

## Abstract book

Conference on Inter-Individual Variation in Resistance Training

Faculty of Sport and Health Sciences, University of Jyväskylä, Finland

November 19-21, 2025

## Oral presentations

The Effect of Resistance Training Volume on Individual-Level Skeletal Muscle Adaptations: A Novel Randomized Replicated Within-Participant Unilateral Trial

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There is growing emphasis on investigating heterogeneity in resistance training (RT) outcomes, likely motivated by observations of substantial gross variability in training effects. However, gross variability does not necessarily represent true inter-individual response variation (IRV) and can be obscured by measurement error, sampling variance, and biological variability. This study explores a novel study design (i.e., randomized replicated within-participant unilateral trial) to demonstrate a methodological framework necessary to distinguish IRV from these confounding sources of within-participant variation. 16 recreationally trained participants performed two 11-week training phases separated by a 6-8 week washout. Lower limbs were randomized to a low volume (~8 sets/week) or high volume (~16 sets/week) training protocol in each phase. We assessed both general (GEN; average response across conditions) and condition-specific (CON; difference between volumes) IRV for vastus lateralis cross-sectional area and leg press one-repetition maximum using a multi-stage statistical approach. Higher weekly set volumes demonstrated a detectable advantage for muscle hypertrophy (1.8 cm<sup>2</sup> [95% HDI: 0.29, 3.41]; 98.77% posterior probability) but not maximal strength (3.48 kg [95% HDI: -5.1, 12.15]; 80.01% posterior probability). Despite substantial gross variability, we failed to detect irrefutable evidence of meaningful IRV. Integrated methods revealed stronger evidence for GEN versus CON IRV, with correlation coefficients ranging from 0.67 to 0.7 for GEN versus 0.04 to 0.06 for CON. Our findings clearly illustrate that gross variability in training outcomes does not necessarily indicate true inter-individual differences, a distinction critical for both research and practice.

# Does Human Muscle Volume Homeostatically Adapt to Bone Volume?

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## Introduction

The 'adipostat' maintains fat around an internal setpoint. Analogously, a 'myostat' may regulate muscle volume in equilibrium with an optimal bone-scaled setpoint (myostatic setpoint). As skeletal muscle's primary role is to move bone, muscle volume should relate to the associated bone volume (e.g., biceps brachii vs. humerus). We investigated whether a normative muscle-to-bone volume ratio exists, independent of stature, and hypothesized that resistance training (RT) would more effectively increase muscle volume in individuals starting below the myostatic setpoint than in those already above it.

## Methods

Untrained males (n=29) and females (n=10), aged  $23 \pm 4$  years, underwent whole-body MRI before and after 12 weeks of RT. Skeletal muscle volumes (n=57) and associated bone volumes were quantified using AI-based segmentation, height-corrected, and converted into sex-specific Z-scores. The pre-RT relationship between mean muscle and bone Z-scores was assessed via linear regression with residuals reflecting deviation from the myostatic setpoint. Positive residuals indicate muscle volume above the setpoint relative to bone volume and vice versa. Changes in mean muscle Z-scores after RT were related to baseline residuals.

## Results

At baseline, mean muscle Z-scores correlated positively with mean bone Z-scores ( $R^2=0.31$ ,  $p<0.0001$ ), showing that a substantial fraction of inter-individual muscle volume variation is explained by bone volume. RT-induced muscle Z-score increases were inversely related to baseline residuals ( $R^2=0.21$ ,  $p=0.015$ ), indicating greater hypertrophy in individuals starting below the myostatic setpoint.

## Conclusion

In untrained males and females, muscle volume is strongly associated with bone volume after adjusting for height. The resulting linear regression line could be considered a myostatic setpoint. RT-induced increases in muscle volume tend to be inversely related to initial bone-scaled muscle volume, supporting the myostat theory. This model could be used to predict normative muscle volume and RT effects based on bone volume, potentially defining upper and lower limits of muscle volume.

## Meta-analytic methods for exploring intervention effect heterogeneity: Examples of application in a large-scale resistance training dataset

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The average effects of resistance training (RT) interventions for strength and hypertrophy are well established. Yet, the presence of gross variability in observed outcomes has fuelled interest in so called “precision” or “personalised” approaches to prescription which assume the existence of interindividual heterogeneity in intervention effects (i.e., person-by-intervention interaction). However, gross variability in observed outcomes is the result of several sources of variance: average intervention effects plus within-person variation, between-person variation, other random variation including measurement error, and potentially true differences in intervention effect between individuals. A first step to identifying interindividual response variation is to determine whether the introduction of an intervention may have impacted variance and this is possible in a randomised controlled trial (RCT) where an intervention is compared to a control. These kinds of comparisons though are poorly powered in the typical RCT of RT interventions. Most meta-analyses in RT focus on average intervention effects, but meta-analytic comparisons of variation can also address the statistical power concerns of small studies. This work demonstrates how meta-analytic approaches can be applied to detect inter-individual response variation in RT. Using data from 111 RCTs of RT (total  $n = 5032$ ), we introduce effect size statistics and modelling approaches for variation, including the standard deviation of individual responses (SDir), log variability ratio (lnVR), log coefficient of variation ratio (lnCVR), and meta-regression of log standard deviation on log means. Assumptions of these modelling approaches will be highlighted, and we will demonstrate that careful selection of appropriate modelling approaches is essential to understanding whether an intervention may have resulted in true interindividual heterogeneity in effects. Results of our analyses suggest that there is little evidence of RT interventions exhibiting meaningful interindividual heterogeneity in effects. As such, recommendations regarding RT can likely be made assuming generalisability of intervention effect magnitudes.

