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SYMPOSIA

S1- THE STUDY OF MUSCLE, MOBILITY AND AGING (SOMMA): AN OVERVIEW AND PRELIMINARY RESULTS.

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Communication 1: *The Study of Muscle, Mobility and Aging (SOMMA): An Overview of the Cohort,* Anne B. Newman[1], Stephen B. Kritchevsky[2], Russell T. Hepple[3], Bret H. Goodpaster[4], Paul M. Coen[4], Peggy M. Cawthon[5], Steven R. Cummings[5] (1. Research Institute, California Pacific Medical center and Department of Epidemiology and Biostatistics, University of California, San Francisco, CA, USA; 2. Department of Epidemiology, University of Pittsburgh, Pittsburgh, PA USA; 3. Department of Internal Medicine: Gerontology & Geriatric Medicine and The Sticht Center for Healthy Aging and Alzheimer's Prevention, Wake Forest School of Medicine, Winston-Salem, NC, USA; 4. Department of Physical Therapy, University of Florida, Gainesville, FL USA; 5. Translational Research Institute, AdventHealth, Orlando, FL, USA; 6. Research Institute, California Pacific Medical Center and Department of Epidemiology and Biostatistics, University of California, San Francisco, CA, USA)

SOMMA is a new cohort study conducted at Wake Forest and University of Pittsburgh, coordinated by the San Francisco Coordinating Center, with management of biological specimens by Adventist Health Research Institute. We aim to discover the biological basis of mobility disability and have collected tissues and measurements for future studies of the biology of human aging. We screened approximately 4200 individuals to enroll 881 including 41% men and 59% women with a mean age =73.4 ± 5SD years; 13% were Black, 85% White and 2% of other race and ethnic groups. We will add 80 individuals aged 30-69 years. Exclusions included unstable medical conditions and inability to walk 400 meters(m). The median baseline 400m gait speed at usual pace was 1.05 ± 0.18SD m/s. To assess mitochondrial energetics in muscle, respiration assays were performed on biopsies of the vastus lateralis and the capacity to generate ATP (ATPmax) was determined by 31P MR spectroscopy. Other properties examined in biopsies include denervation, autophagy, and oxidative damage. We archive ~150mg for ancillary science. In a subset, we obtained biopsies of subcutaneous adipose for measurements including cell senescence and for archiving. To assess body composition, SOMMA used whole body MR for quadriceps volume and D3 Creatine dilution for total skeletal muscle mass. We measured fitness by cardiopulmonary exercise testing. Participants also had many other assessments of physical and cognitive performance including chair stands, balance, gait speed, leg power, stair climbing, the Montreal Cognitive Assessment and patterns of physical activity by actigraphy. We will repeat a 400 m walk along with core physical and cognitive batteries annually for 3 years of follow-up. In this symposium, we will describe the baseline characteristics of the cohort and will also describe how to obtain data and specimens for analyses and ancillary studies.

Communication 2: *Skeletal muscle mitochondrial energetics is associated with leg power generation and cardiorespiratory fitness in older adults in the Study of Muscle Mobility and Aging Study (SOMMA),* Theresa Mau[1], Paul M. Coen[2], Li-Yung Lui[1], David J. Marcinek[3], Anthony J. A. Molina[4], Giovanna Distefano[2], Russell T. Hepple[5], Bret Goodpaster[2], Philip Kramer[6], Adam J. Santanasto[7], Frederico G.S. Toledo[8], Kate A. Duchowny[9], Sofhia Ramos[2], Lauren Sparks[2], Peggy M. Cawthon[1,9], Stephen B. Kritchevsky[6], Anne B. Newman[7], Steven R. Cummings[1,9] (1. Research Institute, California Pacific Medical Center, San Francisco, CA, USA; 2. Translational Research Institute, AdventHealth, Orlando, FL, USA; 3. Department of Radiology, University of Washington, Seattle, WA, USA; 4. Department of Medicine; Division of Geriatrics, Gerontology, and Palliative Care, University of California San Diego, La Jolla, CA, USA; 5. Department of Physical Therapy, University of Florida, Gainesville, FL USA; 6. Department of Internal Medicine: Gerontology & Geriatric Medicine and The Sticht Center for Healthy Aging and Alzheimer's Prevention, Wake Forest School of Medicine, Winston-Salem, NC, USA; 7. Department of Epidemiology, University of Pittsburgh, Pittsburgh, PA USA; 8. Department of Medicine, Division of Endocrinology and Metabolism, University of Pittsburgh, USA; 9. Department of Epidemiology and Biostatistics, University of California, San Francisco, CA, USA)

