amino acids for incorporation into protein (8). In the absence of exogenous amino acids, an increase in MPB ensues to replenish amino acids within the intracellular pool (7, 8, 14). However, in the presence of exogenous amino acids, MPB is attenuated and MPS predominates, such that protein balance is positive (7). The ingestion of protein is therefore required following RE to achieve a net positive protein balance (7).

1.2 Dietary protein

Skeletal muscle is the largest labile reservoir of amino acids (AA) in the body that can be liberated in times of need (i.e. fasting, disease, or malnutrition). Proteins are composed of twenty amino acids, nine of which are essential and must be consumed in the diet. In 1982, Professor Michael Rennie and colleagues observed positive whole-body protein balance following ingestion of protein, indicating a net retention of protein (10), which was attributed to a large increase in skeletal MPS (10). Bohe et al (11) confirmed this hypothesis by measuring the incorporation of an isotopically-labelled tracer into skeletal muscle following amino acid infusion. The researchers discovered a ~2.8 fold elevation of MPS compared to rest at 2 hours post infusion but, interestingly, MPS rates quickly returned to basal levels thereafter, despite continued hyperaminoacidemia (11). These data suggest that AA are themselves potent stimulators of MPS, but that the MPS response to their elevation is transient (11). This phenomenon has been termed the

'muscle full' effect and has been further characterized (71, 72). Thus, simply ingesting protein in isolation will not induce muscle hypertrophy.

While ingestion of protein or infusion of AA stimulates MPS at rest, the infusion of AA following RE, results in a large and sustained increase in MPS (7). Thus, following RE, infusion of AA is sufficient to induce a positive protein balance (7). To determine if oral supplementation of AA could enhance post-exercise MPS, Tipton et al (17) fed participants 40 g of essential AA (EAA) or a mixed AA supplement (EAA+non-EAA). It was hypothesized that skeletal MPS in response to an oral dose of amino acids was driven primarily by EAA (17). This investigation showed no difference in MPS and it was proposed that the amount of EAA in the mixed supplement (21 g) exceeded the maximal dose required to stimulate MPS (17, 73). When, however, a relatively small dose of EAA (6 g) (73) was compared to a mixed supplement (3 g EAA + 3 g non-EAA) the anabolic effect of EAA would be more pronounced (74). Borsheim et al (75) observed that 6 g of EAA increased net protein balance to a greater extent than previously published data examining the anabolic effects of a mixed drink (3 g EAA + 3 g non-EAA (74). These authors suggested a dose response of EAA in skeletal muscle and that non-EAA contribute little to the stimulation of MPS (75). As a result of the anabolic influence of EAA on protein turnover, this group, and others advocate for the inclusion of EAA into nutrient beverages (73-75).

Although supplementation with EAA can stimulate MPS at rest or following RE, a full complement of amino acids is required to synthesize proteins. Intact proteins that contain all EAA and non-EAA, such as animal and milk proteins, are considered high

quality. Wilkinson et al (76) examined the ingestion of fluid low fat milk compared to an isonitrogrenous isoenergetic soy beverage and demonstrated that milk proteins enhance MPS to a greater extent than soy proteins (76). The acute results observed by Wilkinson (76) were then followed up with a training study and found to be concordant over a 12-week period in which Hartman et al (77) demonstrated superior gains in LBM and type 2 fibre CSA with the consumption of milk versus soy proteins (77).

### 1.2.1 Protein source

Protein digestion is initiated in the stomach, whereas absorption of free amino acids occurs primarily in the small intestine (19). In a recent investigation, Groen et al (78) demonstrated that 45% of intrinsically-labelled amino acids were absorbed by the splanchnic tissues. Of the 55% available in the peripheral circulation, only 11% of amino acids were used for de novo protein synthesis by skeletal muscle (78, 79).

The speed of amino acid absorption can influence postprandial metabolic responses (19). Bovine milk-derived protein, for example, is composed of two fractions: whey protein which is rapidly digested and, casein protein which clots in the stomach and is slowly digested (19). Tipton et al (20) examined the acute response of muscle protein balance to whey and casein protein following RE. Participants ingested placebo, 20 g whey, or 20 g casein protein one hour following RE (20). Plasma leucine peaked significantly faster after ingesting whey protein, however both protein sources induced a comparable net protein balance. This work was followed by a study from Tang et al (80) who examined the acute MPS response to whey, casein and soy proteins at rest and following RE. MPS was elevated to a greater extent with whey protein at rest (93%

greater than casein), and following RE (122% greater than casein) (80). These data support the utility of whey protein to enhance RE-induced anabolism acutely and over the longer term (81, 82).

### 1.2.2 Protein dose

In addition to the contribution of protein source to muscle anabolism, protein dose must also be considered. Cuthbertson et al (83) observed a curvilinear saturable dose response of MPS to the ingestion of EAA such that 10 g (~20g of protein) was sufficient to maximally stimulate MPS at rest in young men with no further stimulation beyond that dose. The increase in MPS with EAA is independent of insulin or IGF-1 and is mediated by mTORC1 associated translation initiation and elongation (84). Moore et al (85) examined the MPS response to intact protein at varying doses following RE. Healthy young males ingested 5, 10, 20 and 40 g of egg protein. The authors observed that 20 g of protein was sufficient to maximally stimulate MPS and intake ≥ 20 g resulted in elevated leucine oxidation (85). Witard et al (21) utilized a similar protocol to examine a dose response of myofibrillar protein synthesis to graded intakes of whey protein. In support of the findings of Moore and colleagues (85), the authors demonstrated that 20 g of whey protein maximally stimulated myofibrillar protein synthesis (21). It is therefore well-accepted that ~20 g of high quality protein, which equates to a per meal dose of ~0.25-0.3 g/kg, is sufficient to enhance RE-induced anabolism (21, 85, 86).

Although all EAA and non-EAA are required to synthesis proteins, protein synthetic machinery can be stimulated by an isolated amino acid. Leucine is a branched-

chain amino acid (BCAA) now thought to be the primary EAA in protein that stimulates skeletal muscle growth processes (24, 25, 74, 87, 88). Preclinical models identified that the ingestion or infusion of leucine alone can independently stimulate mTORC1, which is a key protein kinase that activates MPS (24-26, 87, 88). Ingestion of leucine alone or enriched in an EAA and carbohydrate supplement also stimulates mTORC1 and MPS in humans (84, 89). Fujita et al (84) observed a 94% increase in the rate of MPS following the ingestion of a leucine-rich EAA- and carbohydrate-containing supplement. Of note, ingestion of the same leucine-EAA supplement following RE induced a greater magnitude of MPS (145%) and mTORC1 signaling (89). It is clear that leucine alone or in combination with other nutrients contributes to the anabolism of a nutrient drink consumed following RE (84, 89, 90). Recently, it was shown that a suboptimal dose (i.e., lower than previously shown to be maximally effective in stimulating MPS) of whey protein (6.25 g) enriched with leucine (3 g) stimulated MPS to a similar extent as an optimal dose of whey protein (25 g) (23). Nonetheless, Churchvard-Venne et al (23) demonstrated that an optimal dose of whey protein sustained post-exercise MPS for a longer duration, and may be better suited to increase exercise-induced muscle mass accretion. Although, enriching a suboptimal dose of whey protein with leucine is effective (23), a near optimal dose (16.6 g) of whey protein enriched with leucine (3.4 g) provided little additional stimulation of MPS indicating there is a maximal upper limit to AA-induced stimulation of anabolism (91)

1.3 Beta-hydroxy beta-methylbutyrate (HMB)

Of all AA, leucine is characterized by its ability to enhance muscle anabolism by binding to a protein called sestrin2 that subsequently results in the activation of mTORC1 (92) and MPS (23-26, 84, 87). Research has led to an interest in a metabolite of leucine, beta-hydroxy beta-methylbutyrate (HMB) (2, 3), demonstrated to enhance anabolism in animals and humans. In human skeletal muscle, leucine undergoes rapid but reversible transamination to its keto-acid, α-ketoisocaproate (α-KIC), that is catalyzed by branched chain amino acid transferase. The α-KIC is in rapid equilibrium across the muscle membrane and so its concentration is elevated with leucine ingestion. It is estimated that 5-10% of α-KIC is metabolized in the liver by the hepatocyte cytosolic enzyme KIC

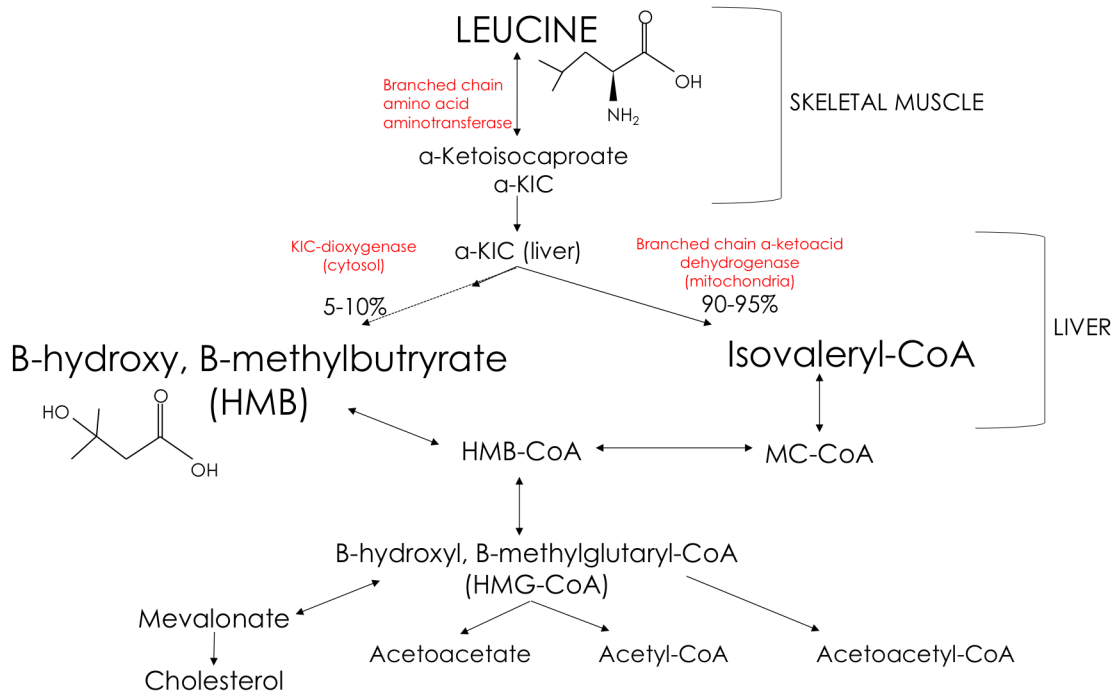


**Figure 1.** Leucine metabolism to HMB (2, 3)

dioxygenase generating HMB (2, 3); however, humans have a very low activity of the dioxygenase enzyme (3).

Endogenous HMB derived from leucine is converted to beta-hydroxyl, beta-methylglutaryl CoA (HMG-CoA) and serves as a precursor for cholesterol synthesis (Figure 1) (3). The endogenous cholesterol synthesis from HMB is proposed to contribute to the anti-catabolic effects of HMB. HMB supplementation may contribute to enhanced membrane integrity and repair with a reduction in subsequent reduction in exercise induced muscle damage (3).

In addition, as a leucine metabolite, HMB is claimed to be anabolic, but the low endogenous production of HMB, 2-5% of leucine in ruminants and fowl (2) and 0.7% of leucine in humans (93), has led to investigation of HMB supplementation (94). Preclinical models, have demonstrated that HMB attenuates suppression of protein synthesis induced by cachectic stimuli (95-97). As such, the first investigation of HMB supplementation in humans, Nissen et al (94), hypothesized that HMB supplementation would decrease RE-induced proteolysis. Support for such a thesis comes from a study of 41 participants that engaged in 3 weeks of RT who were supplemented with 0 g/d (placebo), 1.5 g/d or 3 g/d of HMB. In those ingesting HMB there was an decrease in urinary 3-methylhistidine (an indirect marker of myofibrillar proteolysis) and reduced blood CK activity during RT (94). These authors concluded that HMB suppressed muscle myofibrillar proteolysis and attenuated RE-induced muscle damage (94). Recently, a direct assessment of MPB was used to investigate the role of HMB in muscle protein turnover in humans. Wilkinson et al (1) provided 3.42 g of HMB-FA or 3.42 g of leucine to 8 young men and found that

ingestion of HMB attenuated MPB by 57% (1) (Figure 2B). However, the ability of leucine to attenuate MPB was not tested and it could not be deduced whether or not HMB was superior to leucine in this regard (1). However, leucine is an insulinogenic AA and so ingestion of leucine resulted in a relative hyperinsulinemia (1), to which proteolysis is remarkably sensitive (98). To provide mechanistic insight into the changes observed, Wilkinson et al (1) monitored the gene expression of proteolytic components – MuRF1, Mafbx, Beclin 1, Cathepsin L and Calpain 1 – at different times throughout their investigation.

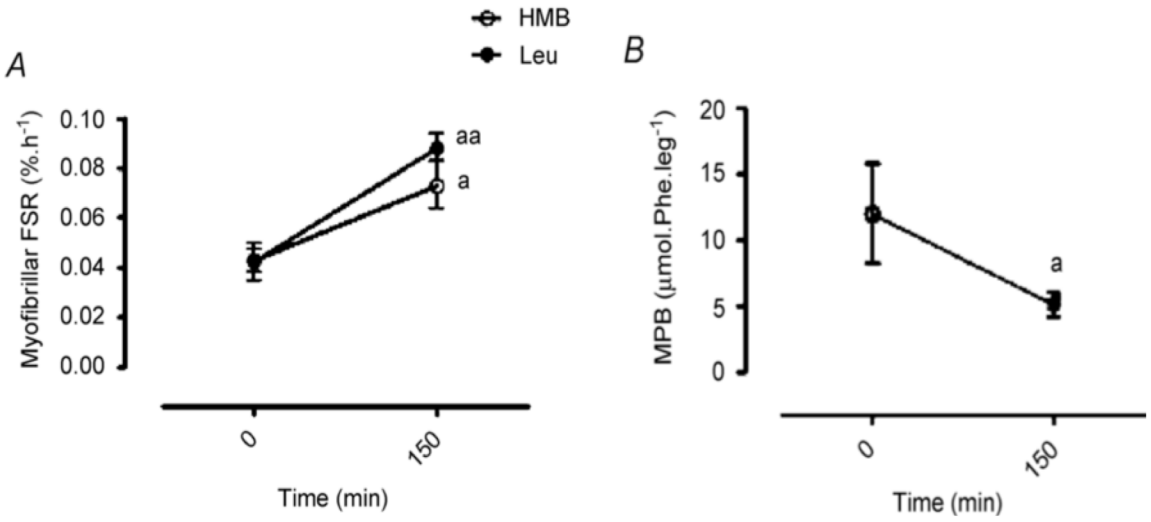


**Figure 2 A.** Myofibrillar MPS **(A)** and MPB **(B)** following oral ingestion of 3.42 g HMB-FA and 3.42 g leucine (A- only) in young healthy men. From Wilkinson et al (1)

Surprisingly, they failed to detect any changes in these gene targets with the ingestion of HMB (1). Thus, although limited data exists to substantiate the claims that HMB prevents increments in MPB (1), future research is required to examine the time course of these effects. In addition to its anti-catabolic effects, HMB is also a purported anabolic

compound (28, 30, 94, 99-102). Early work in chickens and pigs demonstrated that HMB increased body mass, lean mass and improved immune function (103-105). Thus, Nissen et al (94) examined the effects of HMB on RT-induced hypertrophy in humans and observed a trend for a dose response of HMB supplementation on lean mass ($p<0.1$) (94). In Study 2, from the same manuscript (94), 37 trained participants consumed CHO or 75 g of protein + 3 g of HMB during 7 weeks of RT. Nissen et al (94) observed slight increases in upper body strength with no pre-post changes in lean body mass. The contribution of HMB to the gains in strength could not be parsed out from this trial (94), since the supplement contained far more protein than what is required to maximally stimulate MPS (106). To separate the influence of protein and HMB, Kreider et al (107) utilized a similar supplementation regime, but provided 28 participants with a nutrient powder (75 g of protein) or the nutrient powder+HMB (75 g protein+ 3 g HMB). Contrary to Nissen (94), the authors reported no differences in mass and strength between groups. Other groups have since examined the utility of HMB to enhance RT-induced hypertrophy with conflicting results (107-111).

Thomson et al (112) reported a 'trivial' (the term applied using magnitude-based inferential statistics used in their analysis) increase in average strength (1.6%) and a negligible effect on body composition (112) after 9 weeks of 3 g of HMB-Ca supplementation in RT men. An international position stand stated that the ability of HMB to enhance RT-induced hypertrophy is dependent on the interaction between the athletes training status (UT or TR) and the rigor of the training program (102). It is suggested that HMB is able to enhance recovery after RE by reducing muscle damage

(102). In the UT state, muscle damage following a bout of RT is high because of the unaccustomed training stimulus (47, 113). For this reason, it is claimed that HMB supplementation in UT persons can attenuate RT-induced muscle damage (102). In TR persons, however, the RT program must be of sufficient intensity to induce muscle damage upon which HMB can be maximally effective (47, 113), such as a supervised periodized RT program for ≥ 6 weeks (102). It has been suggested that the failure of previous investigations (107, 108, 112) to employ a supervised, periodized RT program ≥ 6 weeks in TR participants may explain the inconsistency of RT-induced hypertrophy with HMB (102). The difference in results between studies may also be related to the form in which HMB is delivered.

HMB is available in two forms: a calcium-bound form (HMB-Ca) and a free-acid-bound form (HMB-FA). Fuller et al (114) examined the plasma appearance and retention of HMB-Ca vs. HMB-FA. It was observed that HMB-FA resulted in rapid time to peak plasma concentration (30 vs. 120 mins) two times greater in magnitude than HMB-Ca (114). This improved bioavailability of HMB-FA has led some to claim that HMB-FA is more anabolic than HMB-Ca (28, 30, 102). Recently however, Wilkinson et al (1) examined the effect of HMB-FA supplementation on muscle anabolism in humans. HMB-FA and leucine stimulated MPS (70% and 110%, respectively, Figure 2A), and increased mTORC1 and p70S6K signaling to a similar extent. In a similar investigation, Wilkinson et al (27) demonstrated that 3 g of HMB-Ca increased MPS to a similar extent as HMB-FA. Thus, despite differing bioavailability, there is no apparent difference in the acute stimulation of MPS to either HMB-FA or HMB-Ca (1, 27).

Despite similar anabolic effects, at least based on acute MPS results, induced by HMB-Ca or HMB-FA (1, 27), recent investigations have developed a training regime and supplementation protocol purported to maximize the efficacy of HMB supplementation in TR participants. Wilson et al (28) provided 3 g of HMB-FA to TR participants during 12 weeks of a daily undulating periodized RT program. A single bout of RE from this protocol was demonstrated to increase muscle damage and anabolic hormones in TR men (115). Therefore, this design would ensure that TR participants achieve a potent stimulus to induce muscle damage upon which supplementation with HMB-FA would be maximally effective (28, 102). Wilson et al (28) observed substantial increases in LBM compared to a corn syrup-based placebo. However, the increases in mass and strength observed by Wilson et al (28) are difficult to reconcile with extant published reports of what is typical of RT-induced hypertrophy. For instance, a recent meta-analysis from our laboratory (116) showed that, in young participants (<35y; n=624) engaging in ~12 weeks of RT, gains in LBM averaged 1.2 ± 1.1 kg and protein supplementation resulted in only an additional 0.4 kg increase (116). The gains in fat- and bone-free mass (FBFM, often referred to as LBM) reported by Wilson et al (28) amounted to 7.4 kg, which is significantly (6.1 – 4.6-fold) greater than reports from our recent meta-analysis (1.2-1.6 kg) (116). Despite substantial criticism (117, 118), Lowery et al (30) examined 3 g of HMB-FA + 400 mg ATP during 12 weeks of the same RT program in TR participants and observed an 8.5 kg increase in FBFM. The results from both trials were attributed to the efficacy of the training protocol to maximize the anabolic potential of HMB-FA (28, 30). However, the form of HMB likely contributed little to the gains in lean mass reported

in Wilson et al (28) and Lowery et al (30) and the results they report simply seem implausible. Similar, to previous reports (28, 30), Kraemer et al (100) provided TR participants with HMB-Ca combined with other nutrients and observed even greater gains in lean mass (~9 kg) during RT in young men. Although data exist supporting substantial anabolic properties of HMB-FA and HMB-Ca (1, 27), the gains reported in these trials (28, 30, 100) greatly exceed that what is typical of RT-induced hypertrophy (31).

To gain a greater understanding of the LBM accretion typically observed following HMB supplementation during RT, a meta-analysis was performed with the aim of examining the efficacy of HMB-Ca and HMB-FA supplementation to augment skeletal muscle mass and strength with training in older and younger adults. A systematic search of Medline, Embase, CINAHK and SportDiscus, from 1996-November 2017 comprised the meta-analysis. All articles met the following eligibility criteria 1) randomized controlled trial (RCT), with resistance exercise training or sprint/high intensity interval training ≥ 3 weeks (training sessions at least 2 x/week) and 2) supplementation with β-hydroxy, β-methylbutyrate (HMB) in the calcium (HMB-Ca) or free acid form (HMB-FA) with or without protein or amino acids. Random-effects meta-analyses were performed in RevMan (Review Manager (RevMan), V.5.3 Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014). The present meta-analysis included 8 studies that fit our inclusion criteria, for which data were available or provided on request, and subject to risk of bias assessment. A total of 269 participants were included, and the mean study duration was 9 ± 6 weeks with a training frequency of 3 ± 1

days/week. Data from 5/8 studies included trained participants. Data from 7/8 studies supplemented with HMB-Ca (3 g/d) and 1/8 with HMB-FA (3 g/d).