## Individual responses to multicomponent physical training in older adults – secondary analysis of controlled trial

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### Background

Responses to physical training vary between individuals, but the factors underlying this variation in older adults are not well known. We investigated individual variation in strength, muscle mass, and walking responses to a one-year multicomponent physical training and associations between health-related factors and responsiveness to training among older adults.

### Methods

Participants (n=314; mean age 75.1±3.8 years; 60 % of women) were randomized into physical training (PT) and physical and cognitive training (PTCT) groups. Physical training for all included resistance, walking, balance, and mobility training. CT included computer-based executive function training. Maximal isometric grip and knee extension strength, muscle mass, walking speed, and six-minute walking distance were measured. No significant differences were observed in outcome changes between the PT and PTCT groups, and groups were combined for further analysis. For each outcome, participants were categorized either into a high or low response group whether the change exceeded or remained below the variance-based threshold value. Logistic regressions were conducted to explore associations between health-related factors and high responses.

### Results

The rate of high responders was 27% for grip strength, 46% for knee extension strength, 17% for muscle mass, 30% for walking speed, and 44% for walking distance. More than one high response was present in 56% of the participants. Multimorbidity (OR 3.08, p<.001), higher body mass index (OR 1.18, p=0.017), male sex (OR 4.62, p<.001), younger age (OR .87, p<.001), and higher adherence to strength training (OR 1.03, p<0.001) associated with having more than one high response across the outcomes.

### Conclusion

A one-year combined physical training results in substantial individual variability in physical functioning outcomes. Younger individuals, men, and those with multimorbidity or a higher body mass index demonstrate greater potential for improvement across multiple measures of physical functioning.

The effect of 12-week time-specific strength-aerobic training programme on body composition, metabolic health and muscle strength in elderly females

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Aging is a natural multisystem process that progressively impairs neural, cardiovascular, respiratory, metabolic, and musculoskeletal functions, leading to reduced physical fitness and independence in older adults. The circadian system, which regulates the timing of many physiological processes, is also affected by aging. Time-specific training may help mitigate these alterations. This study aimed to examine the effects of a 12-week time-specific strength–aerobic training program on metabolic health, muscle strength, and body composition in elderly females.

A total of 26 women (69.1 years; BMI: 27.14) were divided into three groups: morning training group (MTG;  $n = 10$ ; BMI = 27.26), afternoon training group (ATG;  $n = 10$ ; BMI = 26.77), and control group (CON;  $n = 6$ ; BMI = 27.55). Participants were tested before and after the intervention. Body composition was assessed using dual-energy X-ray absorptiometry (DXA), including skeletal muscle mass, fat mass, and bone mineral density. Fasting venous blood samples were analysed for glucose metabolism and lipid profile. Lower-limb strength was evaluated with an isometric knee dynamometer.

Whole-body bone density significantly increased over time ( $p = 0.03$ ), particularly in the ATG (from  $0.97 \pm 0.03$  to  $0.99 \pm 0.03$  g/cm<sup>2</sup>;  $p = 0.005$ ). Maximal isometric knee extension moment improved in both MTG ( $164.6 \pm 17.5$  Nm vs.  $205.7 \pm 20.8$  Nm;  $p = 0.04$ ) and ATG ( $177.4 \pm 22.9$  Nm vs.  $250.2 \pm 10.7$  Nm;  $p < 0.0001$ ). Additionally, glucose metabolism and lipid profile indicators improved significantly compared with controls.

In conclusion, the time-specific training program enhanced multiple aspects of physical fitness, including BMI, bone density, muscle strength, and walking speed, although it had no significant impact on sleep parameters. Morning training showed a trend toward better stability of movement rhythmicity, though without statistical confirmation.

Funding: Slovak Research and Development Agency (APVV-21-0164), VEGA 0554/24, VEGA 1/0482/23

## Glucose as a building block in muscle growth

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### Background and purpose:

Skeletal muscle is the main consumer of glucose after a mixed meal, and resistance exercise further increases muscle glucose uptake. Emerging evidence suggests that glucose in muscles is not only stored as glycogen or used as a fuel but can also be incorporated into other biomass during growth. We aimed to study the utilization of glucose-derived carbons for protein, RNA, and lipid synthesis during human skeletal muscle (HSkM) cell growth. We also investigated whether muscle growth in vivo by resistance training (RT) affects the abundance of metabolites and enzymes required for these processes in human muscle.