Skeletal muscle mitochondrial function declines with age, and few studies have examined how these declines relate to physical function in older adults. Here, we examined associations between measures of mitochondrial energetics with leg power and cardiorespiratory fitness in SOMMA. Thigh muscle (vastus lateralis) biopsies were collected from older women and men to assess mitochondrial function (n=468, mean=76.9yr). Max OXPHOS (maximal complex I and II supported state 3 respiration) was determined in vitro by high-resolution respirometry of permeabilized muscle fibers, and ATPmax was determined in vivo by 31P magnetic resonance spectroscopy. Maximum leg extension power (mean=174.6Watts) was measured with a Keiser press system, and VO2 peak (mean=1494.6mL/min) was acquired using a standardized cardiopulmonary exercise test. Beta coefficients (β) and coefficient of determination (R2) were calculated using multivariate linear regression models adjusted for age, sex, race, technician/site, height, weight, and body size. Max OXPHOS was strongly associated with leg power (β= 10.7 Watts per 1 SD increment, $p<0.001$) and peak VO2 (β= 83.7 mL/min, $p<0.001$). ATPmax had weak associations with leg power (β= 4.2 Watts per SD increment, $p<0.13$). In contrast to its weaker relationship with leg power, ATPmax

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was strongly associated with VO2 peak (β= 70.1 mL/min per SD increment, p<0.001). In models that included ATPmax, Max OXPHOS, age, sex, race, technician/site, and body size as independent variables, the R2 was 0.6 for maximal leg power as the dependent variable, and 0.7 for VO2 peak as the dependent variable. In conclusion, skeletal muscle mitochondrial energetics were strong determinants of leg power and VO2 peak in these older adults, independent of age, sex, and race. These measures of mitochondrial function, along with age, sex, race, explain a large proportion of the variance in leg power and VO2 peak in this population. Our findings support an important role for mitochondrial energetics in aging muscle health.

Communication 3: *Cognitive and Physical Function Relationships in the SOMMA study,* Stephen B. Kritchevsky[1], Eileen Johnson[2], Christina E. Hugenschmidt[1], Paul M. Coen[3], Russell T. Hepple[4], Anne B. Newman[5], Anthony J. A. Molina[6], Michael E. Miller[7], Peggy M. Cawthon[2,8], Theresa Mau[2], Nancy Glynn[5], Steven R. Cummings[2,8] (1. Department of Internal Medicine: Gerontology & Geriatric Medicine and The Sticht Center for Healthy Aging and Alzheimer's Prevention, Wake Forest School of Medicine, Winston-Salem, NC, USA; 2. Research Institute, California Pacific Medical Center, San Francisco, CA, USA; 3. Translational Research Institute, AdventHealth, Orlando, FL, USA; 4. Department of Physical Therapy, University of Florida, Gainesville, FL USA; 5. Department of Epidemiology, University of Pittsburgh, Pittsburgh, PA USA; 6. Department of Medicine; Division of Geriatrics, Gerontology, and Palliative Care, University of California San Diego, La Jolla, CA, USA; 7. Division of Public Health Sciences and The Sticht Center for Healthy Aging and Alzheimer's Prevention, Wake Forest School of Medicine, Winston-Salem, NC, USA; 8. Department of Epidemiology and Biostatistics, University of California, San Francisco, CA, USA)

There is interest in the interplay between cognitive and physical function. However, relatively few studies include measures which allow for their simultaneous consideration. We used canonical correlation (n=424) to examine the relationships between a set of physical function measures (400m usual pace, chair stands/sec, 4m walk pace, standing balance times, VO2 peak, muscle power, four-square step test (FSST) time, stair climb time and stair climb power) and a set of cognitive measures (Trail Making Test B (sec), Digit Symbol Substitution Test (DSST), the Montreal Cognitive Assessment, and California Verbal Learning Test. Canonical correlation derives synthetic variables comprised of linear combinations within each set of variables (physical and cognitive) that maximize the correlations between synthetic variables. The full set of 7 synthetic variables explained 39% of the shared variance between the physical and cognitive sets [Wilk's lambda = 0.61; F=1.92 (77, 1739.3), p < 0.001]. Only the first canonical function was statistically significant and explained 27.4% of the shared variability between the two variable sets. The physical assessments most strongly associated with the physical synthetic variable were: 400 m pace; 4 m Pace; chair stand rate; FSST time; and stair climb time (all structure coefficients > |0.5|). The cognitive assessments most strongly associated with the cognitive synthetic variable were: DSST (# correct), and Trails B time (structure coefficients > |0.73|). The FSST was the most cognitively challenging physical task and was most strongly correlated with the cognitive synthetic variable (- 0.42). The DSST score, which measures perceptual speed, was the cognitive measure most strongly correlated with the physical synthetic variable (0.48). It is notable that only the timed cognitive and physical tests are inter-associated. Whether this is secondary to age or reflects an intrinsic pace remains to be explored.