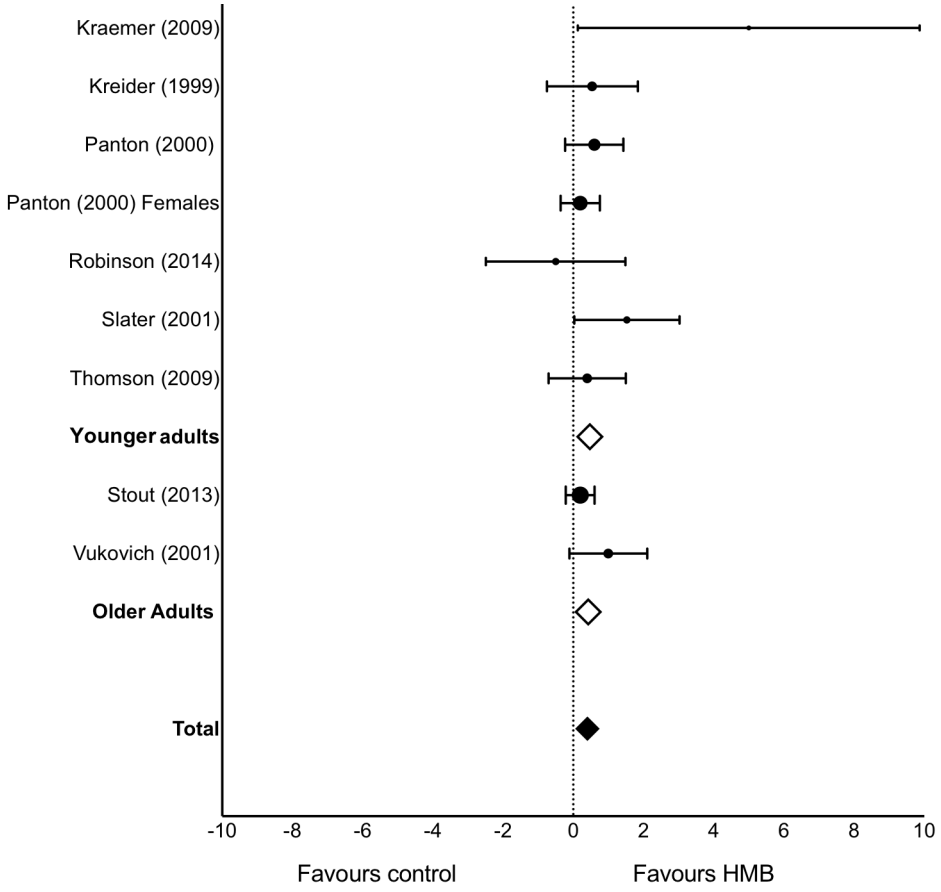


**Figure 3.** Forest plot of the results from a random-effects meta-analysis shown as mean difference with 95% CIs on changes in lean mass (kg) in younger and older participants. For each study, the circle represents the mean difference of the intervention effect with the horizontal line intersecting it as the lower and upper limits of the 95% CI. The size of each circle is indicative of the relative weight that study carried in the meta-analysis. The rhombi represent the weighted younger, older and total group's mean difference. Older adults n=67: z=1.18, 0.43 kg (-0.28,1.13) p=0.24. Younger adults n=202; z=2.04, 0.47 kg (0.02, 0.93), p=0.04). Total: n=269, z=2.51, 0.40 kg (0.09, 0.72), p=0.01.

The meta-analysis demonstrated that HMB-FA and HMB-Ca did not significantly influence RT-induced gains in total body mass, 0.43 kg (95% confidence interval [CI]: -0.22, 1.08; p=0.19), fat mass, -0.01 kg (95% CI: -0.49, 0.47; p=0.97), or 1-RM strength (upper and lower body), 1.76 kg (95% CI: -0.72, 4.25; p=0.16), during resistance training compared to placebo. HMB-Ca and HMB-FA augmented resistance training-induced gains in LBM by 0.40 kg (95% CI: 0.09, 0.72; p=0.01, Figure 3).

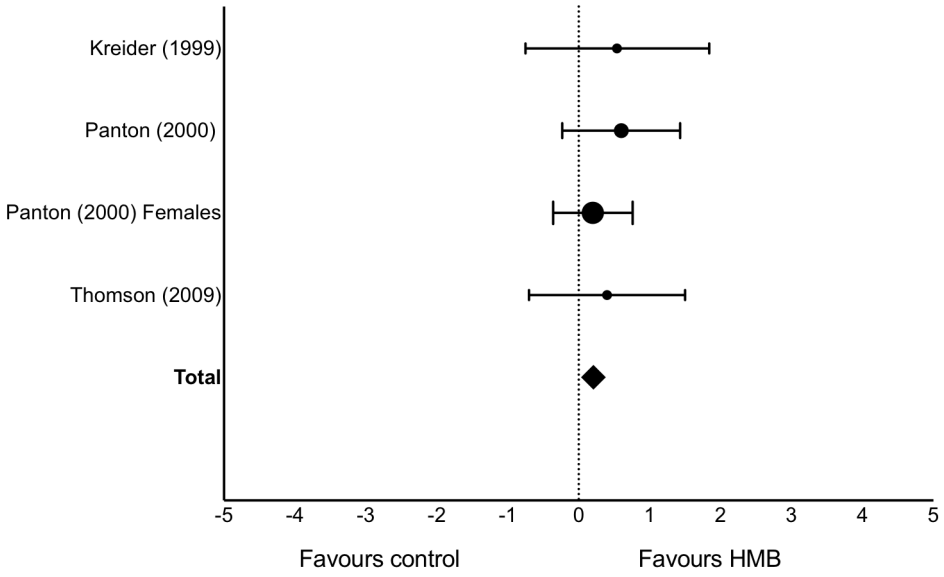


**Figure 4.** Forest plot of the results from a random-effects meta-analysis shown as mean difference with 95% CIs on Lean mass (kg) in younger and older participants. Studies with ≥ 2 criteria of unclear/high risk of bias removed from the analysis. Total: n=137, z=1.72, 0.36 kg (-0.05, 0.76), p=0.09.

However, when studies (5 of 8) containing an unclear/high risk of bias on ≥2 categories (specified in RevMan) were removed, the effect of HMB was no longer significant 0.36 kg (95% CI: -0.05, 0.76, p=0.09, Figure 4). This meta-analysis demonstrated that supplementation with HMB-FA or HMB-Ca had no effects on RT-induced gains in total body mass, fat mass or 1-RM strength. The limited number of high quality trials investigating HMB-Ca and HMB-FA complicates the ability to draw conclusions in regard to the effectiveness of the supplement on lean mass. There may be a small effect of HMB to enhance RT-induced gains in LBM, however, a number of trials investigating HMB showed a high risk of bias. Our conclusions are supported by other meta-analyses which reported little or no effect of HMB on LBM gains during RT in TR participants (112).

1.4 Statement of the problem and hypotheses

Based on examination of our own meta-analysis and others (112), we are unable to explain the large gains in LBM reported by Kraemer et al (100), Wilson et al (28) and Lowery et al

(30) that

were ~9 kg,

7.4 kg and 8.5 kg (all in 12 weeks of RT), respectively. In previous investigations (28, 30), the placebo comparator to HMB-FA was simply carbohydrate. In one investigation, the HMB supplement also contained other ingredients (arginine, glutamine, taurine and dextrose) while the placebo was simply maltodextrin (100). A more ecologically valid study rather than a comparison of HMB to placebo would incorporate normal practices of

resistance trainees known to be efficacious. Given the knowledge of the beneficial effect that protein (116) and leucine (see section 1.2.1 above) have on hypertrophy and stimulation of MPS combined with the fact that protein supplements are a frequent choice of resistance trainees (119, 120), future research is needed that directly compares the anabolic influence of HMB with protein against protein with equivalent quantities of leucine. Such a comparison would result in generation of new knowledge as to whether HMB is truly more anabolic than its parent metabolite, leucine.

The overarching aim of the study comprising my thesis was to conduct a randomized, double-blind, pragmatic trial comparing the ingestion of whey protein with HMB-Ca, as this form of the supplement was previously reported to result in the greatest gains in FBFM (100), versus whey protein plus the parent compound of HMB, leucine. We assessed muscle hypertrophy using multiple indices, and strength via one repetition-maximum (1-RM), utilizing a highly effective program of undulating periodized RT in young relatively trained men (28, 30). In line with previous investigations (28, 30), we hypothesized that whey protein enriched with HMB would elicit substantially superior gains in lean mass and strength compared to whey protein enriched with leucine.

# CHAPTER 2: MANUSCRIPT

## Equivalent hypertrophy and strength gains in HMB or leucine supplemented men

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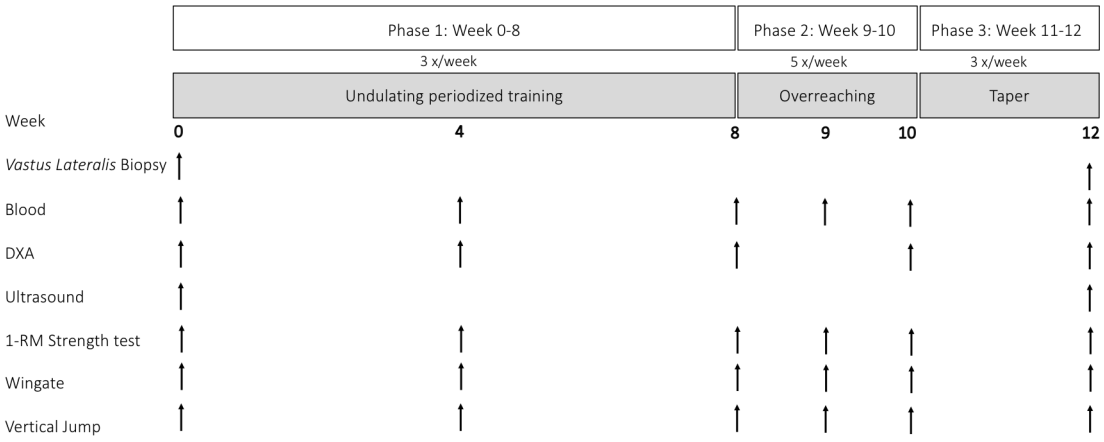
## 2.1 Methods

### 2. 1.1 Study Design

A schematic overview of the study design is shown in (Figure 5). We employed a randomized, double-blind repeated measures design. A third, independent party performed the randomization and codes were not revealed to study personel or participants until all data had been analyzed. Participants were randomized, according to a list generated at randomize.com, with block sizes varying from 2-6 matched for baseline FBFM, to ingest: whey protein (25 g) plus HMB (1.5 g) (Whey+HMB; n=13) or whey protein (25 g) enriched with an equivalent mass of leucine (1.5 g) (Whey+Leu; n=13), twice daily during a 12-week, 3-phase RT program as described extensively previously (28, 30, 100). The RT program was selected as it has been demonstrated to elicit muscle damage in trained participants upon which HMB is maximally effective (28-30, 100). Briefly, phase 1 was 8 weeks of undulating periodized RT thrice weekly; phase 2 was an overreaching phase (5 weekly training sessions); followed by phase 3, which was a two-week taper (3 sessions/week). Body composition and 1-RM strength tests were performed at baseline, weeks 4, 8, 9, 10, and upon completion of the RT program (week 12) as illustrated in Figure

5. Supplements were prepared by Infinit Nutrition (Windsor, ON, Canada) matched for flavor (citrus) and consistency and were in powder form, which dissolved freely into 250




mL of water. A sample of the supplement was analyzed using documented ISO17025 accredited LGC (LGC, Queens Road, Teddington, Middlesex, TW11 0LY, UK) methods for the compounds specified within the Service Level Agreement: Nutritional Supplements V2.0. Results, GCMS: None were found, LCMS: None were found. LGC Reference: 204545. On training days, supplements were consumed following training and prior to sleep. On non-training days, supplements were consumed in the morning and prior to sleep.

2.1.2 Familiarization and 1-RM strength testing

One week prior to the start of the training program participants attended a familiarization session at a research dedicated training facility located within McMaster University, and ≥ 72 hours later (42), a 1-RM strength test for squat, bench press and deadlift. The 1-RM tests were performed in the same order: squat, bench press and deadlift and followed strict guidelines as established by the National Strength and

**Figure 5.** Schematic representation of Study design

Conditioning Association (NSCA). One investigator conducted all strength tests. Strength tests began with a 5-min warm-up on a cycle ergometer, that was followed by 5-8 repetitions at 50%, followed by 3-5 repetitions at 75% of the predicted 1-RM load. Following 5 mins of seated rest the 1-RM load was increased by 10-20 % until 1-RM was achieved. Participants had their form critiqued and adjusted if necessary by qualified personal trainers. Total 1-RM strength was calculated as the sum of mass lifted (kilograms, kg) for 1-RM of squat, bench press and deadlift.

2.1.3 Dietary Records

Protein intake was assessed at weeks 0, 8, and 12, using a 3-day food diary (2 weekdays, 1 weekend day), and was analyzed using the NutriBase dietary analysis software (Nutribase11 Professional Edition, version 11.5, Cybersoft Inc., Phoenix, AZ, USA). Food diaries were completed on both training and non-training days.

2.1.4 Resistance Training Intervention

Replicating a program described extensively elsewhere, (28, 30, 100), participants engaged in a supervised 3-Phase RT program. Our program followed this program exactly with participants performing: Squat, bench press, deadlifts, dumbbell shoulder press, pull-ups/dips, bent over row, biceps curls/lying triceps extensions, with leg press and close-grip bench press performed in weeks 9 and 10. Loads were decreased (5-10%) between sets to ensure participants achieved the prescribed repetition ranges.

2.1.5 Body composition

Body composition was assessed using dual- energy x-ray absorptiometry (DXA; GE Lunar iDXA total body scanner, GE Medical Systems, Madison, WI, USA) between

06:00-09:00 following a ≥10 hour fast and after participants had voided their bladders. Participants refrained from physical activity for ≥24 hours except during Phase 2 (training 5 x/week). Scans were performed and analyzed with software in the medium scan mode. Total body water was assessed using a Bioelectrical impedance analysis (BIA, BIA-101A; RJL Systems, Mt. Ckemens, MI). All body composition assessments were performed by the same technician to minimize variability. Based on scans of a whole-body phantom (Oscar Jr. Orthometrix, Naples, FL), intra-assay coefficient of variation (CV) of this scanner for FBFM (i.e., the body compartment of interest) is 1.2% and less than 1.7% on inter-assay 12 wks apart.

2.1.6. Ultrasound Muscle thickness and Cross-sectional area

Muscle thickness (MT) of the *vastus lateralis* was assessed by the same investigator using a B-mode ultrasound (Vivid q; GE Medical Systems, Horten, Norway) and a 50 mm, 12.5 linear-array probe. Ultrasound assessments were performed fasted and at the same time as the body composition testing. Participants laid supine for 10 mins with their right leg in full extension in a custom mount. Thickness was assessed at fifty percent of the distance between the greater trochanter and the lateral epicondyle of the knee (121). Tracing paper was used to record the reference point and the probe was placed transversally on the leg. An experienced investigator used water-based gel to ensure good acoustic contact and applied no pressure to the skin to rule out tissue compression as a potential confounding influence (122). A second investigator ensured the images were clear and possessed identifiable superficial/deep aponeurosis and the MT image was stored. To assess muscle cross-sectional area (CSA) sequential images starting

at the border of the *rectus femoris* to the border of the *biceps femoris* in the frontal plane were captured resulting in a total of ~8-10 images of the *vastus lateralis* (123). Images were stored using Echo-PAC, PC Version 110.0.2 (GE Medical Systems, Horten, Norway) and converted from DICOM to JPEG using Sante DICOM Editor (Version 3.1.20; Santesoft Athens, Greece). The MT images were analyzed using AMS II (Version 1.141; Gothenburg, Sweden) at the widest distance between the narrow and deep aponeurosis. Each image was reviewed, and manual corrections were made, if necessary, the algorithm redirected the borders to asssses the thickness accurately (124). The same investigator performed the MT analysis on AMS II software on two separate occasions (intra-class correlation coefficient = 0.96). The muscle CSA images were stitched together using GIMP (GNU Image manipulation program 2.8.22, Creative Common, Mountain View, CA, USA) by aligning the superficial and deep aponeuroses. The muscle CSA was measured using computerized planimetry (i.e., *vastus lateralis* muscle CSA was manually contoured with an 800-dpi mouse) (Madena 3.2.5, EyePhysics, Los Paladinos, USA). The planimetry software was calibrated with fixed distance scales displayed in the ultrasound images. The ultrasound-based technique for determination of muscle CSA has recently been validated against magnetic resonance imaging (123). The stitched images were downloaded to ImageJ and manually traced to encompass the entire *vastus lateralis.* Conversion factor of 69 pixels per cm was used to calculate CSA in $cm^2$. Two experienced investigators performed the analysis with an interclass correlation of 0.97.

2.1.7. Power testing

*Wingate.* Participants performed a 2-minute warm-up (50 watts, W) on an electronically braked cycle ergometer (Veletron, RacerMate, Seattle, WA, USA). Participants were instructed to pedal as fast as possible against the ergometers initial resistance for approximately 2 seconds before the appropriate load was applied by a computer interfaced with the ergometer (Wingate software version 1.11, Lode). Similar to previous investigations (125), a 30-second "all out" effort against a resistance equivalent to 0.075 kg/kg body mass was completed. The total body mass used for all power assessments was derived from the DXA. Participants were verbally encouraged throughout the test. Research assistants were trained at the same time and provided with a standardized set of verbal cues to encourage participants. Peak power, mean power and fatigue index were recorded. Participants then engaged in a 5-minute dynamic cool down.

*OptoJump*. Measurements of specific power (W/kg) were made using OptoJump (Microgate, Via Antonio Stradivari, Italy) and analyzed using OptoJump Next systems software (Microgate, Via Antonio Stradivari, Italy). Participants performed one practice countermovement jump to ensure correct form and completed three countermovement jumps. Data were averaged as specific power (W/kg).

2.1.8 Muscle Fiber and Cross-sectional area

Participants arrived overnight fasted and 72 h after their last training session for a muscle biopsy. Muscle biopsies were obtained at baseline and post-training from the *vastus lateralis.* Muscle biopsies were performed under local anesthesia (2% xylocaine) using a 5-mm Bergstom needle that was modified for manual section. Upon excision, the sample was cleared of connective tissue and fat and was oriented longitudinally before

being embedded in an optimal cutting temperature medium. The mounted sample was frozen in liquid isopentane, cooled by liquid nitrogen and stored at -80°C for analysis. Cross sections (7 μm thick) were cut on a Microm HM550 Cryostat (Thermo Fisher scientific, Waltham, MA, USA), mounted on glass slides and stained. Fiber type and CSA were assessed via immunofluorescent staining of myosin heavy chain (MHC) isoforms and dystrophin as previously described (126). Primary antibodies against MHC1 (BA-F8), MHC11A (SC-71), MHC11X (6H1) and dystrophin (MANDYs; Developmental Studies Hybridoma Bank, Iowa City, IA, USA) followed by isotope-specific fluorescent secondary antibodies for the identification of Type I, Type I /Type IIA, Type IIA, Type IIA/X and Type IIX fibers. Slides were mounted with Prolong Diamond Antifade Reagent (Life Technologies, Burlington, ON, CAN) and imaged the next day. Images were obtained with a Nikon Eclipse 90i microscope at a magnification of 20X and captured with a Photometric Cool SNAP HQ2 florescent camera (Nikon Instrument, Melville, NY). Analysis was performed using the Nikon NIS element AR software (Nikon Instruments) on a large-scale image. The investigator was blinded to the group and time condition of each participant during all analyses. The CSA data pools Type IIA and Type IIX fibers as Type II, due to the number necessary to analyze the CSA for each fiber type (~50-60) per sample (127). Fiber type was assessed by counting all suitable fibers (mean fibres counted: 239 ± 71) whereas fibers along the periphery and those that were obliquely or longitudinally-oriented were not included.

2.1.9 Blood Analysis

Blood samples were obtained to measure creatine kinase and systemic hormones concentrations. A 22-gauge needle was inserted into an antecubital vein and blood was collected and set aside to be allowed to clot and serum was collected after a 10-min spin at 500 *g,* Heparinized-tubes were used to isolate plasma. Whole blood samples were immediately analyzed for creatine kinase (ARCHITECT System, Abbott Laboratories, Abbott Park, IL 60064, USA) while the remaining samples were centrifuged at 4000 g for 10 min at 4° C, aliquoted and frozen at -80℃. Blood samples were analyzed for serum total testosterone (T; ng/dL), free testosterone (fT; ng/dL), cortisol (nM), growth hormone (GH; ng/mL) and insulin-like growth factor 1 (IGF-1; ug/dL) using a two-site chemiluminescence immunometric assays (Immulite; Intermedico, Holliston, MA) or radio-immunoassay (Diagnostics Products Corporation, Los Angeles, CA). The intra- and inter-assay CV for these hormones were all below 5%.