### Materials and methods:

We used human primary HSkM cells, carbon-14-labeled glucose, and anabolic stimuli (IGF-1 or serum stimulation) to study glucose utilization for muscle cell growth. Muscle biopsies were obtained from a human resistance training (RT) study. We used liquid chromatography-mass spectrometry (LC-MS) to analyze metabolites and enzymes involved in glucose utilization for anabolism. Lastly, we used lentiviral-based gene knockdown and overexpression experiments in HSkM cells.

### Results:

We found that differentiated HSkM cells incorporated glucose-derived carbon into proteins, RNA, and lipids, and anabolic stimulation further increased these processes. Ten weeks of RT increased essential metabolites and enzymes for nucleotide, serine, and glycine synthesis, including phosphoglycerate dehydrogenase (PHGDH) in muscle. We also examined whether the PHGDH enzyme, branching from glycolysis, is essential for new muscle formation (myogenesis), and indeed, PHGDH was revealed to be important for myogenesis.

### Conclusion:

The data suggest that glucose is not only used for ATP or glycogen generation but also as a building block in human muscle cell growth. The PHGDH enzyme, which directs a glycolytic intermediate to anabolism, was highlighted as important for myogenesis. The results open new avenues for studies investigating the mechanisms of RT and muscle growth in improving muscle glucose metabolism.

## Is There a Volume Ceiling for Muscle Hypertrophy in Trained Athletes?

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**Objectives:** This study investigated whether extremely high resistance training (RT) volumes (>60 weekly sets per muscle group) enhance muscle strength and hypertrophy compared to moderate volumes, and whether greater volume influences non-responsiveness in trained athletes.

**Methods:** 27 strength-trained male athletes completed a 10-week RT intervention, followed by a 7-week experimental phase, in which they were split into normal (NOR, n = 12) and extra volume (XTR, n = 15) groups, with XTR performing 1.5 times more weekly sets. Muscle thickness in the Vastus Lateralis (VL) and Biceps Femoris (BF) was measured via ultrasound, and strength through back squat (BS), deadlift (DL), isometric squat, broad jump, and peak power.

**Results:** VL and BF thickness increased significantly during the initial 10-week RT (pre to mid: VL:  $7.0\% \pm 9.8$ ,  $p = 0.003$ ; BF:  $8.6\% \pm 10.3$ ,  $p < 0.001$ , pre to post: VL:  $6.1\% \pm 11.8$ , ns.; BF:  $4.2\% \pm 8.0$ ,  $p = 0.050$ ), along with substantial improvements in strength (BS:  $19.1\% \pm 10.95$ ; DL:  $12.5\% \pm 8.3$ , both  $p < 0.001$ ). During the final 7 weeks, increasing weekly volume by 1.5× did not yield additional hypertrophy in VL or BF, either in the total sample or among initial non-responders ( $< 2 \times$  typical error in VL thickness during the first 10 weeks). For strength, only DL differed between groups, favouring lower volume ( $p = 0.043$ ).

**Conclusions:** Substantially increasing RT volume did not enhance muscle hypertrophy or strength in athletes. Furthermore, non-response was unaffected by increased RT volume.

## Assessment of Individual Response Variation to Resistance Training: Study Design of TraDeRe Research Project and Statistical Insights

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**Purpose:** Individual response variation (IRV) is generally attributed to differences in trainability across individuals, but recent evidence using novel analytical approaches challenges this assumption. This study investigated the presence of IRV in responses of maximal leg press strength (1RM) and vastus lateralis cross-sectional area (VL CSA) following resistance training (RT) .

**Methods:** 248 untrained participants completed a 12-week RT intervention (INT), while 60 participants engaged in a non-training control period followed by the 12-week RT intervention (CON). A linear mixed model for between- (BTW) and within-group (WTH) analyses was conducted to assess training effects. True IRV was estimated using statistics of absolute (standard deviation of individual responses, SDIR) and relative variation (log ratio coefficient of variation, InCVR). The likelihood that a new subject from the studied population would benefit or not from the prescribed training intervention was assessed by calculating the proportion of response (%).

**Results:** Both analyses showed significant gains in primary outcomes in INT compared to CON ( $p < 0.001$ ). True IRV estimates showed a small SDIR effect size (ESIR) for both BTW (1RM = 0.26; VL CSA = 0.19) and WTH (1RM = 0.25; VL CSA = 0.29) analyses, respectively. A negative InCVR indicated higher relative variation introduced by the CON compared to the INT condition. Proportion of response ranged from 94 to 98% in muscle strength and size outcomes.