S2- FRAILTY AND SURGERY: INTEGRATING EVIDENCE FOR RISK PREDICTION AND BEYOND.

Qian-Li Xue *(Department of Medicine Division of Geriatric Medicine, Johns Hopkins University School of Medicine and Johns Hopkins Center on Aging and Health, Baltimore, Maryland, USA)*

Communication 1: *Implementation of a Frailty-Focused Perioperative Care Pathway: Is This Value-Based Care?* April Ehrlich[1], Joshua Mostales[1], Oluwafemi Owodunni[3], Dianne Bettick[2], Susan Gearhart[3] (1. Department of Medicine Division of Geriatric Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA; 2. Quality Management, Johns Hopkins Bayview Medical Center, Baltimore, MD, USA; 3. Department of Surgery, Johns Hopkins School of Medicine, Johns Hopkins University, Baltimore, MD, USA)

Background: Individuals 65 years and older account for 40% of the inpatient surgical population and 1 out of 5 patients in this age group are considered frail and at risk for poor postoperative outcomes. In 2018, we implemented a Geriatric Surgery Pathway (GSP) in accordance with the American College of Surgeons' Geriatric Surgery Verification Standards and supported by the Age-Friendly Hospital Program to identify and address the unique challenges of caring for frail older surgical patients. **Objectives:** An observational pre-post GSP study was conducted to examine the effect of the GSP on postoperative outcomes and cost of care among frail patients. **Methods:** Data from EHR geriatric dashboard for patients ≥65 years undergoing inpatient surgery from 2016-2020 was merged with the national ACS-NSQIP registry. GSP patients (2018-2020) were identified by preoperative frailty screening (Edmonton Frail Scale). The GSP intervention for patients screening positive for frailty included a multidisciplinary preoperative discussion, perioperative anesthesia/acute pain team consultation, and postoperative co-management with Geriatric Medicine. Postoperative outcomes included loss of independence (LOI), length of stay (LOS), major complications (CD II-IV), and total and direct cost of inpatient care. Linear regressions were computed adjusting for age, sex, race, operative stress score, and case mix index. **Results:** 533 (300 pre-GSP, 233 GSP) served as the study sample. Frailty was identified in 82 patients (26%) in the pre-GSP cohort and 74 (32%) patients in the GSP cohort. Frail patients

before and after GSP implementation were similar in baseline characteristics. On multivariable analysis, frail patients in the GSP cohort experienced decreased risk for LOI (OR 0.30 [0.25, 0.37] $p < 0.001$) and major complications (OR 0.31 [0.24, 0.40] $p < 0.001$), and a reduction in LOS (IRR 0.97 [0.96, 0.98], $p < 0.001$). Comparing our frail pre-GSP to our GSP cohort, the mean total cost ($29,752+/-$4,333 vs. $28,237+/-$3,452, p=0.02) and direct cost of inpatient care ($13,892+/-$1,950 vs. $12,765+/-$1,566, p=0.02) decreased. **Conclusions:** This study demonstrates that high-value care can be achieved in a diverse frail patient population with implementation of a GSP. Future studies to examine pathway compliance would promote the identification of further interventions.

Communication 2: *Frailty Assessment as a Component of Comprehensive Geriatric Assessment for Geriatric Trauma Patients,* Maria Cantu-Cooper[1], Ashley McGinity[2], Alex Bokov[1], Sara Espinoza[1] (1. Department of Medicine, Division of Geriatrics, Gerontology & Palliative Medicine, University of Texas Health Science Center at San Antonio, San Antonio, TX, USA; 2. Department of Surgery, Division of Trauma and Emergency Surgery, University of Texas Health Science Center at San Antonio, San Antonio, TX, USA)