2.1.10 Statistical analyses

All variables were assessed for normality using the Kolmogorov-Smirnov test ($p>0.05$). Baseline characteristics were assessed using independent-t tests. A two-way (group by time) mixed-model ANOVA was assessed for muscle thickness, fibre CSA, fibre distribution and total 1-RM strength and hormone concentrations. Tukey's HSD was performed in excel when the ANOVA was significant. Significance was set at $p<0.05$. To compare the changes in body composition (FBFM, MT, CSA) and strength tests (1-RM, Wingate peak power and Optojump) between groups independent t-tests were performed. Intra-class correlation estimates for muscle thickness were calculated based on a single rater, absolute-agreement, 2-way mixed-effects model. The interclass correlation for

muscle cross-sectional area was assessed using a mean-raters (k=2), consistency-agreement, 2-way mixed-effects model. All analysis was performed using SPSS statistical package version 23 (IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY). Values are expressed as means ± standard deviation (SD) or using box and whisker plots to illustrate the full variance of the data.

## 2.2 RESULTS

### 2.2.1 Participant Characteristics

Baseline anthropometric characteristics are provided in Table 1. There were no significant differences between groups for any study variables ($p>0.05$, Table 1).

Table 1. Participant characteristics

| | Whey +HMB (n=13) | Whey+ Leu (n=13) | p |
|---|---|---|---|
| Age, years | 22 ± 1 | 23 ± 3 | 0.73 |
| Height, cm | 179 ± 6 | 180 ± 6 | 0.89 |
| Body mass, kg | 81.6 ± 9.6 | 83.4 ± 13.1 | 0.68 |
| Lean mass, kg | 63.1 ± 5.7 | 62.9 ± 8.7 | 0.95 |
| Total fat mass, kg | 15.2 ± 5.2 | 17.2 ± 6.4 | 0.39 |
| Percent body fat, % | 19.0 ± 4.6 | 21.1 ± 5.8 | 0.33 |
| Squat kg/kg BM | 1.7 ± 0.2 | 1.7 ± 0.3 | 0.64 |
| Bench kg/kg BM | 1.2 ± 0.2 | 1.2 ± 0.3 | 0.97 |
| Deadlift kg/kg BM | 1.9 ± 0.3 | 1.9 ± 0.2 | 0.94 |
| Total Strength kg/kg BM | 4.8 ± 0.6 | 4.8 ± 0.7 | 0.88 |
| Protein intake g/kg/day | 1.8 ± 0.4 | 1.9 ± 0.6 | 0.40 |

Abbreviations; Body Mass (BM). Values are mean±SD.

There was no significant difference in dietary protein intake (g/kg/day) between groups at baseline or week 12 ($p>0.05$, Table 2).

Table 2. Macronutrient distribution

| | Whey +HMB (n=13) | Whey+ Leu (n=13) |
|---|---|---|
| Baseline | | |
| %PRO | 23 ± 5 | 24 ± 6 |
| %CHO | 40 ± 9 | 43 ± 13 |
| %FAT | 37 ± 7 | 31 ± 9 |
| Post | | |
| %PRO | 23 ± 5 | 23 ± 7 |
| %CHO | 43 ± 8 | 44 ± 10 |
| %FAT | 34 ± 7 | 34 ± 12 |

Abrv. PRO: Protein, CHO: carbohydrates.

2.2.2 Body composition

FBFM changed in the Whey+HMB from 63.1 ± 5.7 kg to 65.4 ± 5.9 kg. For Whey+Leu, FBFM changed from 62.9 ± 8.7 kg to 65.6 ± 8.6 kg, pre to post-invention, respectively (Figure 6A). The change in FBFM for Whey+HMB (2.3 ± 1.2 kg) and Whey+Leu (2.6 ± 1.9 kg) were not significantly different (p=0.59; Figure 6B). Fat mass remained unchanged (p=0.19) in both groups (Whey+HMB: -0.1 ± 0.9 kg and Whey+Leu: -0.5 ± 1.3 kg; p=0.41). For both groups, total body water remained unchanged throughout the intervention (p=0.62, data not shown).

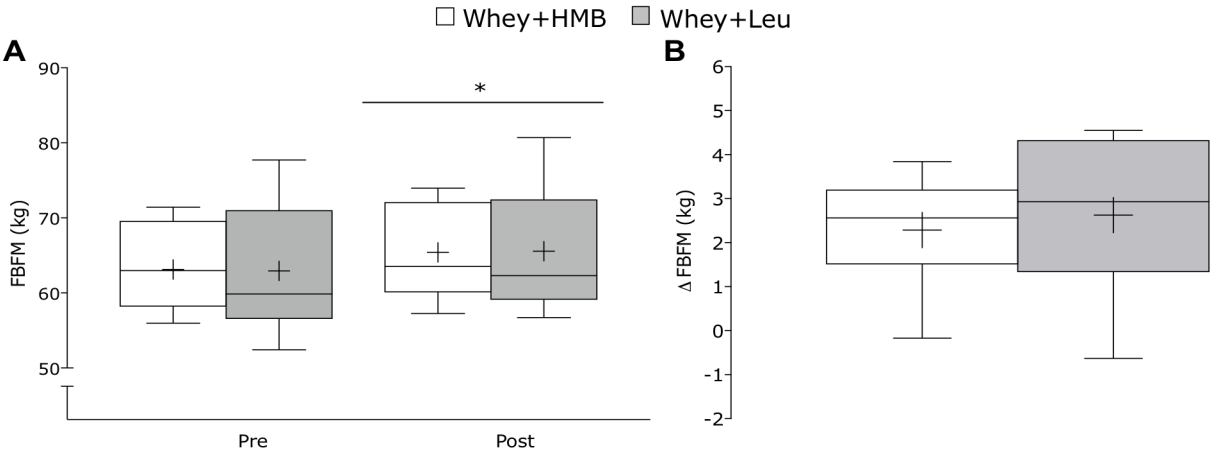



**Figure 6. A)** Absolute values pre- and post training and **B)** Change in fat-and bone free mass (FBFM) for Whey+HMB (n=13, open box) and Whey+Leu (n=13, grey box) following 12 weeks of resistance training. Values are presented as median (lines) with the interquartile range (boxes) ± minimum and maximum values (whiskers) and where + indicates the mean. *Significantly different ($p<0.05$) from pre-training.

2.2.3 Ultrasound

Whey+HMB and Whey+Leu exhibited comparable changes in MT. Whey+HMB increased from 31 ± 2 mm to 32 ± 2 mm and Whey+Leu increased from 30 ± 3 mm to 32 to 4 mm (5 ± 6 % and 5 ± 6 %, respectively; $p=0.97$, Figure 7A). The mid-thigh CSA increased from 34.1 ± 4.0 $cm^2$ to 36.4 ± 4.8 $cm^2$ in Whey+HMB and from 33.9 ± 5.8 $cm^2$ to 36.1 ± 6.3 $cm^2$ in Whey+Leu (Figure 7C).

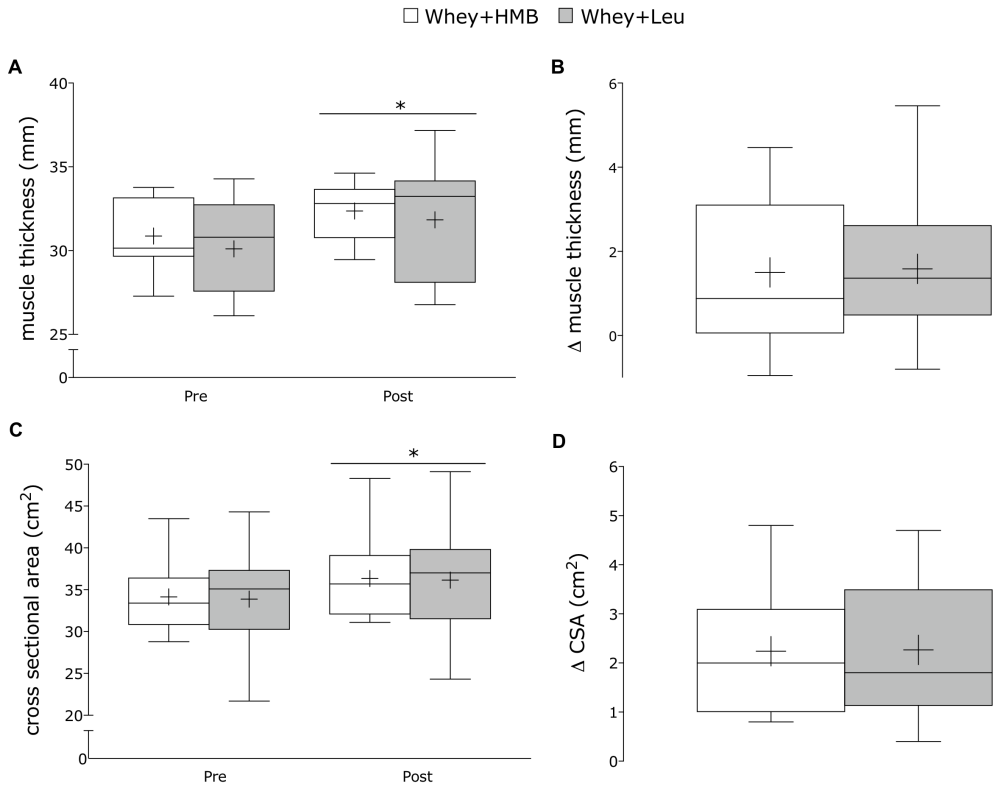



Figure 7. A) Absolute values pre- and post-training and B) Change in *vastus lateralis* muscle thickness for Whey+HMB (n=13, open box) and Whey+Leu (n=12, grey box) following 12 weeks of undulating periodized resistance training. C) Absolute change and D) Delta change in *vastus lateralis* cross-sectional area for Whey+HMB and Whey+Leu. Values are presented as median (lines) with the interquartile range (boxes) ± minimum and maximum values (whiskers) and where + indicates the mean. *Significantly different ($p<0.05$) from pre-training.

The change in muscle CSA for Whey+HMB (2.2 ± 1.4 $cm^2$) and Whey+Leu (2.3 ± 1.4 $cm^2$) was not different ($p=0.96$, Figure 7D). The percent for change in CSA for Whey+HMB (6 ± 4 %) and Whey+Leu (7 ± 4 %) in CSA was similar between groups ($p=0.92$).

2.3.4 Fiber CSA

Following the intervention, there was an increase in Type 2 CSA with no difference between groups or fibers ($p>0.05$, Table 3).

Table 3. Muscle fiber cross-sectional area and distribution

| | Pre | | | Post | | | p |
|---|---|---|---|---|---|---|---|
| Type 1 fCSA $\mu m^2$ | | | | | | | |
| HMB | 5106 | ± | 572 | 5450 | ± | 610 | 0.058 |
| Leu | 5152 | ± | 375 | 5378 | ± | 462 | |
| Type 2 fCSA $\mu m^2$ | | | | | | | |
| HMB | 5785 | ± | 555 | 6363 | ± | 573 | <0.01 |
| Leu | 6312 | ± | 572 | 6719 | ± | 603 | |
| Distribution | | | | | | | |
| Type 1 % | | | | | | | |
| HMB | 36 | ± | 12 | 41 | ± | 16 | 0.69 |
| Leu | 39 | ± | 16 | 37 | ± | 7 | |
| Type 2 (2a+2x) % | | | | | | | |
| HMB | 63 | ± | 12 | 58 | ± | 18 | 0.79 |
| Leu | 60 | ± | 17 | 63 | ± | 7 | |
| Type 2a % | | | | | | | |
| HMB | 50 | ± | 14 | 52 | ± | 16 | 0.15 |
| Leu | 57 | ± | 18 | 58 | ± | 7 | |
| Type 2x % | | | | | | | |
| HMB | 11 | ± | 9 | 1 | ± | 2 | 0.03 |
| Leu | 6 | ± | 8 | 4 | ± | 7 | |

Abbreviations; Fiber cross-sectional area (fCSA). Values are mean±SD.

There were no group, time or group-by-time interactions for Type 1 or Type 2 fiber-type distributions ($p>0.05$). A significant shift pre- to post-training in Type 2x from 11 ± 9 %

to 1 ± 2 % in Whey+HMB and 6 ± 8 % to 4 ± 7 % in Whey+Leu; p=0.03, Table 3) was observed.

2.2.5 Maximal Strength

In response to 12 weeks of RT, 1-RM strength for squat, bench press and deadlift increased ($p<0.01$). There was an increase post-training in squat 1-RM for Whey+HMB (33 ± 10 kg) and Whey+Leu (35 ± 17 kg, Table 4). The increase in bench press 1-RM was similar for Whey+HMB (11 ± 5 kg) and Whey+Leu (11 ± 7 kg, Table 4). The increase in deadlift 1-RM for Whey+HMB (25 ± 12 kg) was similar to Whey+Leu (34 ± 22 kg, Table 4). There were no significant differences in any 1-RM strength test from baseline to week 12 between for Whey+HMB and Whey+Leu ($p>0.05$). Following 12 weeks of training, there was a significant increase in total strength for Whey+HMB (70 ± 21 kg) and Whey+Leu (80 ± 40 kg) with no significant difference between groups ($p=0.41$). Upon completion of week 1 to week 8 (Phase 1) both groups experienced similar changes in squat 1-RM (21± 11 kg and 27 ± 11 kg, $p=0.24$), bench press (10 ± 4 kg and 10 ± 5 kg, $p=0.89$) and deadlift (18 ± 7 kg and 25 ± 19 kg, $p=0.22$) for Whey+HMB and Whey+Leu respectively. Upon completion of Phase 2 (overreaching), both groups experienced similar changes in squat (3 ± 7 kg and -2 ± 9 kg, $p=0.24$), bench press (-2 ± 4 kg and -1 ± 3 kg, $p= 0.43$) and deadlift (-2 ± 8 kg and -6 ± 11 kg, $p=0.15$), Whey+HMB and Whey+Leu, respectively. The decrement in total strength following week 8 to week 10 (overreaching) was 1 ± 12 kg for Whey+HMB and 8 ± 19 kg for Whey+Leu. ($p=0.29$). Following a 2-week taper (Phase 3), total 1-RM strength recovered similarly between groups ($p=0.25$) from overreaching: Whey+HMB (20 ± 9 kg) and

Whey+Leu (28 ± 22 kg). There was a significant increase in total 1-RM strength from (Week 8 to Week 12) with no difference in Whey+HMB (21 ± 10 kg) and Whey+Leu (18 ± 18 kg, p=0.59).

Table 4. Maximal strength (kg) and peak Wingate power (W) pre- and post-training

| | HMB | | | | | | | | | LEU | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Pre | | | Post | | | Δ | | | Pre | | | Post | | | Δ | | |
| SQ | 140 | ± | 19 | 173 | ± | 22* | 33 | ± | 10 | 139 | ± | 24 | 174 | ± | 28* | 35 | ± | 17 |
| BP | 99 | ± | 18 | 111 | ± | 17* | 11 | ± | 5 | 102 | ± | 19 | 113 | ± | 23* | 11 | ± | 7 |
| DL | 151 | ± | 23 | 177 | ± | 28* | 25 | ± | 12 | 155 | ± | 24 | 189 | ± | 28* | 34 | ± | 22 |
| Total | 392 | ± | 53 | 461 | ± | 59* | 70 | ± | 21 | 396 | ± | 61 | 476 | ± | 72* | 80 | ± | 40 |
| Power | 981 | ± | 180 | 1030 | ± | 180* | 49 | ± | 96 | 954 | ± | 90 | 1043 | ± | 109* | 88 | ± | 92 |

Abbreviations; SQ, squat, BP, bench press, DL, deadlift, Total, total 1-RM (kg): SQ+BP+DL, Power, peak power (W) during the Wingate test. Values are means±SD. *Significantly different from Pre ($p<0.05$).

2.2.6 Wingate

There was a significant increase in peak Wingate power (W) following training for Whey+HMB (981 ± 180 W to 1030 ± 180 W) and Whey+Leu (954 ± 90 W to 1043 ± 109 W, p=0.02) with no difference between groups (p=0.39, Table 4). The delta change in peak power was not different between groups (p=0.33), 49 ± 96 W and 88 ± 92 W for Whey+HMB and Whey+Leu, respectively. There was a significant group-by-time interaction in peak power following overreaching (Week 8 to Week 10) for Whey+HMB and Whey+Leu (p=0.03). The decrement in peak power for Whey+HMB was significantly greater (-39 ± 74 W) than Whey+Leu (18 ± 51 W) (p=0.03).

2.2.7 Vertical Jump

Following training, there was a significant increase in Optojump performance (W/kg); Whey+HMB increased from 14.9 ± 1.3 W/kg to 16.1 ± 1.3 W/kg, and Whey+Leu increased from 14.4 ± 1.9 to 15.7 ± 1.9 W/kg ($p<0.01$), with no difference between groups ($p=0.80$). There was no change in average power (W/kg) during overreaching for Whey+HMB (15.2 ± 1.3 W/kg to 15.9 ± 1.5 W/kg) or Whey+Leu (16.0 ± 3.0 W/kg to 16.5 ± 1.9 W/kg, $p=0.80$).

2.2.8 Blood Analysis

There was a significant increase in blood creatine kinase activity from baseline and week 8 to week 9, and week 10 ($p<0.05$), with no significant differences between groups (Table 5). Following overreaching, CK increased 109 ± 115 % and 72 ± 41 % ($p=0.29$, Table 5) for Whey+HMB and Whey+Leu, respectively. Following a 2-week taper (week 10 to week 12) both groups experienced similar decrements in CK -26 ± 44 % and -29 ± 57 %, $p=0.91$ (Table 5, Whey+HMB and Whey+Leu, respectively). There was a significant increase in cortisol from baseline and week 8 to week 9, week 10 (overreaching) and week 12 ($p<0.01$), with no difference between groups. Both groups showed similar increases following overreaching (47 ± 49 % and 47 ± 43 %, $p=0.99$) and a two-week taper (-15 ± 34 % and -10 ± 48 %, $p=0.74$) for Whey+HMB and Whey+Leu, respectively (Table 5). There was no time or group by time effect for IGF-1 ($p=0.14$). There was no significant group by time effect for GH ($p=0.42$) but a significant effect of time ($p=0.017$). In the Whey+HMB and Whey+Leu groups, there was a significant decrease in GH from week 0 to week 10 and week 12 ($p<0.05$). There was a significant

decrease ($p \leq 0.05$) in total testosterone from week 0 to week 10, and a significant increase from week 10 to week 12 ($p < 0.05$) with no between-group differences at any phase. There was a significant increase in free testosterone from baseline to week 8 ($p < 0.05$) and a significant decrease from week 8 to week 10 ($p = 0.05$).

Table 5. Serum creatine kinase activity and plasma hormone concentrations during the protocol

| | Pre | Week 4 | Week 8 | Week 9 | Week 10 | Week 12 |
|---|---|---|---|---|---|---|
| CK, (U/L) | | | | | | |
| HMB | 247 ± 102 | 240 ± 98 | 201 ± 72 | *450 ± 187 | *387 ± 180 | 260 ± 174 |
| Leu | 234 ± 114 | 184 ± 73 | 204 ± 76 | *465 ± 268 | *349 ± 150 | 227 ± 207 |
| Cortisol, nM | | | | | | |
| HMB | 21 ± 3 | 20 ± 3 | 20 ± 2 | *30 ± 8 | *29 ± 10 | *24 ± 7 |
| Leu | 20 ± 3 | 20 ± 3 | 20 ± 3 | *31 ± 9 | *29 ± 7 | *24 ± 6 |
| IGF1, ug/dL | | | | | | |
| HMB | 355 ± 108 | 407 ± 124 | 379 ± 102 | 374 ± 116 | 319 ± 92 | 345 ± 126 |
| Leu | 375 ± 99 | 400 ± 98 | 394 ± 123 | 364 ± 139 | *312 ± 114 | 383 ± 116 |
| GH, ng/mL | | | | | | |
| HMB | 3.3 ± 0.9 | 3.7 ± 0.7 | *3.6 ± 0.9 | 3.2 ± 0.9 | *2.4 ± 0.8 | *2.9 ± 0.8 |
| Leu | 3.7 ± 0.8 | 3.1 ± 0.9 | 3.5 ± 0.8 | *3.0 ± 0.5 | *3.2 ± 1.1 | *3.3 ± 0.8 |
| T, ng/dL | | | | | | |
| HMB | 691 ± 52 | 693 ± 60 | *734 ± 42 | 669 ± 60 | *521 ± 66 | 704 ± 53 |
| Leu | 709 ± 66 | 701 ± 45 | 688 ± 66 | *645 ± 72 | *477 ± 97 | *625 ± 143 |
| fT, ng/dL | | | | | | |
| HMB | 8 ± 3 | 10 ± 3 | *10 ± 3 | 8 ± 2 | *6 ± 2 | *9 ± 3 |
| Leu | 10 ± 3 | 11 ± 2.6 | *9 ± 2 | *7 ± 2 | *7 ± 2 | *8 ± 3 |

CK (Creatine Kinase), cortisol (nM), insulin-like growth factor 1 (IGF-1; ug/dL), growth hormone (GH; ng/mL) total testosterone (T; ng/dL), free testosterone (fT; ng/dL). *Significantly different from Pre ($p < 0.05$).