**Conclusions:** Our findings indicate that while true IRV was observed, random variation (i.e., measurement error, within-subject variability) explain a major part of IRV following RT in previously untrained young-to-middle aged participants. We suggest that RT programs following evidence-based guidelines remain highly effective to induce practically meaningful responses in muscle size and strength in this population.

# Heterogeneity in acute resistance training-induced changes in the reticulospinal excitability in males and females

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**INTRODUCTION** Resistance training (RT)-induced changes in muscle size and strength are only weakly correlated (1), suggesting that neural adaptations may partially explain this heterogeneity, given that muscle strength is influenced by both muscle mass and neural factors. However, inter-individual variability in neural responses to RT remains unknown. The reticulospinal tract (RST) is an important pathway mediating strength adaptations (2), and ipsilateral motor evoked potential (iMEP) is considered a valid proxy of RST excitability (3). Here, we investigated inter-individual heterogeneity in acute iMEP responses to a single bout of resistance exercise.

**METHODS** 119 healthy adults (59 males, 60 females) participated in this study. iMEPs from the non-dominant arm (m. biceps brachii) were elicited using transcranial magnetic stimulation at 100% stimulator output when participants reached an elbow flexion angle of 110° during bilateral biceps curls with 30% of their one-repetition maximum (1RM) load.

**RESULTS** Comparing the average of the first five with the last five iMEPs revealed a significant increase in iMEP amplitude ( $63 \pm 62\%$ ,  $p < 0.001$ ) during 40 repetitions. Eleven (9.7%) subjects were non-responders (relative change,  $\Delta < 0$ ), and 48 (42%) exhibited responses exceeding one standard deviation from the group mean (range from -42% to 387%), without sex difference ( $p = 0.16$ ). Multiple linear regression analysis showed that only  $\Delta$ root mean square amplitude of the background electromyogram ( $\beta = 0.657$ ,  $p = 0.012$ ) was a significant positive predictor of  $\Delta$ iMEP from the first five and the last five trials. This is possibly a reflection of increased motor unit recruitment and/or rate coding due to increased muscle fatigue.

**CONCLUSION** Forty repetitions at 30%1RM led to large variations in iMEP response, independent of age, sex, and strength.

- 1) Ahtiainen et al., J. Age, 2016.
- 2) Akalu et al., Physiol. Rep, 2024
- 3) Ziemann et al., J. Physiol, 1999.

## The Effect of Diet Quality on Skeletal Muscle Hypertrophy

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To maximise skeletal muscle hypertrophy (SMH), diet cannot be neglected. It is not known whether the diet quality differs between higher and lower responders to resistance training (RT). Also, no consensus exists how the consumption of vegetables, grains, and dairy affects SMH. This research aims to examine 1) does the diet quality differ between higher and lower responders to RT and 2) does the consumption of vegetables, grains and dairy affect SMH?

310 participants (130M, 180F) finished a RT period of 12 weeks. 301 participants completed the Healthy Food Intake Index questionnaire at baseline. A cross-sectional area (CSA) of m. vastus lateralis was measured with ultrasound pre- and post-RT. A higher score both within each food group and in the total score across food groups indicated a closer alignment to the Nordic Nutrition Recommendations.

One-way ANOVA was used to compare the diet quality between the responder groups. Group allocation was performed with K-means clustering based on CSA change. Mixed model was used to assess the relationship of the food groups on SMH.

No difference was observed in the diet quality between the groups ( $p=0.763$ ). CSA increased significantly ( $B=3.46\text{cm}^2$  [3.25-3.67],  $p<0.001$ ). Based on estimates, vegetables were negatively associated with CSA increase ( $\beta = -0.14$  [-0.28-0.00],  $p=0.047$ ) and grains were positively associated with CSA increase ( $\beta = 0.19$  [0.06-0.32],  $p=0.005$ ). Both improved the model fit (vegetables  $X^2(1) = 4.00$ ,  $p=0.045$ , grains  $X^2(1) = 8.00$ ,  $p=0.005$ ). Dairy did not affect CSA change ( $p=0.233$ ).

Diet quality did not differ between higher and lower responders to RT. Higher consumption of vegetables and grains was negatively and positively, associated with CSA increase, respectively. All the dietary effects were small in magnitude. Although the used questionnaire reflects diet and its components well in practice, studies with more objective methods are needed.

## Different protein profiles display unequal changes after resistance training and a training break

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High-end proteomics have been used to examine responses of individual proteins and pathways to exercise (1). It can also be used to study protein profiles based on cellular location where their molecular function is known to take place. The present study aims to investigate the effects of resistance training (RT) and detraining (DT) on different protein profiles based on their cellular location.