Background: A growing population, geriatric trauma patients require specialized care to maximize outcomes and reduce complications. Because traumatic injury cannot be anticipated, risk stratification prior to injury is challenging. Prior studies aimed at identifying older adults at risk for poor outcomes examined the effectiveness of combinations of injury severity scale, comorbidities and age; however, these did not accurately predict mortality. **Objectives:** To incorporate frailty screening into a comprehensive geriatric assessment (CGA) model and characterize the prevalence of frailty and its associations with length of stay (LOS) and disposition in a sample of geriatric trauma patients. **Methods:** CGA, including frailty assessment, was conducted for geriatric trauma patients (all aged 65 years or older) at University Hospital, an academic Level I trauma center in San Antonio, TX. Frailty was assessed using the FRAIL Scale, disability status at baseline was assessed with Barthel activities of daily living (ADLs), and Lawton-Brody instrumental activities of daily living (IADLs). A retrospective electronic health record review was conducted for patients evaluated from August 2020 to August 2021, and descriptive statistics were used to examine LOS and disposition. Logistic regression was used to examine odds of disposition to home, with adjustment for comorbidity (Charlson), and baseline ADL and IADL disability. **Results:** Of 270 patients reviewed, 258 had frailty assessment (27% were non-frail, 37% pre-frail, and 34% frail). Compared to non-frail, frailty was associated with longer LOS (9.1 ±9.5 vs. 7.1 ±7.1, p=0.037). Total of 136 (56%) were discharged to home and frail compared to non-frail patients had lower rate of being discharged to home: 31 (35%) vs. 105 (62%), p<0.001). Frail patients had correspondence with 63% lower odds of being discharged to home (odds ratio: 0.37, 95% confidence interval: 0.2-0.57, p<0.001). **Conclusion:** Frailty is associated with longer length of stay and reduced likelihood of home discharge; however, our results are limited by lack of injury severity scale data which we plan to include in the future. FRAIL scale may be a useful tool to identify geriatric trauma patients at risk for poor outcomes.

Communication 3: *Prevalence of Frailty across Different Hospital Types and Association of In-Patient Mortality in Geriatric Surgery,* Daniel S Rubin[1], Maria Lucia L Madariaga[2], Megan Huisingh-Scheetz[3] (1. Department of Anesthesia and Critical Care, University of Chicago, Chicago Illinois, USA; 2. Department of Surgery, Section of Cardiac and Thoracic Surgery, University of Chicago, Illinois, USA; 3. Department of Medicine, Section of Geriatrics and Palliative Care, University of Chicago, Chicago Illinois, USA)

Background: Recent trends in geriatric surgery have identified a shift of in-patient surgical procedures towards urban teaching hospitals. It remains unknown whether the shift is due to the increasing complexity of patients (i.e., frailty) and whether outcomes are similar across health systems. **Objectives:** To determine the prevalence of frailty across hospital types for intermediate risk surgical procedures and the impact of hospital type on in-patient mortality when controlling for frailty. **Methods:** The National Inpatient Sample (NIS) is a systematic random sample of all community hospital discharges in the United States. We used the NIS from 2016-2018 and clinical classification software refined to identify intermediate risk vascular, thoracic, and abdominal surgical procedures in older adults (>65 years of age). Frailty was measured using the Hospital Frailty Risk Score (HFS) based on ICD-10-CM codes, and categorized as low (<5), intermediate (5-15), and high frailty risk (>15). We used a multivariable logistic regression to determine the association between hospital type and in-patient mortality when controlling for frailty, patient and admission characteristics and surgical procedure type. **Results:** The cohort included 139,544 unweighted discharges which represented 697,720 weighted discharges over the 3-year study period. Overall frailty risk prevalence was low-frailty risk (66.7%), intermediate frailty risk (31.4%) and high-frailty risk (1.9%). In-hospital mortality among the three groups was 0.7%, 10.7%, and 20.0% respectively. The prevalence of frailty (low, intermediate, high) across hospital systems was rural hospitals (67.1%, 31.2%,1.7%; n=47,830), urban non-teaching (64.4%, 33.4%, 2.2%; n=148,780) and urban teaching hospitals (67.3%, 30.8%, 1.9%; n=501,110) (P<0.001). Urban teaching hospitals were associated with a higher odds of in-patient mortality (OR: 1.15; 95% CI: 1.02, 1.29; P=0.024) as compared to rural hospitals after adjusting for covariates. **Conclusion:** High-risk frailty is prevalent among older adult surgical patients across all hospital systems, including rural and urban non-teaching hospital systems. Interventions to improve outcomes for frail older adults should be generalizable to all types of health systems.