## 2.3 DISCUSSION

We discovered that in young men undertaking an undulating periodized RT program, that the ingestion of whey protein (50 g) with HMB-Ca (3 g daily) versus whey protein with the same amount of leucine (3 g daily) resulted in no differences in training-induced gains in FBFM, muscle size, strength, or power. We did not detect group differences in blood hormones and serum creatine kinase, an often-used proxy marker of muscle damage. Thus, contrary to our initial hypothesis, and in direct contradiction to several reports using either HMB-Ca (100) or HMB-FA (28, 30), we conclude that HMB ingestion does not lead to an enhancement of hypertrophy or strength in comparison to ingestion of leucine. We observed similar increases in DXA-derived FBFM for Whey+HMB (2.3 ± 1.2 kg) and Whey+Leu (2.6 ± 1.9 kg). We also assessed total body water content at the time of the DXA scan and found no differences between each participant's scans that would have accounted for changes in FBFM. The DXA-measured changes in FBFM we observed were ~3-3.7 times lower than the gains previously reported (28, 30, 100). We cannot explain why the gains in FBFM we report are so much lower than these previous studies (28, 30, 100), but suggest that some methodological issues may contribute to the discrepancies (117). We find the lower gains in FBFM we observed versus previous work (28, 30, 100) particularly perplexing given that: we used the identical training program, we ensured our participants had more than adequate dietary protein and energy intake, and we had participants that were of comparable training status, at least based on FBFM and strength measures. However, we view the gains in FBFM we report as being more in line with typical gains in lean mass for

participants engaging in ~12 weeks of resistance training as reported in a recent meta-analysis from our laboratory (128).

Muscle thickness and CSA were assessed using ultrasound, which has been shown to be a reliable alternative to magnetic resonance imaging (121, 129). The Whey+HMB and Whey+Leu groups in our study demonstrated a 5% increase in muscle thickness, which is in-line with a previous 12 wk RT study (121). In contrast to our results, Lowery et al (30) observed ~3 times greater increase in quadriceps muscle thickness of (7.8 ± 0.4 mm) in participants supplemented with 3 g HMB-FA + 400 mg ATP relative to a placebo group (2.4 ± 0.7 mm). The only other investigation to report such dramatic increases in muscle thickness was from the same study in a group receiving HMB-FA alone (28).

There is no real consensus on the ability of HMB to augment RT-induced muscle strength. Some trials report no effect (107, 130, 131), a trivial effect (112, 132) or considerable effect (28, 30, 100) of HMB to augment muscle mass and strength with RT. Previous work demonstrated significantly greater increases in total strength (3 times) for participants supplemented with HMB-FA (77 ± 18 kg) (28) and HMB+ATP (96 ± 8 kg) (30) compared to placebo (25 ± 22 kg). However, using the same training program as used previously (28, 30), we observed similar increases in total strength for Whey+HMB (70 ± 21 kg) and Whey+Leu (80 ± 40 kg). Following overreaching, both Whey+HMB and Whey+Leu groups experienced similar decrements in total strength (-0.5 ± 3 % and -2 ± 5 %) and subsequent recovery (5 ± 2 % and 6 ± 5 %). In addition, following overreaching, the Whey+HMB group experienced decrements in wingate peak power that were, surprisingly, not observed in the Whey+Leu group indicating a superior ability of

Whey+Leu to protect against declines in performance when overreaching. Again, our results are in sharp contrast with previous investigations (28, 30, 100) in which HMB markedly attenuated the declines in muscle strength and power following overreaching (28, 30). Our data indicate that Whey+HMB and Whey+Leu have a similar ability to augment RT-induced strength gains, attenuate decrements following overreaching, and facilitate recovery during a taper.

We report muscle hypertrophy and strength data that differ from recent investigations that utilized the same RT program (28, 30, 100). Nonetheless, our findings are analogous to previous investigations of HMB-Ca supplementation that did not observe a superior effect on hypertrophy and strength (94, 107). Nissen et al (94) examined HMB-Ca at varying doses 0 g, 1.5 g, 3 g in untrained participants. The authors suggested a dose-response effect on fat-free mass to increasing doses of HMB-Ca (94). Critically, there were no statistically significant increases in fat-free mass following HMB supplementation (94). In a subsequent investigation [Study 2 from (94)], trained participants were supplemented with 3 g HMB-Ca plus a nutrient powder (75 g protein) during 7 weeks of RT. The HMB+nutrient powder group increased fat-free mass on days 14-39 compared to controls (94). Nonetheless, the increase in fat-free mass was not significantly different between groups following training (94). In a separate study, 3 g of HMB-Ca was included in a protein supplement (75 g) given to trained participants, no difference was observed between HMB-Ca or protein groups (107). In spite of these results, the work of Nissen et al (94) is frequently, and incorrectly, cited to illustrate the anabolic effects of HMB (94). An independent effect of HMB on muscle mass accretion,

due to the inclusion of protein in the same supplement, is impossible to elucidate from this trial (94). Critics attribute the discrepancies between these trials (94, 107) to the short supplementation protocol (28 days) and propose a longer period is required to elicit the anabolic effects of HMB (28, 30, 102). Nonetheless, we employed a highly effective training program used previously (28, 30, 100). Our data are in broad agreement with the conclusions of Kreider et al (107) who showed that a protein supplement with HMB does not enhance lean mass, strength or power compared to a protein supplement alone.

The training program used in the present and previous investigations (28, 30) is stated to induce muscle damage and a favourable hormone milieu upon which HMB would be maximally effective (28, 30, 100). The program, adapted from Kraemer et al (100), was designed to increase anabolic hormones by first performing multi-joint, compound lifts, followed by accessory lifts targeting smaller muscle groups. In fact, a single bout of training adapted from this program has been demonstrated to increase systemic hormones (115). Nonetheless, we and others (42, 67, 69) have showed that there is no anabolic effect that arises due to the acute, RT-induced rise in systemic hormones.

In the present investigation, we assessed various hormone concentrations at multiple time points and report no difference in hormones between groups at any phase. In addition, we assessed creatine kinase (CK), a frequently measured, but poor indicator of skeletal muscle damage (49, 133). A recent meta-analysis observed that HMB supplementation was effective in reducing serum levels of CK in studies $\geq$ 6 weeks (133). However, there is extensive debate as to the validity of CK, as serum levels are subject to substantial variation (49). The appearance of CK may reflect a disturbance to energy

control processes and does not independently indicate structural damage to muscle cells (49). Following overreaching, CK (109 % and 72 %) and cortisol (47 % and 47 %) increased similarly in the Whey+HMB and Whey+Leu groups, respectively. The elevations in CK and cortisol recovered similarly during the 2-week taper. Our data support other investigations that have failed to observe any beneficial effect of HMB on CK release or cortisol (110, 130, 134-136).

The principle strengths of the present study stem from the practical applications of our findings. We supplemented participants with whey protein because post-exercise consumption of a high-quality protein, such as whey, is standard nutritional practice (120, 137), and augments hypertrophy (128). We propose that persons undertaking RT to gain strength and muscle mass would not forgo the notable benefits of high-quality protein supplementation (128) and take only an isolated compound such as HMB, alone. Rather, we propose that most resistance exercisers would augment their nutritional program to include a supplement such as HMB in addition to a high-quality protein, especially given the ostensibly substantial anabolic advantage HMB has been shown to provide (28, 30, 100). We used multiple methods to assess changes in muscle: FBFM by DXA, muscle thickness, muscle CSA, and muscle fiber CSA. There are, however, some limitations that are important to acknowledge. In the present analysis, we did not employ a control group. Although the mass and strength in the Whey+HMB and Whey+Leu groups are consistent with previous reports (128), we acknowledge that a non-supplemented control group would have improved the robustness of our findings. Secondly, we recognize that our supplementation protocol differs slightly from what is recommended for HMB: 1 g thrice

daily as 30 minutes before exercise (102, 107). Finally, in contrast to previous investigations in which HMB-FA was used (28, 30), we utilized HMB in its calcium form (HMB-Ca), as this was the form associated with the greatest gains in muscle mass of ~9 kg versus only ~4 kg in the placebo group (100). However, we propose that the form of the HMB likely matters very little since recent work from Wilkinson et al (27) suggests that despite slightly differing bioavailability (114), HMB-Ca and HMB-FA are equivalent in their stimulation of MPS. And critically, HMB as a metabolite of leucine stimulates MPS, and inhibits muscle protein breakdown, through many of the same canonical signaling pathways as leucine (1, 27). Importantly, this is the first investigation to compare HMB to its parent metabolite during RT in young men and not merely a non-protein (usually carbohydrate) placebo. Indeed, our intention was to mimic the nutritional practices of athletes and recreational exercisers who frequently supplement with high-quality protein (120). As a result, our data is of practical relevance to athletes and recreational exercisers who hope to maximize their RT-induced gains through good nutritional and supplementation practices. In conclusion, our results show that there is no benefit of HMB when added to whey compared to whey protein with leucine.

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# Appendix A: Raw Data

Table 1. Baseline Characteristics assessed by DXA

| ID | Code | Age | Height | BM_kg_BL | FBFM_kg_BL | FatMass_kg_BL |
|---|---|---|---|---|---|---|
| H02 | 2 | 29.00 | 178.00 | 70.50 | 57.30 | 12.80 |
| H03 | 1 | 23.00 | 189.00 | 89.90 | 67.90 | 17.60 |
| H04 | 2 | 21.00 | 181.00 | 79.40 | 57.96 | 18.40 |
| H05 | 1 | 22.00 | 182.00 | 75.60 | 59.30 | 13.30 |
| H07 | 1 | 26.00 | 179.00 | 89.00 | 71.38 | 12.80 |
| H09 | 1 | 22.00 | 171.00 | 67.10 | 55.96 | 8.50 |
| H10 | 1 | 22.00 | 177.00 | 78.60 | 58.28 | 16.90 |
| H11 | 2 | 19.00 | 176.00 | 80.10 | 53.94 | 22.60 |
| H12 | 1 | 22.00 | 180.00 | 72.60 | 62.99 | 6.34 |
| H13 | 2 | 22.00 | 184.00 | 88.40 | 66.51 | 17.92 |
| H14 | 1 | 22.00 | 173.00 | 75.60 | 58.09 | 14.87 |
| H15 | 2 | 27.00 | 176.00 | 80.00 | 55.76 | 21.56 |
| H16 | 2 | 22.00 | 183.00 | 94.60 | 77.72 | 13.71 |
| H17 | 1 | 22.00 | 180.00 | 74.90 | 56.94 | 14.47 |
| H18 | 1 | 22.00 | 188.00 | 87.60 | 63.96 | 19.73 |
| H19 | 2 | 22.00 | 168.00 | 71.70 | 52.42 | 16.60 |
| H20 | 1 | 20.00 | 177.00 | 95.87 | 71.42 | 24.45 |
| H21 | 2 | 25.00 | 175.00 | 85.40 | 65.06 | 16.45 |
| H23 | 2 | 23.00 | 190.00 | 112.60 | 76.15 | 31.55 |
| H24 | 1 | 23.00 | 171.00 | 73.20 | 59.84 | 10.59 |
| H25 | 1 | 23.00 | 177.00 | 82.90 | 63.27 | 16.29 |
| H26 | 2 | 22.00 | 175.00 | 69.70 | 57.89 | 8.35 |
| H28 | 2 | 20.00 | 182.00 | 74.10 | 59.87 | 10.99 |
| H29 | 2 | 20.00 | 183.00 | 75.60 | 62.08 | 10.07 |
| H30 | 1 | 22.00 | 185.00 | 97.40 | 71.29 | 22.15 |
| H32 | 2 | 23.00 | 182.00 | 102.50 | 75.55 | 22.77 |

Table 2. Baseline Strength normalized to body mass (kg/kg body mass)

| ID | Code | Squat kg/kg BM | Bench kg/kg BM | Deadlift kg/kg BM | Total kg/kg BM |
|---|---|---|---|---|---|
| H02 | 2 | 2.22 | 1.67 | 2.22 | 6.11 |
| H03 | 1 | 1.44 | 0.78 | 1.74 | 3.96 |
| H04 | 2 | 1.34 | 1.23 | 1.94 | 4.51 |
| H05 | 1 | 1.68 | 1.05 | 1.95 | 4.68 |
| H07 | 1 | 1.76 | 1.35 | 1.99 | 5.10 |
| H09 | 1 | 1.79 | 1.45 | 2.27 | 5.51 |
| H10 | 1 | 1.50 | 1.18 | 1.30 | 3.98 |
| H11 | 2 | 1.44 | 1.05 | 1.81 | 4.30 |
| H12 | 1 | 2.03 | 1.28 | 1.84 | 5.16 |
| H13 | 2 | 1.72 | 1.15 | 1.62 | 4.49 |
| H14 | 1 | 1.71 | 1.44 | 1.89 | 5.04 |
| H15 | 2 | 1.45 | 0.99 | 1.79 | 4.23 |
| H16 | 2 | 1.94 | 1.37 | 2.18 | 5.49 |
| H17 | 1 | 1.79 | 1.24 | 1.79 | 4.82 |
| H18 | 1 | 1.42 | 1.06 | 1.48 | 3.96 |
| H19 | 2 | 1.74 | 1.23 | 1.87 | 4.84 |
| H20 | 1 | 1.87 | 1.44 | 2.01 | 5.32 |
| H21 | 2 | 1.99 | 1.67 | 2.26 | 5.92 |
| H23 | 2 | 1.43 | 0.95 | 1.47 | 3.85 |
| H24 | 1 | 2.26 | 1.36 | 2.26 | 5.89 |
| H25 | 1 | 1.72 | 1.40 | 2.00 | 5.12 |
| H26 | 2 | 1.92 | 1.27 | 1.66 | 4.85 |
| H28 | 2 | 1.50 | 1.13 | 1.99 | 4.62 |
| H29 | 2 | 1.89 | 1.50 | 1.89 | 5.28 |
| H30 | 1 | 1.56 | 1.00 | 1.70 | 4.26 |
| H32 | 2 | 1.31 | 0.86 | 1.62 | 3.78 |

Table 3. Baseline Strength (kg)

| ID | Code | Squat_BL | Bench_BL | Deads_BL | Total_BL |
|---|---|---|---|---|---|
| H02 | 2 | 156.53 | 117.97 | 156.53 | 431.03 |
| H03 | 1 | 129.31 | 70.33 | 156.53 | 356.17 |
| H04 | 2 | 106.62 | 97.55 | 154.26 | 358.44 |
| H05 | 1 | 127.04 | 79.40 | 147.46 | 353.90 |
| H07 | 1 | 156.53 | 120.24 | 176.95 | 453.72 |
| H09 | 1 | 120.24 | 97.55 | 152.00 | 369.78 |
| H10 | 1 | 117.97 | 93.01 | 102.09 | 313.07 |
| H11 | 2 | 115.70 | 83.94 | 145.19 | 344.83 |
| H12 | 1 | 147.46 | 93.01 | 133.85 | 374.32 |
| H13 | 2 | 152.00 | 102.09 | 142.92 | 397.01 |
| H14 | 1 | 129.31 | 108.89 | 142.92 | 381.13 |
| H15 | 2 | 115.70 | 79.40 | 142.92 | 338.02 |
| H16 | 2 | 183.76 | 129.31 | 206.44 | 519.51 |
| H17 | 1 | 133.85 | 93.01 | 133.85 | 360.71 |
| H18 | 1 | 124.77 | 93.01 | 129.31 | 347.10 |
| H19 | 2 | 124.77 | 88.48 | 133.85 | 347.10 |
| H20 | 1 | 179.22 | 138.38 | 192.83 | 510.44 |
| H21 | 2 | 170.15 | 142.92 | 192.83 | 505.90 |
| H23 | 2 | 161.07 | 106.62 | 165.61 | 433.30 |
| H24 | 1 | 165.61 | 99.82 | 165.61 | 431.03 |
| H25 | 1 | 142.92 | 115.70 | 165.61 | 424.23 |
| H26 | 2 | 133.85 | 88.48 | 115.70 | 338.02 |
| H28 | 2 | 111.16 | 83.94 | 147.46 | 342.56 |
| H29 | 2 | 142.92 | 113.43 | 142.92 | 399.27 |
| H30 | 1 | 152.00 | 97.55 | 165.61 | 415.15 |
| H32 | 2 | 133.85 | 88.48 | 165.61 | 387.93 |

Table 4. Body Mass assessed by DXA (kg)

| ID | BM_kg_BL | BM_kg_W4 | BM_kg_W8 | BM_kg_W10 | BM_kg_W12 |
|---|---|---|---|---|---|
| H02 | 70.50 | 74.10 | 73.80 | 73.80 | 74.00 |
| H03 | 89.90 | 94.30 | 94.40 | 93.10 | 92.60 |
| H04 | 79.40 | 79.60 | 81.30 | 80.80 | 80.50 |
| H05 | 75.60 | 79.20 | 80.20 | 81.10 | 79.00 |
| H07 | 89.00 | 88.90 | 89.00 | 91.40 | 91.00 |
| H09 | 67.10 | 69.70 | 68.60 | 70.80 | 69.70 |
| H10 | 78.60 | 80.30 | 79.90 | 80.00 | 79.80 |
| H11 | 80.10 | 82.78 | 79.50 | 85.76 | 85.43 |
| H12 | 72.60 | 73.60 | 72.10 | 74.80 | 75.20 |
| H13 | 88.40 | 87.30 | 88.40 | 88.00 | 87.50 |
| H14 | 75.60 | 76.70 | 75.60 | 76.80 | 77.70 |
| H15 | 80.00 | 84.20 | 80.00 | 85.40 | 86.00 |
| H16 | 94.60 | 95.50 | 94.60 | 98.80 | 96.20 |
| H17 | 74.90 | 76.60 | 74.90 | 77.60 | 76.80 |
| H18 | 87.60 | 88.80 | 87.90 | 88.00 | 87.20 |
| H19 | 71.70 | 72.70 | 71.70 | 74.90 | 74.60 |
| H20 | 95.87 | 101.50 | 98.80 | 102.80 | 103.10 |
| H21 | 85.40 | 86.30 | 85.00 | 87.90 | 86.90 |
| H23 | 112.60 | 115.90 | 112.60 | 117.10 | 116.30 |
| H24 | 73.20 | 72.90 | 74.10 | 73.60 | 74.40 |
| H25 | 82.90 | 82.80 | 83.80 | 82.90 | 82.80 |
| H26 | 69.70 | 71.60 | 73.60 | 74.20 | 73.40 |
| H28 | 74.10 | 74.70 | 73.90 | 74.50 | 72.70 |
| H29 | 75.60 | 77.50 | 80.00 | 81.80 | 89.30 |
| H30 | 97.40 | 97.80 | 98.70 | 99.80 | 100.10 |
| H32 | 102.50 | 100.60 | 99.80 | 101.40 | 100.20 |

Table 5. Fat and Bone free mass (FBFM) assessed by DXA (kg)

| ID | FBFM_kg_BL | FBFM_kg_W4 | FBFM_kg_W8 | FBFM_kg_W10 | FBFM_kg_W12 |
|---|---|---|---|---|---|
| H02 | 57.30 | 57.65 | 58.00 | 57.77 | 58.55 |
| H03 | 67.90 | 72.10 | 72.03 | 71.46 | 71.13 |
| H04 | 57.96 | 59.07 | 60.57 | 59.60 | 59.63 |
| H05 | 59.30 | 62.25 | 63.20 | 64.24 | 62.56 |
| H07 | 71.38 | 72.25 | 72.07 | 73.16 | 73.09 |
| H09 | 55.96 | 58.16 | 56.83 | 58.63 | 57.27 |
| H10 | 58.28 | 60.08 | 59.95 | 60.25 | 60.33 |
| H11 | 53.94 | 56.93 | 57.05 | 58.52 | 57.92 |
| H12 | 62.99 | 64.09 | 64.78 | 65.47 | 66.08 |
| H13 | 66.51 | 65.61 | 65.83 | 66.93 | 65.88 |
| H14 | 58.09 | 60.24 | 60.56 | 60.51 | 61.27 |
| H15 | 55.76 | 60.13 | 58.46 | 59.77 | 60.06 |
| H16 | 77.72 | 78.99 | 79.28 | 81.33 | 79.58 |
| H17 | 56.94 | 58.45 | 60.25 | 60.07 | 59.83 |
| H18 | 63.96 | 65.28 | 66.19 | 65.49 | 67.79 |
| H19 | 52.42 | 54.05 | 56.08 | 56.58 | 56.71 |
| H20 | 71.42 | 72.48 | 71.23 | 74.28 | 73.96 |
| H21 | 65.06 | 65.80 | 66.57 | 67.28 | 66.47 |
| H23 | 76.15 | 80.20 | 81.28 | 82.53 | 80.70 |
| H24 | 59.84 | 59.10 | 59.57 | 59.37 | 59.67 |
| H25 | 63.27 | 63.01 | 64.22 | 63.70 | 63.53 |
| H26 | 57.89 | 60.08 | 61.95 | 62.92 | 62.31 |
| H28 | 59.87 | 60.76 | 60.47 | 61.04 | 59.63 |
| H29 | 62.08 | 63.44 | 64.73 | 65.48 | 66.44 |
| H30 | 71.29 | 72.35 | 71.80 | 74.77 | 73.85 |
| H32 | 75.55 | 76.28 | 77.09 | 79.06 | 78.48 |