Thirty untrained participants were divided into training-detraining-retraining (TDR, n=17) and control (n=13) groups. TDR underwent 10 weeks of RT, and 10 weeks of DT, while the control group remained non-trained for 10 weeks. Biopsies were collected from vastus lateralis in weeks 0, 10, and 20. High-end diaPASEF on the mass spectrometry of the timsTOF Pro 2 platform was used for proteomics analysis. In total, > 3000 unique proteins were quantified. Of these, 50 were classified based on the literature as myofibrillar proteins. Other quantified protein profiles were classified using Uniprot database: mitochondrial (714), enzyme (1257), ECM (158), ribosomal (120), and nuclear (992) proteins.

The relative abundance of myofibrillar and ECM proteins displayed no significant changes between the timepoints, suggesting these protein profiles change in proportion to muscle proteins during RT and DT. Instead, the relative abundance of ribosomal, mitochondrial, and enzyme protein profiles increased during 10 weeks of RT ( $p<0.05$ ) and compared to controls, and there was a trend for increases in nuclear proteins ( $p=0.06$ ). Enzymes and mitochondrial proteins returned to baseline after DT, whereas nuclear and ribosomal proteins remained elevated ( $p<0.05$ ).

Herein we show different temporal changes in protein profiles after resistance training depending on their classified cellular location. Our results suggest relative and persisting expansion of nuclear and ribosomal protein profiles after resistance training and detraining. This may indicate proteomic memory of resistance training-induced hypertrophy.

## References

1. Hulmi et al., The Journal of Physiology, 2025

## Repeatability of skeletal muscle hypertrophy and strength in response to resistance training

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Repeatability of resistance training (RT) responses has been poorly researched. Responses to RT are expected to be repeatable if physiological factors are major determinants of RT responses. This study investigated repeatability of skeletal muscle hypertrophy and maximal strength.

71 participants (40 F, 31 M, age  $38 \pm 6.2$  years) without previous background in systematic RT underwent 12 weeks of RT, consisting of 23 whole-body RT sessions. Exercises for the lower body were bilateral leg press and knee extensions. Three sets were performed per exercise per session, resulting in a weekly volume of 12 sets for the lower body. Based on skeletal muscle size responses, higher, moderate and lower responders were recruited to retraining-intervention after 10 months of detraining. The first 7 weeks of retraining were identical to the first RT phase. Skeletal muscle hypertrophy was evaluated via change in vastus lateralis cross-sectional area (VL CSA) using panoramic ultrasound. Maximal strength was evaluated as a one-repetition maximum in a bilateral leg press (LP 1RM). Correlations between variables was analyzed with Pearson correlation test, or if not normally distributed, Spearman rank correlation test. Responses were analyzed as relative weekly change.

The main results were that skeletal muscle hypertrophy responses displayed moderate correlation ( $p < 0.001$ ,  $R^2 = 0.3$ ) and maximal strength responses displayed weak correlation ( $p = 0.029$ ,  $R^2 = 0.069$ ). The correlation between skeletal muscle hypertrophy and changes in maximal strength in retraining were moderately correlated ( $p < 0.001$ ,  $R^2 = 0.19$ ).

In conclusion, skeletal muscle hypertrophy responses to repeated RT interventions were moderately repeatable, whereas maximal strength responses were poorly repeatable. These results suggest physiological factors have larger influence on skeletal muscle hypertrophy than maximal strength responses. However, a considerable magnitude of skeletal muscle hypertrophy responses to RT remained unexplained by repeated intervention with same training program.

## Poster presentations

### Mast Cells Tryptase and Blood Pressure after Aerobic Exercise

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**Purpose:** Post-exercise hypotension (PEH) is an important marker of peripheral vasodilatation and beneficial blood pressure regulation response after exercise. However, large inter-individual differences have been observed in PEH but the physiological mechanisms for these differences are not known. Mast cell tryptase (MCT), a specific marker for mast cell activation and histamine release, is one of the suggested potential mechanisms for inter-individual differences in PEH.

**Methods:** Normotensive participants (7 males and 7 females, age  $28 \pm 6$  years,  $VO_{2peak}$   $46 \pm 7$  ml/kg/min, body fat %  $17 \pm 7\%$ ) performed 30-min aerobic exercise at the intensity of 60% of maximal workload by cycle ergometer ( $147 \pm 33$  W, heart rate  $73 \pm 5$  % of maximal heart rate). The blood pressure was measured at every 5-min in recovery phase and the area under the curve (AUC) for systolic (SBP) and diastolic (DBP) blood pressure was calculated from the end of exercise until 60-min after exercise. Blood samples were collected at baseline, immediately after exercise, and 60-min after recovery. MCT concentrations were quantified in duplicates using enzyme-linked immunosorbent assay (ELISA). Intra-assay and inter-assay CV were  $< 10\%$ .

**Results:** SBP was  $121 \pm 13$  at baseline and  $110 \pm 13$  mmHg 60-min after exercise ( $p=0.003$ ), and corresponding DBP  $71 \pm 8$  vs.  $70 \pm 8$  mmHg ( $p=ns$ ). AUC for SBP was  $-460 \pm 418$  mmHg·min (range from -1107 to +120 mmHg·min) and for DBP  $8 \pm 260$  mmHg·min (range from -369 to +456 mmHg·min). MCT was  $45 \pm 11$ ,  $46 \pm 11$  and  $45 \pm 7$  ng/ml ( $p=ns$ ) at baseline, immediately after exercise and after 60-min recovery, respectively. The change in MCT from the end of exercise to the end of 60-min recovery was moderately correlated with the AUC for DBP ( $r=-0.61$ ,  $p=0.020$ ) but not with AUC for SBP ( $r=-0.17$ ,  $p=0.573$ ).

**Conclusion:** MCT after aerobic exercise, a specific marker of local histamine release, may partly regulate inter-individual differences in post-exercise DBP

## From Test to Task: Relevance of Basic Physical Fitness Metrics in The Context of Military-Specific Performance

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Physical fitness assessments, such as push-ups, sit-ups, and 12-minute runs, remain central to military readiness evaluation; however, their capacity to explain variance in military-specific task performance remains insufficiently understood. This study investigated the relationship between these generalistic standard physical fitness assessments and performance in six simulated military-specific tasks. Twenty-nine physically active male participants (mean age = 22.4 years, SD = 2.7) completed a battery of laboratory-based measurements including maximal oxygen uptake ( $\text{VO}_{2\text{max}}$ ) and body composition via dual-energy X-ray absorptiometry, and field-based evaluations of aerobic endurance (12-minute run), anaerobic agility (shuttle run), muscular endurance (push-ups, sit-ups, pull-ups), explosive power (countermovement jump, seated medicine ball throw), grip strength, and maximal strength (one-repetition maximum hexagonal barbell deadlift). Six military-specific tasks were performed in standardized 10.4-kilogram combat gear: 2 km loaded march, casualty drag, maximal single lift of a military pack to a platform, repeated lift and carry, modified fire and movement, and water can carry. Most standard assessments showed limited associations with military tasks. The 12-minute run was the only consistent aerobic predictor, relating to the 2 km loaded march ( $\beta = -0.233$ , 95% CI  $[-0.327, -0.140]$ ) and repeated lift-and-carry ( $\beta = -0.062$ ,  $[-0.089, -0.034]$ ). Strength and power measures were task-specific: maximal single lift correlated with seated medicine ball throw ( $\beta = 0.112$ ,  $[0.046, 0.179]$ ) and grip strength ( $\beta = 0.685$ ,  $[0.147, 1.222]$ ), while modified fire-and-movement time was associated with shuttle-run performance ( $\beta = 0.963$ ,  $[0.204, 1.721]$ ). No statistically discernible predictors were identified for casualty drag. Discrete military tasks depend on distinct physical attributes, supporting the integration of task-specific assessments alongside standard tests. These results provide evidence for need to tailor physical training and evaluation protocols to occupational demands of military personnel. Training programs emphasizing aerobic capacity, explosive strength, and load-carrying ability may target the physical qualities most relevant to military performance.

## Psychosocial Well-being and Genetic Predisposition Shape Responsiveness to Lifestyle Coaching: Insights from a Risk-Stratified Intervention Trial

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Lifestyle modifications effectiveness in modulating metabolic signatures and interacting with genetic susceptibility and behavioral determinants of health remains incompletely understood. Psychosocial well-being may both reflect underlying genetic predisposition and influence responsiveness to lifestyle interventions, thus elucidating these relationships is essential for advancing personalized and precision health approaches.

This 10-week longitudinal intervention study assessed the impact of lifestyle coaching on cardiometabolic health among working-age adults at elevated risk based on apolipoprotein B to apolipoprotein A1 ratio ( $N = 709$  screened). Participants in the highest risk category (~15%,  $n = 104$ ) were randomized to either personal coaching (intervention:  $n = 53$ ; control:  $n = 51$ ), while those at medium risk (~30%,  $n = 213$ ) were randomized to group coaching (intervention:  $n = 107$ ; control:  $n = 106$ ) branch. Low-risk individuals ( $n = 394$ ) were excluded after baseline. Interventions followed a standardized curriculum and included personalized or group-based behavioral guidance targeting diet, physical activity, and stress management. Statistical analyses were performed using generalized estimation equations (GEE) for primary analyses.

At baseline, higher polygenic risk scores for BMI associated with greater psychosocial burden, higher adiposity, and more adverse metabolic profiles ( $FDR < 0.05$ ), including elevated high-sensitivity CRP, uric acid, and alanine aminotransferase levels. The 10-week lifestyle intervention did not yield major differential effects on cardiometabolic status between coaching modalities within different risk strata but did result in incremental improvements ( $FDR < 0.05$ ) in psychosocial well-being. Participants with multidomain challenges showed the least responsiveness ( $FDR < 0.05$ ) in adiposity and metabolic signatures. In addition, baseline cardiometabolic status and polygenic risk predisposition shaped intervention responsiveness, influencing adiposity and metabolic signature trajectories.