Table 6. Fat mass (kg) assessed by DXA (kg)

| ID | FatMass_kg_BL | FatMass_kg_W4 | FatMass_kg_W8 | FatMass_kg_W10 | FatMass_kg_W12 |
|---|---|---|---|---|---|
| H02 | 12.80 | 13.45 | 13.17 | 13.06 | 12.51 |
| H03 | 17.60 | 18.18 | 18.19 | 17.64 | 17.39 |
| H04 | 18.40 | 17.39 | 17.75 | 18.04 | 17.68 |
| H05 | 13.30 | 13.53 | 13.54 | 13.40 | 12.97 |
| H07 | 12.80 | 12.66 | 13.02 | 14.18 | 13.87 |
| H09 | 8.50 | 8.50 | 9.05 | 9.11 | 9.29 |
| H10 | 16.90 | 16.72 | 16.66 | 16.16 | 15.98 |
| H11 | 22.60 | 22.52 | 22.75 | 23.87 | 24.11 |
| H12 | 6.34 | 6.24 | 6.09 | 6.03 | 5.87 |
| H13 | 17.92 | 17.75 | 17.29 | 17.15 | 17.69 |
| H14 | 14.87 | 13.64 | 13.11 | 13.44 | 13.57 |
| H15 | 21.56 | 21.07 | 21.76 | 22.57 | 22.86 |
| H16 | 13.71 | 12.56 | 12.91 | 13.46 | 12.63 |
| H17 | 14.47 | 14.52 | 14.03 | 13.91 | 13.42 |
| H18 | 19.73 | 19.50 | 18.85 | 18.56 | 18.45 |
| H19 | 16.60 | 15.75 | 15.54 | 15.45 | 14.97 |
| H20 | 24.45 | 25.66 | 26.90 | 25.25 | 25.82 |
| H21 | 16.45 | 16.60 | 16.74 | 16.73 | 16.55 |
| H23 | 31.55 | 31.77 | 31.15 | 30.71 | 31.77 |
| H24 | 10.59 | 11.02 | 11.69 | 11.43 | 11.87 |
| H25 | 16.29 | 16.46 | 16.23 | 15.87 | 15.88 |
| H26 | 8.35 | 8.04 | 8.11 | 7.77 | 7.61 |
| H28 | 10.99 | 10.62 | 10.15 | 10.15 | 9.75 |
| H29 | 10.07 | 10.68 | 11.85 | 12.82 | 10.09 |
| H30 | 22.15 | 21.52 | 22.82 | 21.04 | 22.21 |
| H32 | 21.06 | 20.16 | 18.59 | 18.19 | 17.59 |

Table 7. Muscle Thickness assessed by Ultrasound (mm)

| **ID** | MT BL | MT W4 | MT W8 | MT W10 | MT W12 | Delta | %increase |
|---|---|---|---|---|---|---|---|
| H02 | 27.6 | 27.5 | 27.0 | 27.5 | 26.8 | -0.8 | -2.9 |
| H03 | 31.5 | 32.3 | 34.2 | 33.5 | 33.7 | 2.2 | 7.1 |
| H04 | 26.3 | 28.6 | 29.6 | 29.5 | 27.8 | 1.5 | 5.8 |
| H05 | 27.3 | 31.1 | 32.4 | 33.8 | 31.7 | 4.4 | 16.3 |
| H07 | 30.1 | 32.2 | 32.5 | 33.5 | 33.1 | 3.1 | 10.2 |
| H09 | 28.8 | 30.4 | 30.1 | 29.8 | 29.5 | 0.7 | 2.4 |
| H10 | 29.6 | 31.0 | 32.0 | 32.3 | 30.3 | 0.7 | 2.3 |
| H11 | 32.1 | 34.3 | 35.9 | 36.2 | 34.8 | 2.7 | 8.4 |
| H12 | 30.0 | 32.0 | 34.7 | 35.0 | 33.1 | 3.1 | 10.5 |
| H13 | 27.6 | 30.1 | 29.0 | 28.7 | 28.3 | 0.8 | 2.9 |
| H14 | 33.8 | 33.7 | 33.9 | 29.9 | 32.8 | -1.0 | -2.8 |
| H15 | 26.1 | 25.7 | 26.4 | 26.2 | 27.3 | 1.2 | 4.6 |
| H16 | 33.1 | 34.3 | 33.2 | 35.8 | 33.8 | 0.8 | 2.4 |
| H17 | 30.2 | 33.9 | 33.4 | 35.1 | 34.6 | 4.5 | 14.8 |
| H18 | 29.7 | 28.9 | 30.2 | 32.2 | 30.9 | 1.3 | 4.3 |
| H19 | 27.6 | 30.0 | 33.0 | 32.6 | 33.0 | 5.5 | 19.8 |
| H20 | 33.4 | 34.7 | 33.6 | 34.7 | 34.3 | 0.9 | 2.6 |
| H21 | 31.3 | 31.9 | 34.6 | 32.0 | 33.2 | 1.9 | 6.0 |
| H23 | 34.3 | 37.2 | 37.2 | 35.7 | 37.2 | 2.9 | 8.4 |
| H24 | 32.9 | 31.7 | 33.4 | 33.7 | 32.4 | -0.5 | -1.5 |
| H25 | 30.5 | 29.8 | 30.5 | 31.0 | 30.5 | 0.0 | 0.1 |
| H26 | 32.2 | 33.4 | 35.6 | 35.7 | 34.5 | 2.3 | 7.3 |
| H28 | 30.2 | 28.7 | 32.5 | 32.1 | 30.1 | -0.2 | -0.6 |
| H29 | 33.0 | 33.0 | 34.5 | 33.5 | 33.3 | 0.4 | 1.2 |
| H30 | 33.6 | 32.2 | 33.0 | 33.6 | 33.7 | 0.1 | 0.2 |
| H32 | | 33.2 | 34.6 | 31.9 | 33.6 | | |

Table 8. Muscle CSA assessed by ultrasound ($cm^2$)

| **Participant ID** | Avrg_Pre | Avrg_Post | Percent_change |
|---|---|---|---|
| H02 | 30.3 | 31.3 | 1.0 |
| H04 | 28.1 | 29.9 | 1.8 |
| H11 | 35.5 | 37.1 | 1.5 |
| H13 | 30.2 | 32.0 | 1.8 |
| H15 | 21.7 | 24.3 | 2.6 |
| H16 | 37.3 | 39.1 | 1.8 |
| H19 | 32.4 | 36.9 | 4.5 |
| H21 | 34.7 | 35.1 | 0.4 |
| H23 | 44.3 | 49.1 | 4.7 |
| H26 | 36.8 | 40.5 | 3.8 |
| H28 | 37.4 | 38.3 | 1.0 |
| H29 | 37.8 | 40.1 | 2.3 |
| H03 | 28.8 | 31.1 | 2.4 |
| H05 | 31.8 | 34.1 | 2.3 |
| H07 | 38.5 | 39.5 | 1.0 |
| H09 | 30.4 | 32.1 | 1.8 |
| H10 | 30.5 | 31.7 | 1.2 |
| H12 | 36.1 | 39.7 | 3.6 |
| H14 | 31.1 | 32.0 | 0.9 |
| H17 | 33.4 | 38.1 | 4.7 |
| H18 | 32.3 | 33.0 | 0.8 |
| H20 | 43.5 | 48.3 | 4.8 |
| H24 | 36.0 | 38.5 | 2.6 |
| H25 | 34.7 | 35.7 | 1.0 |
| H30 | 36.8 | 38.8 | 2.0 |

Table 9. Wingate Peak Power (W)

| ID | PP BL | PPW4 | PPW8 | PPW9 | PPW10 | PPW12 |
|---|---|---|---|---|---|---|
| H02 | 940.00 | 965.00 | 887.00 | 908.00 | 934.00 | 971.00 |
| H03 | 1087.00 | 1239.00 | 1242.00 | 1169.00 | 1191.00 | 1177.00 |
| H04 | 941.00 | 1007.00 | 1028.00 | 1169.00 | 1031.00 | 968.00 |
| H05 | 932.00 | 980.00 | 1043.00 | 1055.00 | 930.00 | 918.00 |
| H07 | 1189.00 | 1191.00 | 1141.00 | 1084.00 | 1046.00 | 1095.00 |
| H09 | 772.00 | 902.00 | 713.00 | 809.00 | 732.00 | 815.00 |
| H10 | 1020.00 | 1017.00 | 1009.00 | 933.00 | 968.00 | 1049.00 |
| H11 | 1018.00 | 1103.00 | 1075.00 | 1025.00 | 988.00 | 1108.00 |
| H12 | 807.00 | 772.00 | 779.00 | 836.00 | 847.00 | 860.00 |
| H13 | 1128.00 | 1133.00 | 1139.00 | 1028.00 | 1154.00 | 1061.00 |
| H14 | 820.00 | 903.00 | 897.00 | 894.00 | 972.00 | 921.00 |
| H15 | 890.00 | 994.00 | 989.00 | 999.00 | 1063.00 | 1130.00 |
| H16 | 985.00 | 1066.00 | 1060.00 | 1043.00 | 1018.00 | 1118.00 |
| H17 | 813.00 | 913.00 | 887.00 | 1008.00 | 888.00 | 754.00 |
| H18 | 950.00 | 1041.00 | 1123.00 | 1119.00 | 987.00 | 1241.00 |
| H19 | 909.00 | 947.00 | 918.00 | 985.00 | 991.00 | |
| H20 | 1259.00 | 1312.00 | 1324.00 | 1360.00 | 1355.00 | 1231.00 |
| H21 | 942.00 | 1014.00 | 994.00 | 1043.00 | 1068.00 | 1019.00 |
| H23 | | 1218.00 | 1154.00 | 1160.00 | 1219.00 | 1343.00 |
| H24 | 794.00 | 871.00 | 882.00 | 764.00 | 818.00 | 921.00 |
| H25 | 1056.00 | 949.00 | 1250.00 | 1072.00 | 1100.00 | 1095.00 |
| H26 | 809.00 | 807.00 | 920.00 | 912.00 | 924.00 | 822.00 |
| H28 | 819.00 | 905.00 | 958.00 | 889.00 | 918.00 | |
| H29 | 870.00 | 942.00 | 912.00 | 945.00 | 935.00 | 1022.00 |
| H30 | 1265.00 | 1236.00 | 1313.00 | 1225.00 | 1266.00 | 1322.00 |
| H32 | 1026.00 | 1185.00 | 1283.00 | 1253.00 | 1312.00 | 1213.00 |

Table 10. Squat 1-RM (kg)

| ID | Squat_BL | Squat_W4 | Squat_W8 | Squat_W9 | Squat_W10 | Squat_W12 |
|---|---|---|---|---|---|---|
| H02 | 156.53 | 165.61 | 172.41 | 174.68 | 174.68 | 174.68 |
| H03 | 129.31 | 154.26 | 167.88 | 167.88 | 167.88 | 172.41 |
| H04 | 106.62 | 129.31 | 136.12 | 136.12 | 129.31 | 133.85 |
| H05 | 127.04 | 156.53 | 163.34 | 167.88 | 172.41 | 172.41 |
| H07 | 156.53 | 176.95 | 183.76 | 179.22 | 183.76 | 192.83 |
| H09 | 120.24 | 140.65 | 149.73 | 156.53 | 145.19 | 156.53 |
| H10 | 117.97 | 127.04 | 142.92 | 142.92 | 133.85 | 142.92 |
| H11 | 115.70 | 142.92 | 142.92 | 147.46 | 152.00 | 156.53 |
| H12 | 147.46 | 152.00 | 156.53 | 142.92 | 156.53 | 165.61 |
| H13 | 152.00 | 156.53 | 156.53 | 156.53 | 142.92 | 156.53 |
| H14 | 129.31 | 142.92 | 152.00 | 152.00 | 156.53 | 156.53 |
| H15 | 115.70 | 142.92 | 147.46 | 142.92 | 133.85 | 156.53 |
| H16 | 183.76 | 204.17 | 208.71 | 208.71 | 208.71 | 210.98 |
| H17 | 133.85 | 142.92 | 138.38 | 142.92 | 142.92 | 152.00 |
| H18 | 124.77 | 133.85 | 142.92 | 133.85 | 142.92 | 152.00 |
| H19 | 124.77 | 138.38 | 149.73 | 149.73 | 152.00 | 165.61 |
| H20 | 179.22 | 188.29 | 192.83 | 192.83 | 197.37 | 206.44 |
| H21 | 170.15 | 188.29 | 195.10 | 197.37 | 190.56 | 210.98 |
| H23 | 161.07 | 183.76 | 206.44 | 188.29 | 206.44 | 215.52 |
| H24 | 165.61 | 174.68 | 174.68 | 183.76 | 188.29 | 199.64 |
| H25 | 142.92 | 156.53 | 170.15 | 165.61 | 174.68 | 179.22 |
| H26 | 133.85 | 172.41 | 183.76 | 188.29 | 197.37 | 206.44 |
| H28 | 111.16 | 120.24 | 142.92 | 136.12 | 136.12 | 133.85 |
| H29 | 142.92 | 154.26 | 161.07 | 156.53 | 149.73 | 176.95 |
| H30 | 152.00 | 172.41 | 174.68 | 179.22 | 188.29 | 204.17 |
| H32 | 133.85 | 142.92 | 156.53 | 152.00 | 161.07 | 170.15 |

Table 11. Bench 1-RM (kg)

| ID | Bench_BL | Bench_W4 | Bench_W8 | Bench_W9 | Bench_W10 | Bench_W12 |
|---|---|---|---|---|---|---|
| H02 | 117.97 | 117.97 | | | 106.62 | 120.24 |
| H03 | 70.33 | 79.40 | 83.94 | 83.94 | 83.94 | 86.21 |
| H04 | 97.55 | 102.09 | 104.36 | 104.36 | 108.89 | 106.62 |
| H05 | 79.40 | 83.94 | 95.28 | 97.55 | 97.55 | 97.55 |
| H07 | 120.24 | 124.77 | 129.31 | 124.77 | 129.31 | 133.85 |
| H09 | 97.55 | 102.09 | 106.62 | 102.09 | 106.62 | 106.62 |
| H10 | 93.01 | 102.09 | 108.89 | 111.16 | 106.62 | 106.62 |
| H11 | 83.94 | 88.48 | 93.01 | 111.16 | 97.55 | 97.55 |
| H12 | 93.01 | 102.09 | 102.09 | 102.09 | 102.09 | 108.89 |
| H13 | 102.09 | 97.55 | 106.62 | 106.62 | 102.09 | 106.62 |
| H14 | 108.89 | 117.97 | 124.77 | 124.77 | 115.70 | 122.50 |
| H15 | 79.40 | 83.94 | 86.21 | 83.94 | 83.94 | 88.48 |
| H16 | 129.31 | 129.31 | 133.85 | 133.85 | 129.31 | 136.12 |
| H17 | 93.01 | 97.55 | 106.62 | 102.09 | 102.09 | 106.62 |
| H18 | 93.01 | 95.28 | 97.55 | 93.01 | 93.01 | 95.28 |
| H19 | 88.48 | 93.01 | 102.09 | 102.09 | 97.55 | 102.09 |
| H20 | 138.38 | 142.92 | 152.00 | 147.46 | 142.92 | 152.00 |
| H21 | 142.92 | 152.00 | 161.07 | 156.53 | 161.07 | 172.41 |
| H23 | 106.62 | 124.77 | 124.77 | 120.24 | 124.77 | 124.77 |
| H24 | 99.82 | 102.09 | 104.36 | 104.36 | 104.36 | 102.09 |
| H25 | 115.70 | 120.24 | 122.50 | 122.50 | 122.50 | 122.50 |
| H26 | 88.48 | 97.55 | 102.09 | 102.09 | 102.09 | 102.09 |
| H28 | 83.94 | 88.48 | 90.74 | 88.48 | 90.74 | 88.48 |
| H29 | 113.43 | 117.97 | 120.24 | 115.70 | 120.24 | 122.50 |
| H30 | 97.55 | 106.62 | 102.09 | 106.62 | 108.89 | 108.89 |
| H32 | 88.48 | 97.55 | 102.09 | 97.55 | 97.55 | 99.82 |

Table 12. Deadlift1-RM (kg)

| ID | Deads_BL | Deads_W4 | Deads_W8 | Deads_W9 | Deads_W10 | Deads_W12 |
|---|---|---|---|---|---|---|
| H02 | 156.53 | 172.41 | 179.22 | 156.53 | 165.61 | 174.68 |
| H03 | 156.53 | 174.68 | 174.68 | 179.22 | 165.61 | 170.15 |
| H04 | 154.26 | 147.46 | 156.53 | 167.88 | 167.88 | 183.76 |
| H05 | 147.46 | 165.61 | 172.41 | 174.68 | 183.76 | 190.56 |
| H07 | 176.95 | 197.37 | 201.91 | 197.37 | 206.44 | 210.98 |
| H09 | 152.00 | 165.61 | 170.15 | 174.68 | 170.15 | 176.95 |
| H10 | 102.09 | 124.77 | 129.31 | 138.38 | 124.77 | 138.38 |
| H11 | 145.19 | 158.80 | 170.15 | 138.38 | 179.22 | 183.76 |
| H12 | 133.85 | 120.24 | 142.92 | 142.92 | 124.77 | 142.92 |
| H13 | 142.92 | 152.00 | 165.61 | 165.61 | 142.92 | 174.68 |
| H14 | 142.92 | 142.92 | 158.80 | 142.92 | 152.00 | 161.07 |
| H15 | 142.92 | 165.61 | 179.22 | 165.61 | 161.07 | 179.22 |
| H16 | 206.44 | 224.59 | 231.40 | 231.40 | 231.40 | 235.93 |
| H17 | 133.85 | 138.38 | 142.92 | 142.92 | 142.92 | 147.46 |
| H18 | 129.31 | 138.38 | 138.38 | 133.85 | 133.85 | 142.92 |
| H19 | 133.85 | 152.00 | 156.53 | 152.00 | 156.53 | 163.34 |
| H20 | 192.83 | 206.44 | 210.98 | 197.37 | 206.44 | 215.52 |
| H21 | 192.83 | 199.64 | 204.17 | 206.44 | 197.37 | 215.52 |
| H23 | 165.61 | 206.44 | 215.52 | 215.52 | 215.52 | 233.67 |
| H24 | 165.61 | 170.15 | 183.76 | 183.76 | 183.76 | 186.03 |
| H25 | 165.61 | 174.68 | 183.76 | 201.91 | 192.83 | 206.44 |
| H26 | 115.70 | 170.15 | 183.76 | 183.76 | 183.76 | 188.29 |
| H28 | 147.46 | 152.00 | 142.92 | 147.46 | 142.92 | 133.85 |
| H29 | 142.92 | 156.53 | 174.68 | 152.00 | 152.00 | 192.83 |
| H30 | 165.61 | 183.76 | 192.83 | 192.83 | 183.76 | 206.44 |
| H32 | 165.61 | 174.68 | 183.76 | 174.68 | 174.68 | 192.83 |

Table 13. Total Strength (sum of Squat, Bench press and Deadlift) 1-RM (kg)

| ID | Total_BL | Total_W4 | Total_W8 | Total_W9 | Total_W10 | Total_W12 |
|---|---|---|---|---|---|---|
| H02 | 431.03 | 455.99 | | | 446.91 | 469.60 |
| H03 | 356.17 | 408.35 | 426.50 | 431.03 | 417.42 | 428.77 |
| H04 | 358.44 | 378.86 | 397.01 | 408.35 | 406.08 | 424.23 |
| H05 | 353.90 | 406.08 | 431.03 | 440.11 | 453.72 | 460.53 |
| H07 | 453.72 | 499.09 | 514.97 | 501.36 | 519.51 | 537.66 |
| H09 | 369.78 | 408.35 | 426.50 | 433.30 | 421.96 | 440.11 |
| H10 | 313.07 | 353.90 | 381.13 | 392.47 | 365.25 | 387.93 |
| H11 | 344.83 | 390.20 | 406.08 | 397.01 | 428.77 | 437.84 |
| H12 | 374.32 | 374.32 | 401.54 | 387.93 | 383.39 | 417.42 |
| H13 | 397.01 | 406.08 | 428.77 | 428.77 | 387.93 | 437.84 |
| H14 | 381.13 | 403.81 | 435.57 | 419.69 | 424.23 | 440.11 |
| H15 | 338.02 | 392.47 | 412.89 | 392.47 | 378.86 | 424.23 |
| H16 | 519.51 | 558.08 | 573.96 | 573.96 | 569.42 | 583.03 |
| H17 | 360.71 | 378.86 | 387.93 | 387.93 | 387.93 | 406.08 |
| H18 | 347.10 | 367.51 | 378.86 | 360.71 | 369.78 | 390.20 |
| H19 | 347.10 | 383.39 | 408.35 | 403.81 | 406.08 | 431.03 |
| H20 | 510.44 | 537.66 | 555.81 | 537.66 | 546.73 | 573.96 |
| H21 | 505.90 | 539.93 | 560.34 | 560.34 | 549.00 | 598.91 |
| H23 | 433.30 | 514.97 | 546.73 | 524.05 | 546.73 | 573.96 |
| H24 | 431.03 | 446.91 | 462.79 | 471.87 | 476.41 | 487.75 |
| H25 | 424.23 | 451.45 | 476.41 | 490.02 | 490.02 | 508.17 |
| H26 | 338.02 | 440.11 | 469.60 | 474.14 | 483.21 | 496.82 |
| H28 | 342.56 | 360.71 | 376.59 | 372.05 | 369.78 | 356.17 |
| H29 | 399.27 | 428.77 | 455.99 | 424.23 | 421.96 | 492.29 |
| H30 | 415.15 | 462.79 | 469.60 | 478.68 | 480.94 | 519.51 |
| H32 | 387.93 | 415.15 | 442.38 | 424.23 | 433.30 | 462.79 |