These findings underscore the importance of personalized, multidimensional approaches for optimizing prevention strategies towards cardiometabolic health. Genetic risk together with psychosocial well-being shape both baseline status and potential for change and intervention responsiveness.

Awareness about digital rehabilitation among Physiotherapist in Pakistan.

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Digital rehabilitation, also termed as tele rehabilitation enables the distant delivery of rehabilitation services, thereby increasing accessibility and efficacy. Worldwide, the healthcare service sector is gradually admitting the advantages of digital rehabilitation. Digital rehabilitation offers a resourceful means for providing suitable physical therapy facilities to patients at the comfort of their homes. The objective of the study was to evaluate level of awareness, attitudes, perceptions and barriers concerning digital rehabilitation services among the Physiotherapists in Pakistan. The data was collected using a cross-sectional survey research design from 255 physiotherapists via online google form. The study population includes 76 (33%) male and 154 females (67%). Participants having an advance knowledge of Information technology showed a significant inclination to attend training programs ( $p < 0.05$ ).

Digital rehabilitation offers an optimistic approach to enhance physiotherapy facilities in Pakistan. Inadequate amenities, poor set-up, lack of knowledge and insufficient funding determine failures in continuing the practice of digital rehabilitation. The findings also indicated that the existing courses do not incorporate the proficiencies required for professionals suggesting the need to incorporate such programs in the syllabuses.

These obstacles must be addressed so that the physiotherapist's community in Pakistan can reinforce digital rehabilitation to improve patient outcomes and promote the profession.

## Supervised Exercise in Prostate Cancer Patients: Implications of inter-individual differences in Precision Medicine

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### Background and Purpose

Individuals adaptations to resistance training (RT) vary widely—an issue with direct relevance to the benefits of exercise in oncological endpoints. We present (1) outcomes from an RCT of supervised vs. home-based exercise during androgen deprivation therapy (ADT) for prostate cancer (PCa), and (2) phase III RCT, testing whether adding atorvastatin to supervised aerobic+RT enhances PCa treatment outcomes.

### Materials and Methods

Study1 (Patient School): Localized or metastatic PCa on long-term ADT (n=44) were randomized 1:1 to supervised, twice-weekly exercise (aerobic+RT) or an unsupervised home-based program for 3 months, with 3-month follow-up. Outcomes included quality of life(QoL), strength, body composition, and metabolic profile.

Study2 (MOVES): A pilot study with three-arm, open-label randomization during first-line systemic therapy in metastatic breast, kidney, ovarian, or prostate cancer. Participants complete 3 months of supervised group exercise, supervised exercise plus atorvastatin 40 mg/day, or non-guided exercise, with a 2-year follow-up for disease progression and mortality. The study characterises tumor-agnostic responses of exercise and their association with cancer outcomes.

### Primary Results

Study 1: Supervised training was safe even for patients with bone metastasis and demonstrated significant improvement in emotional functioning ( $Z = -2.102$ ,  $p = 0.036$ ) and all exercise performance metrics ( $p < 0.001$ ), with the most pronounced gains observed in the leg press ( $Z = -4.17$ ,  $p < 0.001$ ). However, only participants who had strength improvements experienced enhanced physical function ( $p < 0.001$ ). No significant differences were found in other outcomes.

Study 2: Expect to show that exercise combined with atorvastatin reduces tumor hypoxia, affects serum immune parameters beneficially, and improves time until biochemical or clinical progression and death. We assume the benefits depend on individual adaptations to exercise.

### Conclusions

In conclusion, even in metastatic PCa patients, aerobic+RT improves emotional wellbeing, lower- and upper-body strength. However, the exercise benefits depend on individual exercise adaptations.

## Deciphering the role of vasculature in cancer cachexia

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**Background:** Cancer cachexia is characterized by involuntary weight loss, muscle atrophy and inflammation. Bimagrumab, an antibody directed against activin type II receptors (ActRII), has demonstrated anabolic effects on skeletal muscle offering a therapeutic strategy for cachexia management. The aim of this study is to decipher the role of vascular system in the development and progression of cancer cachexia and identify potential therapeutic strategies.

**Methods:** The self-produced bimagrumab and mAb27 (a FLT1-blocking antibody that increases VEGF-A availability and angiogenesis via VEGFR2) antibodies were first tested in healthy C57BL/6J female mice. To study their effects in cancer cachexia, we used the KPC pancreatic adenocarcinoma (PDAC) cachexia mouse model. Adult C57BL/6J female mice (n=30) were divided into control, PDAC, PDAC + bimagrumab and PDAC + mAb27 groups. KPC cells (106) were injected intraperitoneally. Body weights were monitored regularly. Three-dimensional analyses of whole muscle vasculature and investigation of tumor-secreted cachexia-inducing factors are currently ongoing.