Table 14. OptoJump Values (W/kg)

| **Participant ID** | Apower_W0 | W8 | W9 |
|---|---|---|---|
| H02 | 13.7 | 13.6 | 13.7 |
| H03 | 13.9 | 14.7 | 14.5 |
| H04 | 13.1 | 18.3 | 16.0 |
| H05 | 17.6 | 17.5 | 18.0 |
| H07 | 14.6 | 14.7 | 14.7 |
| H09 | 13.8 | 13.2 | 15.3 |
| H10 | 13.6 | 14.0 | 13.2 |
| H11 | 12.9 | 13.4 | 14.1 |
| H12 | 14.8 | 16.3 | 16.9 |
| H13 | 11.7 | 14.3 | 13.9 |
| H14 | 14.5 | 14.9 | 15.2 |
| H15 | 13.8 | 13.4 | 12.7 |
| H16 | 15.3 | 24.5 | 16.6 |
| H17 | 13.8 | 15.6 | 18.1 |
| H18 | 14.6 | 16.9 | 15.7 |
| H19 | 18.3 | 17.2 | 18.9 |
| H20 | 15.6 | 16.0 | 15.9 |
| H21 | 15.3 | 15.5 | 15.6 |
| H23 | 11.9 | 14.5 | 14.9 |
| H24 | 16.0 | 14.0 | 15.4 |
| H25 | 15.1 | 15.7 | 15.8 |
| H26 | 14.8 | 17.6 | 19.0 |
| H28 | 14.7 | 14.8 | 15.5 |
| H29 | 17.3 | 15.9 | 15.8 |
| H30 | 16.8 | 14.0 | 18.0 |
| H32 | 14.6 | 15.4 | 15.1 |

Table 15. Activity levels of CK

| ID | CK_BL | CK_W4 | CK_W8 | CK_W9 | CK_W10 | CK_W12 |
|---|---|---|---|---|---|---|
| H02 | 200 | 226 | 190 | 333 | 376 | 887 |
| H03 | 262 | 239 | 265 | 514 | 413 | 749 |
| H04 | 124 | 150 | 154 | 250 | 174 | 223 |
| H05 | 100 | 130 | 188 | 366 | 257 | 231 |
| H07 | 153 | 320 | 155 | 332 | 182 | 202 |
| H09 | 273 | 210 | 232 | 625 | 450 | 248 |
| H10 | 292 | 261 | 272 | 414 | 523 | 205 |
| H11 | 225 | 366 | 337 | 389 | 431 | 274 |
| H12 |  | 298 | 235 | 710 | 576 | 277 |
| H13 | 132 | 69 | 93 | 216 | 155 | 142 |
| H14 | 250 | 133 | 124 | 217 | 96 | 130 |
| H15 | 199 | 134 | 147 | 220 | 290 | 155 |
| H16 | 439 | 132 | 207 | 424 | 240 | 196 |
| H17 | 262 | 144 | 127 | 350 | 251 | 136 |
| H18 | 249 | 169 | 89 | 177 | 310 | 135 |
| H19 | 225 | 240 | 228 | 535 | 476 | 230 |
| H20 | 185 | 264 | 271 | 731 | 428 | 225 |
| H21 | 248 | 235 | 275 | 551 | 513 | 159 |
| H23 | 114 | 161 | 135 | 233 | 267 | 137 |
| H24 | 437 | 237 | 288 | 782 | 607 | 218 |
| H25 | 394 | 514 | 264 | 473 | 405 | 201 |
| H26 | 478 | 167 | 263 | 816 | 664 | 254 |
| H28 | 128 | 230 | 320 | 861 | 436 | 89 |
| H29 | 228 | 184 | 168 | 987 | 305 | 104 |
| H30 | 107 | 203 | 138 | 422 | 725 | 443 |
| H32 | 302 | 105 | 136 | 231 | 210 | 105 |

Table 16. Concentration of Cortisol (nM)

| ID | Cortisol_BL | Cortisol_W4 | Cortisol_W8 | Cortisol_W9 | Cortisol_W10 | Cortisol_W12 |
|---|---|---|---|---|---|---|
| **H02** | 20.8 | 24.6 | 21 | 37 | 19 | 18.9 |
| **H03** | 24.2 | 19.4 | 22.1 | 21.4 | 42.8 | 18 |
| **H04** | 15.2 | 19.3 | 23.7 | 36 | 22.1 | 26.5 |
| **H05** | 15.9 | 20.3 | 19.2 | 23.4 | 28.5 | 30.1 |
| **H07** | 19.7 | 21.9 | 23.5 | 23.1 | 32.3 | 34 |
| **H09** | 23.2 | 23.4 | 20.2 | 44.2 | 24.2 | 30.1 |
| **H10** | 16.3 | 21.2 | 21.6 | 43.4 | 21.3 | 15.3 |
| **H11** | 24.4 | 15.2 | 17.4 | 40.6 | 36.1 | 16.4 |
| **H12** | 24.6 | 23.9 | 19.5 | 39.6 | 34.9 | 26.1 |
| **H13** | 17.9 | 22.7 | 24.3 | 44.1 | 18.6 | 23.7 |
| **H14** | 23.5 | 16.2 | 20.2 | 24.8 | 44.7 | 23.3 |
| **H15** | 24.4 | 18.5 | 22.5 | 24.3 | 25.7 | 18.4 |
| **H16** | 21.9 | 18.3 | 15.9 | 32.8 | 22.8 | 32.8 |
| **H17** | 21 | 23.1 | 23.6 | 36.3 | 44.6 | 15.3 |
| **H18** | 17.9 | 16.1 | 17 | 30 | 21.9 | 30.6 |
| **H19** | 19.4 | 23.5 | 20.1 | 20.6 | 33.4 | 17.5 |
| **H20** | 21.3 | 15.7 | 18.3 | 24.5 | 23.8 | 20.5 |
| **H21** | 20.7 | 21.5 | 18.5 | 17.6 | 32 | 29.7 |
| **H23** | 20 | 20.6 | 19.7 | 31.8 | 28.9 | 22.9 |
| **H24** | 18.1 | 19.6 | 21.9 | 30.8 | 15.8 | 17.8 |
| **H25** | 23.5 | 18 | 21.7 | 27.2 | 17.4 | 18.9 |
| **H26** | 15.7 | 19.3 | 18.2 | 33.5 | 28.3 | 26.1 |
| **H28** | 21.2 | 19.6 | 18.4 | 40.5 | 39.3 | 24.6 |
| **H29** | 20.1 | 16.6 | 24.1 | 15.8 | 41.2 | 32.8 |
| **H30** | 18.8 | 22.9 | 15.8 | 23.4 | 33.8 | 29.3 |
| **H32** | 15.6 | 23.5 | 18.9 | 26.2 | 31.1 | 27.7 |

Table 17. Growth Hormone

| **ID** | GH_BL | GH_W4 | GH_W8 | GH_W9 | GH_W10 | GH_W12 |
|---|---|---|---|---|---|---|
| H03 | 3.80 | 3.00 | 4.20 | 2.00 | 1.10 | 2.20 |
| H05 | 2.30 | 4.70 | 3.80 | 2.60 | 2.60 | 2.90 |
| H07 | 4.00 | 3.40 | 3.30 | 3.80 | 4.00 | 2.10 |
| H09 | 4.80 | 3.30 | 4.70 | 3.30 | 3.40 | 2.30 |
| H10 | 3.80 | 2.60 | 4.60 | 4.80 | 1.50 | 4.00 |
| H12 | 2.40 | 3.80 | 4.50 | 2.60 | 2.40 | 3.90 |
| H14 | 3.00 | 3.70 | 3.30 | 3.50 | 2.00 | 4.80 |
| H17 | 2.20 | 4.70 | 2.40 | 3.30 | 2.00 | 2.10 |
| H18 | 4.20 | 3.60 | 3.00 | 2.00 | 3.50 | 2.70 |
| H20 | 3.90 | 4.40 | 2.90 | 2.70 | 2.90 | 2.20 |
| H24 | 2.40 | 4.70 | 2.50 | 4.90 | 2.20 | 3.10 |
| H25 | 3.70 | 2.80 | 2.60 | 3.70 | 2.30 | 3.10 |
| H30 | 2.50 | 4.10 | 4.60 | 2.90 | 1.80 | 2.80 |
| H02 | 2.80 | 2.20 | 3.80 | 2.40 | 2.30 | 2.50 |
| H04 | 2.60 | 3.10 | 2.90 | 3.20 | 2.40 | 3.70 |
| H11 | 2.90 | 2.10 | 4.20 | 2.60 | 3.60 | 2.20 |
| H13 | 3.50 | 2.00 | 4.10 | 3.70 | 3.00 | 3.10 |
| H15 | 4.70 | 2.80 | 3.60 | 3.50 | 4.70 | 2.70 |
| H16 | 3.20 | 3.90 | 4.60 | 3.50 | 4.60 | 3.70 |
| H19 | 4.90 | 4.60 | 2.30 | 2.40 | 4.10 | 4.30 |
| H21 | 4.30 | 3.20 | 2.70 | 2.70 | 4.30 | 4.40 |
| H23 | 4.40 | 4.10 | 3.60 | 3.20 | 4.30 | 3.10 |
| H26 | 4.30 | 3.10 | 3.70 | 2.80 | 2.60 | 4.80 |
| H28 | 3.40 | 4.90 | 4.70 | 2.50 | 2.00 | 2.40 |
| H29 | 3.70 | 2.10 | 3.40 | 3.10 | 1.30 | 2.70 |
| H32 | 3.30 | 2.40 | 2.30 | 3.60 | 2.00 | 2.80 |

Table 18. IGF1

| **ID** | IGF1_BL | IGF1_W4 | IGF1_W8 | IGF1_W9 | IGF1_W10 | IGF1_W12 |
|---|---|---|---|---|---|---|
| H03 | 405.00 | 204.10 | 424.20 | 468.10 | 293.20 | 256.00 |
| H05 | 328.70 | 417.90 | 328.30 | 302.50 | 435.90 | 221.30 |
| H07 | 363.10 | 270.50 | 450.30 | 543.90 | 456.00 | 556.30 |
| H09 | 326.40 | 507.00 | 316.50 | 366.30 | 166.50 | 272.50 |
| H10 | 434.50 | 310.30 | 479.20 | 295.50 | 291.30 | 281.50 |
| H12 | 233.20 | 303.20 | 252.40 | 379.80 | 347.00 | 491.90 |
| H14 | 238.90 | 527.80 | 259.80 | 213.70 | 324.60 | 479.30 |
| H17 | 299.70 | 283.20 | 547.20 | 280.50 | 186.10 | 279.40 |
| H18 | 340.50 | 586.80 | 209.70 | 231.10 | 214.60 | 245.80 |
| H20 | 575.60 | 350.50 | 337.30 | 389.50 | 294.40 | 266.80 |
| H24 | 202.20 | 412.50 | 450.50 | 326.70 | 393.80 | 259.70 |
| H25 | 514.90 | 576.70 | 442.20 | 478.60 | 331.20 | 321.80 |
| H30 | 354.90 | 537.20 | 439.20 | 581.10 | 409.70 | 557.60 |
| H02 | 437.50 | 463.50 | 572.80 | 260.40 | 257.90 | 404.20 |
| H04 | 333.00 | 261.40 | 313.70 | 320.60 | 371.90 | 379.60 |
| H11 | 519.90 | 327.70 | 203.60 | 244.10 | 198.00 | 256.40 |
| H13 | 345.10 | 520.60 | 472.00 | 484.60 | 407.10 | 486.80 |
| H15 | 456.40 | 217.80 | 591.60 | 228.30 | 448.50 | 238.60 |
| H16 | 254.40 | 341.30 | 467.80 | 235.60 | 182.70 | 263.20 |
| H19 | 520.80 | 526.60 | 419.00 | 589.30 | 367.80 | 534.20 |
| H21 | 332.90 | 372.00 | 320.70 | 563.20 | 193.90 | 369.90 |
| H23 | 359.70 | 402.90 | 387.70 | 359.50 | 296.60 | 365.50 |
| H26 | 478.00 | 373.30 | 233.70 | 557.00 | 172.00 | 335.50 |
| H28 | 231.90 | 387.00 | 259.30 | 372.40 | 478.80 | 575.20 |
| H29 | 334.10 | 456.10 | 401.90 | 201.80 | 454.90 | 249.40 |
| H32 | 266.80 | 554.90 | 472.80 | 312.30 | 231.40 | 516.90 |

Table 19. Total testosterone

| ID | Total Test BL | Total Test W4 | Total Test W8 | Total Test W9 | Total Test W10 | Total Test W12 |
|---|---|---|---|---|---|---|
| H03 | 657.70 | 637.40 | 797.90 | 704.10 | 524.10 | 715.20 |
| H05 | 753.70 | 768.20 | 758.90 | 732.70 | 521.40 | 640.00 |
| H07 | 630.40 | 775.60 | 720.30 | 692.50 | 581.70 | 657.10 |
| H09 | 659.10 | 723.50 | 656.20 | 650.30 | 406.60 | 795.70 |
| H10 | 730.40 | 662.20 | 760.60 | 561.70 | 575.10 | 751.30 |
| H12 | 621.90 | 788.00 | 743.30 | 632.50 | 444.60 | 769.50 |
| H14 | 780.30 | 737.10 | 677.70 | 768.50 | 580.50 | 696.50 |
| H17 | 708.20 | 606.00 | 773.80 | 651.70 | 570.50 | 734.60 |
| H18 | 614.20 | 675.60 | 714.00 | 663.30 | 546.70 | 642.90 |
| H20 | 723.30 | 600.50 | 712.70 | 564.90 | 548.80 | 640.40 |
| H24 | 684.30 | 710.20 | 780.50 | 676.40 | 591.10 | 725.50 |
| H25 | 694.90 | 645.20 | 752.30 | 680.20 | 446.60 | 657.90 |
| H30 | 608.80 | 724.60 | 630.10 | 622.10 | 410.60 | 294.50 |
| H02 | 792.40 | 719.60 | 612.40 | 711.40 | 514.80 | 644.10 |
| H04 | 763.00 | 756.50 | 622.50 | 696.90 | 387.60 | 454.40 |
| H11 | 619.60 | 647.60 | 796.90 | 654.60 | 221.10 | 702.70 |
| H13 | 756.00 | 700.70 | 716.70 | 718.70 | 447.50 | 699.10 |
| H15 | 653.70 | 655.20 | 793.40 | 762.10 | 564.60 | 784.50 |
| H16 | 731.20 | 662.70 | 610.60 | 624.50 | 472.90 | 430.10 |
| H19 | 790.10 | 770.40 | 715.40 | 603.30 | 581.90 | 676.50 |
| H21 | 700.50 | 690.50 | 730.20 | 664.00 | 520.50 | 708.70 |
| H23 | 632.60 | 736.40 | 643.50 | 510.20 | 534.50 | 762.90 |
| H26 | 659.80 | 644.90 | 675.50 | 647.80 | 533.20 | 654.50 |
| H28 | 750.60 | 755.50 | 750.40 | 643.30 | 457.50 | 660.90 |
| H29 | 760.20 | 644.10 | 653.40 | 521.60 | 557.30 | 647.50 |
| H32 | 727.10 | 682.50 | 698.80 | 716.80 | 430.30 | 725.30 |

Table 20. free testosterone

| **ID** | freeTest BL | freeTest W4 | freeTest W8 | freeTest W9 | freeTest W10 | freeTest W12 |
|---|---|---|---|---|---|---|
| H03 | 9.60 | 14.70 | 9.50 | 7.50 | 9.40 | 10.00 |
| H05 | 5.20 | 7.50 | 9.20 | 6.80 | 6.20 | 10.90 |
| H07 | 7.80 | 10.40 | 13.90 | 9.20 | 3.60 | 14.40 |
| H09 | 9.10 | 11.20 | 9.60 | 7.90 | 4.90 | 13.00 |
| H10 | 5.90 | 13.80 | 13.10 | 8.90 | 8.30 | 9.00 |
| H12 | 12.10 | 13.70 | 14.90 | 9.10 | 4.80 | 7.80 |
| H14 | 14.70 | 5.30 | 8.50 | 8.30 | 9.20 | 12.90 |
| H17 | 8.00 | 11.00 | 6.50 | 9.30 | 3.70 | 11.90 |
| H18 | 7.00 | 12.10 | 5.60 | 3.30 | 5.20 | 10.70 |
| H20 | 5.30 | 6.40 | 8.30 | 5.80 | 7.50 | 5.20 |
| H24 | 5.20 | 5.00 | 6.40 | 9.10 | 4.30 | 5.40 |
| H25 | 6.50 | 12.10 | 7.50 | 4.40 | 6.10 | 5.50 |
| H30 | 13.50 | 5.10 | 14.30 | 8.70 | 4.80 | 6.00 |
| H02 | 12.00 | 13.60 | 5.10 | 6.90 | 8.90 | 5.70 |
| H04 | 9.60 | 10.00 | 12.60 | 3.50 | 8.40 | 8.00 |
| H11 | 8.20 | 9.10 | 8.70 | 9.30 | 6.40 | 5.80 |
| H13 | 5.00 | 10.80 | 6.00 | 6.60 | 8.10 | 9.20 |
| H15 | 7.30 | 10.10 | 10.70 | 7.30 | 9.60 | 6.70 |
| H16 | 14.70 | 13.40 | 5.10 | 8.30 | 8.30 | 7.10 |
| H19 | 13.20 | 12.40 | 8.10 | 7.40 | 6.40 | 5.70 |
| H21 | 14.90 | 7.10 | 14.30 | 9.40 | 7.70 | 8.80 |
| H23 | 9.40 | 9.70 | 8.80 | 7.40 | 5.40 | 9.50 |
| H26 | 10.30 | 13.10 | 6.60 | 5.90 | 3.40 | 6.50 |
| H28 | 10.40 | 13.50 | 12.60 | 9.20 | 3.90 | 12.80 |
| H29 | 6.10 | 5.30 | 6.40 | 3.10 | 4.20 | 9.70 |
| H32 | 13.70 | 13.50 | 14.70 | 7.80 | 7.20 | 14.70 |

# Appendix B: Statistical Outputs

## Objective 1. Baseline characteristics: Body composition

**Independent Samples Test**

| | | Levene's Test for Equality of Variances | | t-test for Equality of Means | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | 95% Confidence Interval of the Difference | |
| | | F | Sig. | t | df | Sig. (2-tailed) | Mean Difference | Std. Error Difference | Lower | Upper |
| Age | Equal variances assumed | 4.608 | .042 | -.354 | 24 | .726 | -.30769 | .86915 | -2.10153 | 1.48615 |
| | Equal variances not assumed | | | -.354 | 16.991 | .728 | -.30769 | .86915 | -2.14152 | 1.52613 |
| Height | Equal variances assumed | .001 | .971 | -.138 | 24 | .891 | -.30769 | 2.22590 | -4.90173 | 4.28634 |
| | Equal variances not assumed | | | -.138 | 23.952 | .891 | -.30769 | 2.22590 | -4.90221 | 4.28682 |
| DXA_BM_kg_BL | Equal variances assumed | .680 | .418 | -.416 | 24 | .681 | -1.87154 | 4.49425 | -11.14722 | 7.40415 |
| | Equal variances not assumed | | | -.416 | 22.014 | .681 | -1.87154 | 4.49425 | -11.19170 | 7.44863 |
| DXA_FBFM_kg_BL | Equal variances assumed | 2.636 | .117 | .064 | 24 | .949 | .18538 | 2.88197 | -5.76271 | 6.13348 |
| | Equal variances not assumed | | | .064 | 20.740 | .949 | .18538 | 2.88197 | -5.81258 | 6.18335 |
| DXA_FatMass_kg_BL | Equal variances assumed | .416 | .525 | -.872 | 24 | .392 | -1.98308 | 2.27321 | -6.67474 | 2.70859 |
| | Equal variances not assumed | | | -.872 | 22.997 | .392 | -1.98308 | 2.27321 | -6.68560 | 2.71945 |
| DXA_FatM_percent_BL | Equal variances assumed | 1.183 | .288 | -1.000 | 24 | .327 | -2.06923 | 2.06899 | -6.33942 | 2.20095 |
| | Equal variances not assumed | | | -1.000 | 22.851 | .328 | -2.06923 | 2.06899 | -6.35081 | 2.21234 |