**Results:** Body weight began to decline rapidly after 7 days in all PDAC groups, but bimagrumab modestly slowed this loss. Bimagrumab improved overall survival and preserved muscle mass in the tibialis anterior and quadriceps muscles, while mAb27 treatment was associated with reduced survival.

**Conclusions:** Bimagrumab appears to be a promising therapeutic option for the treatment of cachexia, whereas mAb27 seems to impair survival. Future directions of this research aim to investigate the combined effects of bimagrumab, exercise and/or GDF15 inhibition. Muscle samples from the slower progressing ApcMin/+ colorectal cancer model have also been collected and are under investigation.

## Short-term Resistance Training: Strength and Reticulospinal Tract Adaptations

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### Background

Despite growing interest, the contribution of the reticulospinal tract (RST) to strength gains following resistance training (RT) in healthy humans remains unresolved (1). This study examined neural adaptations of RST in response to RT.

### Materials and Methods

Thirty-seven healthy volunteers (20 males, 17 females; age:  $40 \pm 6$  years; height:  $1.72 \pm 0.09$  m; body mass:  $74.7 \pm 12.5$  kg) participated in a six-week, supervised RT targeting upper and lower limb muscles. Training sessions were performed twice weekly: three sets (last set to failure) of 8-10 repetitions per exercise, following a progressive overload principle. Transcranial magnetic stimulation (TMS) elicited ipsilateral and contralateral motor evoked potentials (iMEPs and cMEPs, respectively) in biceps brachii. The iMEPs and ipsilateral-to-contralateral amplitude ratio (ICAR) assessed RST excitability. Single-pulse TMS was delivered at 100% maximum stimulator output with posterior-anterior current flow during preacher curl at 30% maximum load (2). Only iMEP data with latencies  $\geq 4$  ms longer than cMEP were included to ensure ipsilateral origin. MEP amplitudes were normalized to M-max.

### Results

Pre-intervention test-retest showed no significant changes in strength, iMEP or ICAR ( $p > 0.05$ ), confirming no adaptations from repeated testing. RST excitability significantly increased, as indicated by a  $37 \pm 56$  % increase in iMEP amplitude ( $p < 0.001$ ) and a  $32 \pm 60$  % rise in ICAR ( $p = 0.04$ ). One-repetition maximum improved by  $9.4 \pm 6$  % confirming enhanced strength. Changes in iMEP and ICAR were not correlated with strength gains ( $R = -0.14$ ,  $p = 0.46$ ;  $R = -0.06$ ,  $p = 0.75$ ), likely due to high measurement variability (CV = 22.4% and 24.9%).

### Conclusion

These findings suggest short-term RT can increase RST excitability, indicating subcortical pathways may contribute to early neural adaptations to RT.

1. Akalu et al. 2024, Eur J Neurosci 2. Hu et al. 2024, Eur J Neurosci

## Effects of time-of-day specific combined resistance-interval training on muscle strength and bone mass in elderly women

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**Background & Purpose:** Aging is associated with osteosarcopenia, increasing the risk of falls and fractures [1]. While exercise is recommended, the optimal time of day for training specifically for elderly women remains underexplored [2]. This study aimed to determine the effects of a 12-week time-specific (morning vs. afternoon) combined resistance-interval training program on muscle strength and bone mass in elderly women.

**Materials & Methods:** 26 healthy untrained elderly women (age:  $71 \pm 3$ ; BMI:  $18.5 - 35 \text{ kg/m}^2$ ) were divided into three groups: Morning Training (MTG,  $n=10$ ), Afternoon Training (ATG,  $n=10$ ), and Control (CON,  $n=6$ ). The 12-week intervention included supervised sessions (2x/week) and later added home-based sessions (1x/week). Assessments before (PRE) and after (POST) included Dual-energy X-ray Absorptiometry (DXA) for bone/body composition and isometric knee extension dynamometry for strength (tested at both AM and PM times).

**Principal Results:** Relative peak torque significantly increased after the 12-week intervention period ( $p < 0.0001$ ). Post-hoc analysis revealed that only ATG significantly improved strength in both morning ( $p = 0.0202$ ) and afternoon ( $p = 0.0188$ ) tests, whereas the MTG showed no significant post-hoc increases. A significant test time effect ( $p = 0.0129$ ) confirmed a typical diurnal rhythm (PM > AM strength) that persisted in training groups both PRE- and POST-intervention. While Bone Mineral Content (BMC) did not change significantly, Total Body Bone Mineral Density (BMD) and T-scores showed favorable trends ( $p = 0.0529$ ;  $p = 0.0627$ , respectively), with improvements noted specifically in the ATG post-intervention.

**Major Conclusions:** A 12-week time-of-day specific combined resistance-interval training program improves musculoskeletal health in elderly women. Afternoon training appears superior for elderly women, eliciting broader strength adaptations and early favorable shifts in bone mineral density compared to morning training.

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