## Objective 1.1. Baseline characteristics: Strength and Strength normalized to Body Mass

**Independent Samples Test**

| | | Levene's Test for Equality of Variances | | t-test for Equality of Means | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | 95% Confidence Interval of the Difference | |
| | | F | Sig. | t | df | Sig. (2-tailed) | Mean Difference | Std. Error Difference | Lower | Upper |
| Squat_BL | Equal variances assumed | 1.252 | .274 | .164 | 24 | .871 | 1.39615 | 8.52292 | -16.19429 | 18.98660 |
| | Equal variances not assumed | | | .164 | 22.522 | .871 | 1.39615 | 8.52292 | -16.25557 | 19.04788 |
| Bench_BL | Equal variances assumed | .436 | .515 | -.240 | 24 | .813 | -1.74692 | 7.28453 | -16.78146 | 13.28761 |
| | Equal variances not assumed | | | -.240 | 23.757 | .813 | -1.74692 | 7.28453 | -16.78960 | 13.29576 |
| Deads_BL | Equal variances assumed | .012 | .913 | -.394 | 24 | .697 | -3.66308 | 9.30636 | -22.87046 | 15.54431 |
| | Equal variances not assumed | | | -.394 | 23.991 | .697 | -3.66308 | 9.30636 | -22.87085 | 15.54469 |
| Total_BL | Equal variances assumed | .180 | .675 | -.177 | 24 | .861 | -4.01308 | 22.62341 | -50.70549 | 42.67934 |
| | Equal variances not assumed | | | -.177 | 23.452 | .861 | -4.01308 | 22.62341 | -50.76332 | 42.73717 |
| Squat_kg_kg_BM_BL | Equal variances assumed | 2.131 | .157 | .474 | 24 | .640 | .04923 | .10388 | -.16517 | .26363 |
| | Equal variances not assumed | | | .474 | 22.970 | .640 | .04923 | .10388 | -.16568 | .26414 |
| Bench_kg_kg_BM_BL | Equal variances assumed | .355 | .557 | -.033 | 24 | .974 | -.00308 | .09202 | -.19300 | .18684 |
| | Equal variances not assumed | | | -.033 | 22.939 | .974 | -.00308 | .09202 | -.19346 | .18731 |
| Deadlift_kg_kg_BM_BL | Equal variances assumed | .033 | .858 | -.075 | 24 | .941 | -.00769 | .10218 | -.21858 | .20320 |
| | Equal variances not assumed | | | -.075 | 23.742 | .941 | -.00769 | .10218 | -.21870 | .20332 |
| TotalVol_kg_kg_BM_BL | Equal variances assumed | .196 | .662 | .153 | 24 | .880 | .04077 | .26711 | -.51051 | .59205 |
| | Equal variances not assumed | | | .153 | 23.459 | .880 | .04077 | .26711 | -.51119 | .59273 |

## Objective 2. Change in FBFM following Training

**Independent Samples Test**

| | | Levene's Test for Equality of Variances | | t-test for Equality of Means | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | 95% Confidence Interval of the Difference | |
| | | F | Sig. | t | df | Sig. (2-tailed) | Mean Difference | Std. Error Difference | Lower | Upper |
| Delta_FBFM | Equal variances assumed | 4.865 | .037 | -.553 | 24 | .586 | -.33923 | .61397 | -1.60640 | .92794 |
| | Equal variances not assumed | | | -.553 | 20.715 | .587 | -.33923 | .61397 | -1.61712 | .93866 |

## Objective 2.1 Repeated Measures ANOVA (time within, groups between) FBFM

**Multivariate Tests[a]**

| Effect | | Value | F | Hypothesis df | Error df | Sig. |
|---|---|---|---|---|---|---|
| Time | Pillai's Trace | .728 | 64.121[b] | 1.000 | 24.000 | .000 |
| | Wilks' Lambda | .272 | 64.121[b] | 1.000 | 24.000 | .000 |
| | Hotelling's Trace | 2.672 | 64.121[b] | 1.000 | 24.000 | .000 |
| | Roy's Largest Root | 2.672 | 64.121[b] | 1.000 | 24.000 | .000 |
| Time * Code | Pillai's Trace | .013 | .306[b] | 1.000 | 24.000 | .586 |
| | Wilks' Lambda | .987 | .306[b] | 1.000 | 24.000 | .586 |
| | Hotelling's Trace | .013 | .306[b] | 1.000 | 24.000 | .586 |
| | Roy's Largest Root | .013 | .306[b] | 1.000 | 24.000 | .586 |

a. Design: Intercept + Code
Within Subjects Design: Time

b. Exact statistic

**Tests of Within-Subjects Effects**

Measure: MEASURE_1

| Source | | Type III Sum of Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|---|
| Time | Sphericity Assumed | 78.499 | 1 | 78.499 | 64.121 | .000 |
| | Greenhouse-Geisser | 78.499 | 1.000 | 78.499 | 64.121 | .000 |
| | Huynh-Feldt | 78.499 | 1.000 | 78.499 | 64.121 | .000 |
| | Lower-bound | 78.499 | 1.000 | 78.499 | 64.121 | .000 |
| Time * Code | Sphericity Assumed | .374 | 1 | .374 | .306 | .586 |
| | Greenhouse-Geisser | .374 | 1.000 | .374 | .306 | .586 |
| | Huynh-Feldt | .374 | 1.000 | .374 | .306 | .586 |
| | Lower-bound | .374 | 1.000 | .374 | .306 | .586 |
| Error(Time) | Sphericity Assumed | 29.381 | 24 | 1.224 | | |
| | Greenhouse-Geisser | 29.381 | 24.000 | 1.224 | | |
| | Huynh-Feldt | 29.381 | 24.000 | 1.224 | | |
| | Lower-bound | 29.381 | 24.000 | 1.224 | | |

Measure: MEASURE_1

| Source | Time | Type III Sum of Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|---|
| Time | Linear | 78.499 | 1 | 78.499 | 64.121 | .000 |
| Time * Code | Linear | .374 | 1 | .374 | .306 | .586 |
| Error(Time) | Linear | 29.381 | 24 | 1.224 | | |

Objective 2.2 Change in *vastus lateralis* muscle thickness and CSA following training

Muscle Thickness

**Independent Samples Test**

| | | Levene's Test for Equality of Variances | | t-test for Equality of Means | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | F | Sig. | t | df | Sig. (2-tailed) | Mean Difference | Std. Error Difference | 95% Confidence Interval of the Difference | |
| | | | | | | | | | Lower | Upper |
| Delta_Image6_BLW12 | Equal variances assumed | .552 | .465 | -.118 | 23 | .907 | -.08186 | .69561 | -1.52083 | 1.35712 |
| | Equal variances not assumed | | | -.118 | 23.000 | .907 | -.08186 | .69318 | -1.51580 | 1.35209 |
| Percent_Increase_BLW12 | Equal variances assumed | .612 | .442 | -.069 | 23 | .946 | -.16538 | 2.39784 | -5.12570 | 4.79493 |
| | Equal variances not assumed | | | -.069 | 22.989 | .945 | -.16538 | 2.39167 | -5.11306 | 4.78229 |

Objective 2.3 ICC estimates for Muscle Thickness

**Table 2.3**
ICC estimates and their 95% confident intervals were calculated using SPSS statistical package version 23 (SPSS Inc, Chicago, IL) based on a single rater, absolute-agreement, 2-way mixed-effects model. (*) Significantly different from baseline ($p \leq 0.01$).

| | | 95 % Confidence Interval | | F Test with True Value 0 | | | |
|---|---|---|---|---|---|---|---|
| | Intraclass Correlation | Lower Bound | Upper Bound | Value | *df*1 | *df*2 | Sig |
| Single measures | .863 | .811 | .901 | 13.25 | 128 | 128 | .000 |

Objective 2.4 Repeated Measures ANOVA (time within, groups between) *vastus lateralis* CSA

**Tests of Within-Subjects Effects**

Measure: MEASURE_1

| Source | | Type III Sum of Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|---|
| Time | Sphericity Assumed | 62.462 | 1 | 62.462 | 64.112 | .000 |
| | Greenhouse-Geisser | 62.462 | 1.000 | 62.462 | 64.112 | .000 |
| | Huynh-Feldt | 62.462 | 1.000 | 62.462 | 64.112 | .000 |
| | Lower-bound | 62.462 | 1.000 | 62.462 | 64.112 | .000 |
| Time * Code | Sphericity Assumed | .011 | 1 | .011 | .011 | .917 |
| | Greenhouse-Geisser | .011 | 1.000 | .011 | .011 | .917 |
| | Huynh-Feldt | .011 | 1.000 | .011 | .011 | .917 |
| | Lower-bound | .011 | 1.000 | .011 | .011 | .917 |
| Error(Time) | Sphericity Assumed | 22.408 | 23 | .974 | | |
| | Greenhouse-Geisser | 22.408 | 23.000 | .974 | | |
| | Huynh-Feldt | 22.408 | 23.000 | .974 | | |
| | Lower-bound | 22.408 | 23.000 | .974 | | |

**Tests of Between-Subjects Effects**

Measure: MEASURE_1

Transformed Variable: Average

| Source | Type III Sum of Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|
| Intercept | 61604.193 | 1 | 61604.193 | 1122.447 | .000 |
| Code | .729 | 1 | .729 | .013 | .909 |
| Error | 1262.328 | 23 | 54.884 | | |

Objective 2.5 Change in *vastus lateralis* CSA following training

**Independent Samples Test**

| | | Levene's Test for Equality of Variances | | t-test for Equality of Means | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | F | Sig. | t | df | Sig. (2-tailed) | Mean Difference | Std. Error Difference | 95% Confidence Interval of the Difference | |
| | | | | | | | | | Lower | Upper |
| Delta | Equal variances assumed | .005 | .945 | -.051 | 23 | .960 | -.02821 | .55494 | -1.17618 | 1.11977 |
| | Equal variances not assumed | | | -.051 | 22.810 | .960 | -.02821 | .55511 | -1.17707 | 1.12066 |

Objective 2.5 Repeated Measures ANOVA (time within, groups between) Type 1 Fibre CSA

**Multivariate Tests[a]**

| Effect | | Value | F | Hypothesis df | Error df | Sig. |
|---|---|---|---|---|---|---|
| Time | Pillai's Trace | .219 | 4.196[b] | 1.000 | 15.000 | .058 |
| | Wilks' Lambda | .781 | 4.196[b] | 1.000 | 15.000 | .058 |
| | Hotelling's Trace | .280 | 4.196[b] | 1.000 | 15.000 | .058 |
| | Roy's Largest Root | .280 | 4.196[b] | 1.000 | 15.000 | .058 |
| Time * Code | Pillai's Trace | .012 | .180[b] | 1.000 | 15.000 | .678 |
| | Wilks' Lambda | .988 | .180[b] | 1.000 | 15.000 | .678 |
| | Hotelling's Trace | .012 | .180[b] | 1.000 | 15.000 | .678 |
| | Roy's Largest Root | .012 | .180[b] | 1.000 | 15.000 | .678 |

**Tests of Within-Subjects Effects**

Measure: MEASURE_1

| Source | | Type III Sum of Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|---|
| Time | Sphericity Assumed | 686582.520 | 1 | 686582.520 | 4.196 | .058 |
| | Greenhouse-Geisser | 686582.520 | 1.000 | 686582.520 | 4.196 | .058 |
| | Huynh-Feldt | 686582.520 | 1.000 | 686582.520 | 4.196 | .058 |
| | Lower-bound | 686582.520 | 1.000 | 686582.520 | 4.196 | .058 |
| Time * Code | Sphericity Assumed | 29409.814 | 1 | 29409.814 | .180 | .678 |
| | Greenhouse-Geisser | 29409.814 | 1.000 | 29409.814 | .180 | .678 |
| | Huynh-Feldt | 29409.814 | 1.000 | 29409.814 | .180 | .678 |
| | Lower-bound | 29409.814 | 1.000 | 29409.814 | .180 | .678 |
| Error(Time) | Sphericity Assumed | 2454582.72 | 15 | 163638.848 | | |
| | Greenhouse-Geisser | 2454582.72 | 15.000 | 163638.848 | | |
| | Huynh-Feldt | 2454582.72 | 15.000 | 163638.848 | | |
| | Lower-bound | 2454582.72 | 15.000 | 163638.848 | | |

**Tests of Between-Subjects Effects**

Measure: MEASURE_1

Transformed Variable: Average

| Source | Type III Sum of Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|
| Intercept | 941644947 | 1 | 941644947 | 2309.013 | .000 |
| Code | 1504.314 | 1 | 1504.314 | .004 | .952 |
| Error | 6117190.22 | 15 | 407812.681 | | |

Objective 2.7 Repeated Measures ANOVA (time within, groups between) Type 2 Fibre CSA

**Multivariate Tests[a]**

| Effect | | Value | F | Hypothesis df | Error df | Sig. |
|---|---|---|---|---|---|---|
| Time | Pillai's Trace | .391 | 9.623[b] | 1.000 | 15.000 | .007 |
| | Wilks' Lambda | .609 | 9.623[b] | 1.000 | 15.000 | .007 |
| | Hotelling's Trace | .642 | 9.623[b] | 1.000 | 15.000 | .007 |
| | Roy's Largest Root | .642 | 9.623[b] | 1.000 | 15.000 | .007 |
| Time * Code | Pillai's Trace | .019 | .287[b] | 1.000 | 15.000 | .600 |
| | Wilks' Lambda | .981 | .287[b] | 1.000 | 15.000 | .600 |
| | Hotelling's Trace | .019 | .287[b] | 1.000 | 15.000 | .600 |
| | Roy's Largest Root | .019 | .287[b] | 1.000 | 15.000 | .600 |

**Tests of Within-Subjects Effects**

Measure: MEASURE_1

| Source | | Type III Sum of Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|---|
| Time | Sphericity Assumed | 2053377.53 | 1 | 2053377.53 | 9.623 | .007 |
| | Greenhouse-Geisser | 2053377.53 | 1.000 | 2053377.53 | 9.623 | .007 |
| | Huynh-Feldt | 2053377.53 | 1.000 | 2053377.53 | 9.623 | .007 |
| | Lower-bound | 2053377.53 | 1.000 | 2053377.53 | 9.623 | .007 |
| Time * Code | Sphericity Assumed | 61230.004 | 1 | 61230.004 | .287 | .600 |
| | Greenhouse-Geisser | 61230.004 | 1.000 | 61230.004 | .287 | .600 |
| | Huynh-Feldt | 61230.004 | 1.000 | 61230.004 | .287 | .600 |
| | Lower-bound | 61230.004 | 1.000 | 61230.004 | .287 | .600 |
| Error(Time) | Sphericity Assumed | 3200767.94 | 15 | 213384.529 | | |
| | Greenhouse-Geisser | 3200767.94 | 15.000 | 213384.529 | | |
| | Huynh-Feldt | 3200767.94 | 15.000 | 213384.529 | | |
| | Lower-bound | 3200767.94 | 15.000 | 213384.529 | | |

**Tests of Between-Subjects Effects**

Measure: MEASURE_1

Transformed Variable: Average

| Source | Type III Sum of Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|
| Intercept | 1.343E+9 | 1 | 1.343E+9 | 2970.211 | .000 |
| Code | 1652612.76 | 1 | 1652612.76 | 3.656 | .075 |
| Error | 6780694.72 | 15 | 452046.314 | | |

Objective 2.8 Repeated Measures ANOVA (time within, groups between) Fibre Type 1 Distribution

**Multivariate Tests[a]**

| Effect | | Value | F | Hypothesis df | Error df | Sig. |
|---|---|---|---|---|---|---|
| Time | Pillai's Trace | .010 | .156[b] | 1.000 | 15.000 | .698 |
| | Wilks' Lambda | .990 | .156[b] | 1.000 | 15.000 | .698 |
| | Hotelling's Trace | .010 | .156[b] | 1.000 | 15.000 | .698 |
| | Roy's Largest Root | .010 | .156[b] | 1.000 | 15.000 | .698 |
| Time * CODE | Pillai's Trace | .065 | 1.037[b] | 1.000 | 15.000 | .325 |
| | Wilks' Lambda | .935 | 1.037[b] | 1.000 | 15.000 | .325 |
| | Hotelling's Trace | .069 | 1.037[b] | 1.000 | 15.000 | .325 |
| | Roy's Largest Root | .069 | 1.037[b] | 1.000 | 15.000 | .325 |

**Tests of Within-Subjects Effects**

Measure: MEASURE_1

| Source | | Type III Sum of Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|---|
| Time | Sphericity Assumed | 17.117 | 1 | 17.117 | .156 | .698 |
| | Greenhouse-Geisser | 17.117 | 1.000 | 17.117 | .156 | .698 |
| | Huynh-Feldt | 17.117 | 1.000 | 17.117 | .156 | .698 |
| | Lower-bound | 17.117 | 1.000 | 17.117 | .156 | .698 |
| Time * CODE | Sphericity Assumed | 113.839 | 1 | 113.839 | 1.037 | .325 |
| | Greenhouse-Geisser | 113.839 | 1.000 | 113.839 | 1.037 | .325 |
| | Huynh-Feldt | 113.839 | 1.000 | 113.839 | 1.037 | .325 |
| | Lower-bound | 113.839 | 1.000 | 113.839 | 1.037 | .325 |
| Error(Time) | Sphericity Assumed | 1645.965 | 15 | 109.731 | | |
| | Greenhouse-Geisser | 1645.965 | 15.000 | 109.731 | | |
| | Huynh-Feldt | 1645.965 | 15.000 | 109.731 | | |
| | Lower-bound | 1645.965 | 15.000 | 109.731 | | |

**Tests of Between-Subjects Effects**

Measure: MEASURE_1

Transformed Variable: Average

| Source | Type III Sum of Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|
| Intercept | 49886.598 | 1 | 49886.598 | 201.006 | .000 |
| CODE | 4.393 | 1 | 4.393 | .018 | .896 |
| Error | 3722.767 | 15 | 248.184 | | |

Objective 2.9 Repeated Measures ANOVA (time within, groups between) Fibre Type T2A Distribution

**Multivariate Tests[a]**

| Effect | | Value | F | Hypothesis df | Error df | Sig. |
|---|---|---|---|---|---|---|
| Time | Pillai's Trace | .135 | 2.336[b] | 1.000 | 15.000 | .147 |
| | Wilks' Lambda | .865 | 2.336[b] | 1.000 | 15.000 | .147 |
| | Hotelling's Trace | .156 | 2.336[b] | 1.000 | 15.000 | .147 |
| | Roy's Largest Root | .156 | 2.336[b] | 1.000 | 15.000 | .147 |
| Time * CODE | Pillai's Trace | .000 | .000[b] | 1.000 | 15.000 | .992 |
| | Wilks' Lambda | 1.000 | .000[b] | 1.000 | 15.000 | .992 |
| | Hotelling's Trace | .000 | .000[b] | 1.000 | 15.000 | .992 |
| | Roy's Largest Root | .000 | .000[b] | 1.000 | 15.000 | .992 |

**Tests of Within-Subjects Effects**

Measure: MEASURE_1

| Source | | Type III Sum of Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|---|
| Time | Sphericity Assumed | 346.052 | 1 | 346.052 | 2.336 | .147 |
| | Greenhouse-Geisser | 346.052 | 1.000 | 346.052 | 2.336 | .147 |
| | Huynh-Feldt | 346.052 | 1.000 | 346.052 | 2.336 | .147 |
| | Lower-bound | 346.052 | 1.000 | 346.052 | 2.336 | .147 |
| Time * CODE | Sphericity Assumed | .015 | 1 | .015 | .000 | .992 |
| | Greenhouse-Geisser | .015 | 1.000 | .015 | .000 | .992 |
| | Huynh-Feldt | .015 | 1.000 | .015 | .000 | .992 |
| | Lower-bound | .015 | 1.000 | .015 | .000 | .992 |
| Error(Time) | Sphericity Assumed | 2222.190 | 15 | 148.146 | | |
| | Greenhouse-Geisser | 2222.190 | 15.000 | 148.146 | | |
| | Huynh-Feldt | 2222.190 | 15.000 | 148.146 | | |
| | Lower-bound | 2222.190 | 15.000 | 148.146 | | |

**Tests of Between-Subjects Effects**

Measure: MEASURE_1

Transformed Variable: Average

| Source | Type III Sum of Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|
| Intercept | 99518.852 | 1 | 99518.852 | 402.761 | .000 |
| CODE | 22.829 | 1 | 22.829 | .092 | .765 |
| Error | 3706.370 | 15 | 247.091 | | |

Objective 2.10 Repeated Measures ANOVA (time within, groups between) Fibre Type 1T2X Distribution

**Multivariate Tests[a]**

| Effect | | Value | F | Hypothesis df | Error df | Sig. |
|---|---|---|---|---|---|---|
| Time | Pillai's Trace | .287 | 6.038[b] | 1.000 | 15.000 | .027 |
| | Wilks' Lambda | .713 | 6.038[b] | 1.000 | 15.000 | .027 |
| | Hotelling's Trace | .403 | 6.038[b] | 1.000 | 15.000 | .027 |
| | Roy's Largest Root | .403 | 6.038[b] | 1.000 | 15.000 | .027 |
| Time * CODE | Pillai's Trace | .155 | 2.748[b] | 1.000 | 15.000 | .118 |
| | Wilks' Lambda | .845 | 2.748[b] | 1.000 | 15.000 | .118 |
| | Hotelling's Trace | .183 | 2.748[b] | 1.000 | 15.000 | .118 |
| | Roy's Largest Root | .183 | 2.748[b] | 1.000 | 15.000 | .118 |

**Tests of Within-Subjects Effects**

Measure: MEASURE_1

| Source | | Type III Sum of Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|---|
| Time | Sphericity Assumed | 292.299 | 1 | 292.299 | 6.038 | .027 |
| | Greenhouse-Geisser | 292.299 | 1.000 | 292.299 | 6.038 | .027 |
| | Huynh-Feldt | 292.299 | 1.000 | 292.299 | 6.038 | .027 |
| | Lower-bound | 292.299 | 1.000 | 292.299 | 6.038 | .027 |
| Time * CODE | Sphericity Assumed | 133.047 | 1 | 133.047 | 2.748 | .118 |
| | Greenhouse-Geisser | 133.047 | 1.000 | 133.047 | 2.748 | .118 |
| | Huynh-Feldt | 133.047 | 1.000 | 133.047 | 2.748 | .118 |
| | Lower-bound | 133.047 | 1.000 | 133.047 | 2.748 | .118 |
| Error(Time) | Sphericity Assumed | 726.124 | 15 | 48.408 | | |
| | Greenhouse-Geisser | 726.124 | 15.000 | 48.408 | | |
| | Huynh-Feldt | 726.124 | 15.000 | 48.408 | | |
| | Lower-bound | 726.124 | 15.000 | 48.408 | | |

**Tests of Between-Subjects Effects**

Measure: MEASURE_1

Transformed Variable: Average

| Source | Type III Sum of Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|
| Intercept | 1021.192 | 1 | 1021.192 | 19.941 | .000 |
| CODE | 2.634 | 1 | 2.634 | .051 | .824 |
| Error | 768.167 | 15 | 51.211 | | |

Objective 3. Change in Total Strength
Repeated Measures ANOVA (time within, groups between)

**Multivariate Tests[a]**

| Effect | | Value | F | Hypothesis df | Error df | Sig. |
|---|---|---|---|---|---|---|
| Time | Pillai's Trace | .860 | 147.100[b] | 1.000 | 24.000 | .000 |
| | Wilks' Lambda | .140 | 147.100[b] | 1.000 | 24.000 | .000 |
| | Hotelling's Trace | 6.129 | 147.100[b] | 1.000 | 24.000 | .000 |
| | Roy's Largest Root | 6.129 | 147.100[b] | 1.000 | 24.000 | .000 |
| Time * Code | Pillai's Trace | .030 | .738[b] | 1.000 | 24.000 | .399 |
| | Wilks' Lambda | .970 | .738[b] | 1.000 | 24.000 | .399 |
| | Hotelling's Trace | .031 | .738[b] | 1.000 | 24.000 | .399 |
| | Roy's Largest Root | .031 | .738[b] | 1.000 | 24.000 | .399 |

**Tests of Within-Subjects Effects**

Measure: MEASURE_1

| Source | | Type III Sum of Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|---|
| Time | Sphericity Assumed | 73370.456 | 1 | 73370.456 | 147.100 | .000 |
| | Greenhouse-Geisser | 73370.456 | 1.000 | 73370.456 | 147.100 | .000 |
| | Huynh-Feldt | 73370.456 | 1.000 | 73370.456 | 147.100 | .000 |
| | Lower-bound | 73370.456 | 1.000 | 73370.456 | 147.100 | .000 |
| Time * Code | Sphericity Assumed | 368.197 | 1 | 368.197 | .738 | .399 |
| | Greenhouse-Geisser | 368.197 | 1.000 | 368.197 | .738 | .399 |
| | Huynh-Feldt | 368.197 | 1.000 | 368.197 | .738 | .399 |
| | Lower-bound | 368.197 | 1.000 | 368.197 | .738 | .399 |
| Error(Time) | Sphericity Assumed | 11970.734 | 24 | 498.781 | | |
| | Greenhouse-Geisser | 11970.734 | 24.000 | 498.781 | | |
| | Huynh-Feldt | 11970.734 | 24.000 | 498.781 | | |
| | Lower-bound | 11970.734 | 24.000 | 498.781 | | |

**Tests of Between-Subjects Effects**

Measure: MEASURE_1
Transformed Variable: Average

| Source | Type III Sum of Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|
| Intercept | 9666995.25 | 1 | 9666995.25 | 1350.630 | .000 |
| Code | 1132.849 | 1 | 1132.849 | .158 | .694 |
| Error | 171777.531 | 24 | 7157.397 | | |

Objective 3.1 Change in Total strength following training

**Independent Samples Test**

| | | Levene's Test for Equality of Variances | | t-test for Equality of Means | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | 95% Confidence Interval of the Difference | |
| | | F | Sig. | t | df | Sig. (2-tailed) | Mean Difference | Std. Error Difference | Lower | Upper |
| PrePostTotal | Equal variances assumed | 2.271 | .145 | -.859 | 24 | .399 | -10.64385 | 12.38779 | -36.21099 | 14.92330 |
| | Equal variances not assumed | | | -.859 | 18.358 | .401 | -10.64385 | 12.38779 | -36.63330 | 15.34561 |

Objective 3.2 Percent change in Squat, Bench press and Deadlift following overreaching

**Independent Samples Test**

| | | Levene's Test for Equality of Variances | | t-test for Equality of Means | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | 95% Confidence Interval of the Difference | |
| | | F | Sig. | t | df | Sig. (2-tailed) | Mean Difference | Std. Error Difference | Lower | Upper |
| W8W10perc_Squat | Equal variances assumed | 1.817 | .190 | 1.693 | 24 | .103 | 3.14615 | 1.85801 | -.68858 | 6.98089 |
| | Equal variances not assumed | | | 1.693 | 22.214 | .104 | 3.14615 | 1.85801 | -.70497 | 6.99728 |
| W8W10perc_Bench | Equal variances assumed | .185 | .671 | -.253 | 23 | .802 | -.352 | 1.389 | -3.225 | 2.521 |
| | Equal variances not assumed | | | -.255 | 22.848 | .801 | -.352 | 1.379 | -3.206 | 2.502 |
| W8W10_pre_dead | Equal variances assumed | 1.435 | .243 | .608 | 24 | .549 | 1.37692 | 2.26312 | -3.29392 | 6.04777 |
| | Equal variances not assumed | | | .608 | 22.362 | .549 | 1.37692 | 2.26312 | -3.31209 | 6.06594 |

Objective 4. CK activity Repeated Measures ANOVA (time within, groups between)
(Tukey's performed in excel)

**Multivariate Tests[a]**

| Effect | | Value | F | Hypothesis df | Error df | Sig. |
|---|---|---|---|---|---|---|
| Time | Pillai's Trace | .755 | 11.741[b] | 5.000 | 19.000 | .000 |
| | Wilks' Lambda | .245 | 11.741[b] | 5.000 | 19.000 | .000 |
| | Hotelling's Trace | 3.090 | 11.741[b] | 5.000 | 19.000 | .000 |
| | Roy's Largest Root | 3.090 | 11.741[b] | 5.000 | 19.000 | .000 |
| Time * Code | Pillai's Trace | .166 | .755[b] | 5.000 | 19.000 | .593 |
| | Wilks' Lambda | .834 | .755[b] | 5.000 | 19.000 | .593 |
| | Hotelling's Trace | .199 | .755[b] | 5.000 | 19.000 | .593 |
| | Roy's Largest Root | .199 | .755[b] | 5.000 | 19.000 | .593 |

**Tests of Within-Subjects Effects**

Measure: MEASURE_1

| Source | | Type III Sum of Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|---|
| Time | Sphericity Assumed | 1317966.24 | 5 | 263593.249 | 14.394 | .000 |
| | Greenhouse-Geisser | 1317966.24 | 2.818 | 467623.239 | 14.394 | .000 |
| | Huynh-Feldt | 1317966.24 | 3.392 | 388522.768 | 14.394 | .000 |
| | Lower-bound | 1317966.24 | 1.000 | 1317966.24 | 14.394 | .001 |
| Time * Code | Sphericity Assumed | 20206.192 | 5 | 4041.238 | .221 | .953 |
| | Greenhouse-Geisser | 20206.192 | 2.818 | 7169.292 | .221 | .871 |
| | Huynh-Feldt | 20206.192 | 3.392 | 5956.576 | .221 | .902 |
| | Lower-bound | 20206.192 | 1.000 | 20206.192 | .221 | .643 |
| Error(Time) | Sphericity Assumed | 2105910.57 | 115 | 18312.266 | | |
| | Greenhouse-Geisser | 2105910.57 | 64.824 | 32486.572 | | |
| | Huynh-Feldt | 2105910.57 | 78.022 | 26991.329 | | |
| | Lower-bound | 2105910.57 | 23.000 | 91561.329 | | |

**Tests of Between-Subjects Effects**

Measure: MEASURE_1
Transformed Variable: Average

| Source | Type III Sum of Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|
| Intercept | 2057323.38 | 1 | 2057323.38 | 234.798 | .000 |
| Code | 2379.525 | 1 | 2379.525 | .272 | .607 |
| Error | 201528.602 | 23 | 8762.113 | | |

Objective 4.1 Cortisol hormone concentration (nM) Repeated Measures ANOVA (time within, groups between)
(Tukey's performed in excel)

**Multivariate Tests[a]**

| Effect | | Value | F | Hypothesis df | Error df | Sig. |
|---|---|---|---|---|---|---|
| Time | Pillai's Trace | .837 | 20.479[b] | 5.000 | 20.000 | .000 |
| | Wilks' Lambda | .163 | 20.479[b] | 5.000 | 20.000 | .000 |
| | Hotelling's Trace | 5.120 | 20.479[b] | 5.000 | 20.000 | .000 |
| | Roy's Largest Root | 5.120 | 20.479[b] | 5.000 | 20.000 | .000 |
| Time * Code | Pillai's Trace | .020 | .080[b] | 5.000 | 20.000 | .995 |
| | Wilks' Lambda | .980 | .080[b] | 5.000 | 20.000 | .995 |
| | Hotelling's Trace | .020 | .080[b] | 5.000 | 20.000 | .995 |
| | Roy's Largest Root | .020 | .080[b] | 5.000 | 20.000 | .995 |

**Tests of Within-Subjects Effects**

Measure: MEASURE_1

| Source | | Type III Sum of Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|---|
| Time | Sphericity Assumed | 2966.790 | 5 | 593.358 | 15.818 | .000 |
| | Greenhouse-Geisser | 2966.790 | 2.642 | 1123.040 | 15.818 | .000 |
| | Huynh-Feldt | 2966.790 | 3.122 | 950.213 | 15.818 | .000 |
| | Lower-bound | 2966.790 | 1.000 | 2966.790 | 15.818 | .001 |
| Time * Code | Sphericity Assumed | 12.605 | 5 | 2.521 | .067 | .997 |
| | Greenhouse-Geisser | 12.605 | 2.642 | 4.772 | .067 | .967 |
| | Huynh-Feldt | 12.605 | 3.122 | 4.037 | .067 | .980 |
| | Lower-bound | 12.605 | 1.000 | 12.605 | .067 | .798 |
| Error(Time) | Sphericity Assumed | 4501.292 | 120 | 37.511 | | |
| | Greenhouse-Geisser | 4501.292 | 63.402 | 70.996 | | |
| | Huynh-Feldt | 4501.292 | 74.934 | 60.070 | | |
| | Lower-bound | 4501.292 | 24.000 | 187.554 | | |

**Tests of Between-Subjects Effects**

Measure: MEASURE_1

Transformed Variable: Average

| Source | Type III Sum of Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|
| Intercept | 15121.954 | 1 | 15121.954 | 3566.611 | .000 |
| Code | .002 | 1 | .002 | .000 | .985 |
| Error | 101.757 | 24 | 4.240 | | |

Objective 4.2 Percent change in CK activity and Cortisol following overreaching

**Independent Samples Test**

| | | Levene's Test for Equality of Variances | | t-test for Equality of Means | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | 95% Confidence Interval of the Difference | |
| | | F | Sig. | t | df | Sig. (2-tailed) | Mean Difference | Std. Error Difference | Lower | Upper |
| CKW8W10 | Equal variances assumed | 3.101 | .091 | 1.070 | 24 | .295 | 36.46154 | 34.06217 | -33.83934 | 106.76241 |
| | Equal variances not assumed | | | 1.070 | 14.979 | .301 | 36.46154 | 34.06217 | -36.14905 | 109.07213 |
| CortW8W10 | Equal variances assumed | .449 | .509 | -.013 | 24 | .990 | -.23077 | 18.09549 | -37.57802 | 37.11649 |
| | Equal variances not assumed | | | -.013 | 23.610 | .990 | -.23077 | 18.09549 | -37.61069 | 37.14915 |

Objective 4.3 Testosterone concentration (ng/dL) Repeated Measures ANOVA (time within, groups between)

(Tukey's performed in excel)

**Multivariate Tests[a]**

| Effect | | Value | F | Hypothesis df | Error df | Sig. |
|---|---|---|---|---|---|---|
| Time | Pillai's Trace | .894 | 33.583[b] | 5.000 | 20.000 | .000 |
| | Wilks' Lambda | .106 | 33.583[b] | 5.000 | 20.000 | .000 |
| | Hotelling's Trace | 8.396 | 33.583[b] | 5.000 | 20.000 | .000 |
| | Roy's Largest Root | 8.396 | 33.583[b] | 5.000 | 20.000 | .000 |
| Time * Code | Pillai's Trace | .225 | 1.158[b] | 5.000 | 20.000 | .364 |
| | Wilks' Lambda | .775 | 1.158[b] | 5.000 | 20.000 | .364 |
| | Hotelling's Trace | .290 | 1.158[b] | 5.000 | 20.000 | .364 |
| | Roy's Largest Root | .290 | 1.158[b] | 5.000 | 20.000 | .364 |

**Tests of Within-Subjects Effects**

Measure: MEASURE_1

| Source | | Type III Sum of Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|---|
| Time | Sphericity Assumed | 817342.233 | 5 | 163468.447 | 32.155 | .000 |
| | Greenhouse-Geisser | 817342.233 | 3.614 | 226147.642 | 32.155 | .000 |
| | Huynh-Feldt | 817342.233 | 4.511 | 181171.407 | 32.155 | .000 |
| | Lower-bound | 817342.233 | 1.000 | 817342.233 | 32.155 | .000 |
| Time * Code | Sphericity Assumed | 42708.329 | 5 | 8541.666 | 1.680 | .144 |
| | Greenhouse-Geisser | 42708.329 | 3.614 | 11816.822 | 1.680 | .168 |
| | Huynh-Feldt | 42708.329 | 4.511 | 9466.693 | 1.680 | .152 |
| | Lower-bound | 42708.329 | 1.000 | 42708.329 | 1.680 | .207 |
| Error(Time) | Sphericity Assumed | 610045.080 | 120 | 5083.709 | | |
| | Greenhouse-Geisser | 610045.080 | 86.741 | 7032.971 | | |
| | Huynh-Feldt | 610045.080 | 108.274 | 5634.254 | | |
| | Lower-bound | 610045.080 | 24.000 | 25418.545 | | |

**Tests of Between-Subjects Effects**

Measure: MEASURE_1

Transformed Variable: Average

| Source | Type III Sum of Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|
| Intercept | 11146595.0 | 1 | 11146595.0 | 9322.008 | .000 |
| Code | 5062.921 | 1 | 5062.921 | 4.234 | .051 |
| Error | 28697.496 | 24 | 1195.729 | | |

Objective 4.4 free Testosterone concentration (ng/dL) Repeated Measures ANOVA (time within, groups between)

(Tukey's performed in excel)

**Multivariate Tests[a]**

| Effect | | Value | F | Hypothesis df | Error df | Sig. |
|---|---|---|---|---|---|---|
| Time | Pillai's Trace | .693 | 9.010[b] | 5.000 | 20.000 | .000 |
| | Wilks' Lambda | .307 | 9.010[b] | 5.000 | 20.000 | .000 |
| | Hotelling's Trace | 2.253 | 9.010[b] | 5.000 | 20.000 | .000 |
| | Roy's Largest Root | 2.253 | 9.010[b] | 5.000 | 20.000 | .000 |
| Time * Code | Pillai's Trace | .199 | .993[b] | 5.000 | 20.000 | .447 |
| | Wilks' Lambda | .801 | .993[b] | 5.000 | 20.000 | .447 |
| | Hotelling's Trace | .248 | .993[b] | 5.000 | 20.000 | .447 |
| | Roy's Largest Root | .248 | .993[b] | 5.000 | 20.000 | .447 |

a. Design: Intercept + Code

**Tests of Within-Subjects Effects**

Measure: MEASURE_1

| Source | | Type III Sum of Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|---|
| Time | Sphericity Assumed | 293.861 | 5 | 58.772 | 8.580 | .000 |
| | Greenhouse-Geisser | 293.861 | 4.353 | 67.502 | 8.580 | .000 |
| | Huynh-Feldt | 293.861 | 5.000 | 58.772 | 8.580 | .000 |
| | Lower-bound | 293.861 | 1.000 | 293.861 | 8.580 | .007 |
| Time * Code | Sphericity Assumed | 41.083 | 5 | 8.217 | 1.199 | .314 |
| | Greenhouse-Geisser | 41.083 | 4.353 | 9.437 | 1.199 | .315 |
| | Huynh-Feldt | 41.083 | 5.000 | 8.217 | 1.199 | .314 |
| | Lower-bound | 41.083 | 1.000 | 41.083 | 1.199 | .284 |
| Error(Time) | Sphericity Assumed | 822.003 | 120 | 6.850 | | |
| | Greenhouse-Geisser | 822.003 | 104.481 | 7.867 | | |
| | Huynh-Feldt | 822.003 | 120.000 | 6.850 | | |
| | Lower-bound | 822.003 | 24.000 | 34.250 | | |

Objective 4.5 Insulin-like growth factor 1 (IGF-1; ug/dL) Repeated Measures ANOVA (time within, groups between)
(Tukey's performed in excel)

**Multivariate Tests[a]**

| Effect | | Value | F | Hypothesis df | Error df | Sig. |
|---|---|---|---|---|---|---|
| Time | Pillai's Trace | .321 | 1.887[b] | 5.000 | 20.000 | .142 |
| | Wilks' Lambda | .679 | 1.887[b] | 5.000 | 20.000 | .142 |
| | Hotelling's Trace | .472 | 1.887[b] | 5.000 | 20.000 | .142 |
| | Roy's Largest Root | .472 | 1.887[b] | 5.000 | 20.000 | .142 |
| Time * Code | Pillai's Trace | .108 | .483[b] | 5.000 | 20.000 | .784 |
| | Wilks' Lambda | .892 | .483[b] | 5.000 | 20.000 | .784 |
| | Hotelling's Trace | .121 | .483[b] | 5.000 | 20.000 | .784 |
| | Roy's Largest Root | .121 | .483[b] | 5.000 | 20.000 | .784 |

**Tests of Within-Subjects Effects**

Measure: MEASURE_1

| Source | | Type III Sum of Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|---|
| Time | Sphericity Assumed | 113902.942 | 5 | 22780.588 | 1.898 | .100 |
| | Greenhouse-Geisser | 113902.942 | 4.160 | 27379.724 | 1.898 | .114 |
| | Huynh-Feldt | 113902.942 | 5.000 | 22780.588 | 1.898 | .100 |
| | Lower-bound | 113902.942 | 1.000 | 113902.942 | 1.898 | .181 |
| Time * Code | Sphericity Assumed | 11426.526 | 5 | 2285.305 | .190 | .966 |
| | Greenhouse-Geisser | 11426.526 | 4.160 | 2746.682 | .190 | .947 |
| | Huynh-Feldt | 11426.526 | 5.000 | 2285.305 | .190 | .966 |
| | Lower-bound | 11426.526 | 1.000 | 11426.526 | .190 | .666 |
| Error(Time) | Sphericity Assumed | 1440188.75 | 120 | 12001.573 | | |
| | Greenhouse-Geisser | 1440188.75 | 99.843 | 14424.551 | | |
| | Huynh-Feldt | 1440188.75 | 120.000 | 12001.573 | | |
| | Lower-bound | 1440188.75 | 24.000 | 60007.865 | | |

**Tests of Between-Subjects Effects**

Measure: MEASURE_1
Transformed Variable: Average

| Source | Type III Sum of Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|
| Intercept | 21040707.4 | 1 | 21040707.4 | 1124.232 | .000 |
| Code | 2500.802 | 1 | 2500.802 | .134 | .718 |
| Error | 449174.947 | 24 | 18715.623 | | |

Objective 4.6 Growth Hormone (GH; ng/mL) Repeated Measures ANOVA (time within, groups between) (Tukey's performed in excel)

**Multivariate Tests[a]**

| Effect | | Value | F | Hypothesis df | Error df | Sig. |
|---|---|---|---|---|---|---|
| Time | Pillai's Trace | .421 | 3.823[b] | 4.000 | 21.000 | .017 |
| | Wilks' Lambda | .579 | 3.823[b] | 4.000 | 21.000 | .017 |
| | Hotelling's Trace | .728 | 3.823[b] | 4.000 | 21.000 | .017 |
| | Roy's Largest Root | .728 | 3.823[b] | 4.000 | 21.000 | .017 |
| Time * Code | Pillai's Trace | .162 | 1.016[b] | 4.000 | 21.000 | .422 |
| | Wilks' Lambda | .838 | 1.016[b] | 4.000 | 21.000 | .422 |
| | Hotelling's Trace | .193 | 1.016[b] | 4.000 | 21.000 | .422 |
| | Roy's Largest Root | .193 | 1.016[b] | 4.000 | 21.000 | .422 |

**Tests of Within-Subjects Effects**

Measure: MEASURE_1

| Source | | Type III Sum of Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|---|
| Time | Sphericity Assumed | 9.970 | 4 | 2.493 | 3.587 | .009 |
| | Greenhouse-Geisser | 9.970 | 3.557 | 2.803 | 3.587 | .012 |
| | Huynh-Feldt | 9.970 | 4.000 | 2.493 | 3.587 | .009 |
| | Lower-bound | 9.970 | 1.000 | 9.970 | 3.587 | .070 |
| Time * Code | Sphericity Assumed | 3.644 | 4 | .911 | 1.311 | .271 |
| | Greenhouse-Geisser | 3.644 | 3.557 | 1.024 | 1.311 | .274 |
| | Huynh-Feldt | 3.644 | 4.000 | .911 | 1.311 | .271 |
| | Lower-bound | 3.644 | 1.000 | 3.644 | 1.311 | .264 |
| Error(Time) | Sphericity Assumed | 66.706 | 96 | .695 | | |
| | Greenhouse-Geisser | 66.706 | 85.364 | .781 | | |
| | Huynh-Feldt | 66.706 | 96.000 | .695 | | |
| | Lower-bound | 66.706 | 24.000 | 2.779 | | |