S3- THE D3-CREATINE DILUTION METHOD: MEASUREMENT OF MUSCLE MASS ACROSS THE LIFE SPAN: CHILDREN, NEUROMUSCULAR DISEASE, AGING MEN AND WOMEN. Luigi Ferrucci *(National Institute on Aging, Baltimore, MD, USA)*

The assessment of total body skeletal muscle mass has, until recently, been problematic. Skeletal muscle is a significant but not the only component of lean body mass (LBM). In a large number of clinical trials LBM is incorrectly referred to as muscle mass and, as a result use of LBM as a surrogate for muscle mass has resulted in erroneous conclusions on the importance of skeletal muscle in development of late-life dysfunction and risk of chronic disease. The D3-Creatine (D3Cr) dilution method allows a direct and accurate measurement of skeletal muscle mass that is undiluted by hydration status or accumulation of intramyocellular fibrosis or lipid. The method provides a measurement of creatine pool size and, as ~98% of the body creatine pool is located in the sarcomere, muscle mass. Because the method is non-invasive and only requires a single fasting urine sample, the method is ideal to measure muscle mass in large cohort studies. The method has been incorporated into a large prospective longitudinal trial in more than 1,300 older men (MrOS corhort, > 80 yr), older women from the Women's Health Initiative, infants, children, and boys with Duchenne muscular dystrophy (DMD). Results show that D3Cr muscle mass but not DXA derived LBM, is strongly associated with several important functional and health related outcomes including risk of a fall, hip fracture, and disability. In this population of elderly men, D3Cr muscle mass has also been associated with activities of daily living, and instrumental activities of daily living. In a smaller sample of older women, D3Cr muscle is more strongly correlated with functional capacity and indices of glycemic control than LBM. In infants and children, accretion of muscle mass is rapid and associated with indices of growth. However, in boys with DMD, aging is associated with declining muscle mass and function.

Communication 1: *The D3-creatine dilution method,* William J Evans (University of California, Berkeley CA, USA)

Description of pre-clinical and clinical validation studies. How to employ the method into clinical trials including large cohort studies and randomized, controlled trials. This method employs an enteral dose of a tracer quantity of deuterated creatine. The tracer is absorbed and transported into the sarcomere. The D3Cr is irreversibly converted to D3-creatinine (D3Crn) and excreted, thus allowing the measurement of D3Crn enrichment from a single, fasting urine sample. Details of dosing, sampling, and measuring muscle mass in longitudinal studies will be discussed. In addition to MrOS, incorporation of this method into ongoing longitudinal studies including the Framingham offspring, WHI Life and Longevity after Cancer (LILAC), Tobago Longitudinal Aging Study, Study of Muscle, Mobility and Aging (SOMMA), and longitudinal changes in muscle mass in DMD will allow a definition of sarcopenia that is based on an accurate measurement of skeletal muscle mass.

Communication 2: *D3Cr muscle mass and assessment skeletal muscle quality,* Eric Orwoll (Oregon Health & Science University, Portland, OR, USA)

D3Cr muscle mass and assessment skeletal muscle quality. Is Sarcopenic Obesity an anachronistic term? Previous research using estimates of LBM have concluded that increased body fatness represents and additional risk for poor functional capacity than low LMB. Data on the relationship of body fatness and muscle mass on walking speed suggests that sarcopenic obesity may not be a risk factor when muscle mass is accurately measured.

Communication 3: *Muscle mass as a powerful risk factor for health-related outcomes in older people,* Peggy Cawthon (California Pacific Medical Center Research Institute, San Francisco, CA, USA)

Muscle mass as a powerful risk factor for health-related outcomes in older people. The use of inaccurate measurements of muscle has resulted in an assumption that muscle mass is not associated with late-life disability and health related outcomes. Sarcopenia definitions are controversial and none, so far, have used muscle mass. Emerging data indicates that in older men, muscle mass (but not DXA lean mass or appendicular lean mass) is strongly associated with functional status, strength, risk of hip fracture, disability (including IADL), and mortality. We review the current evidence and highlight what additional steps are needed to support the use of D3Cr to define sarcopenia.

S4- NEUROMUSCULAR JUNCTION TRANSMISSION FAILURE IN SARCOPENIA. Matteo Cesari *(University of Milan, italy)*

Communication 1: *Neuromuscular junction transmission failure is associated with weakness and impaired muscle function in aged rodents,* W. David Arnold[1], D. Chugh[1], C.C. Iyer[1], X. Wang[1], R. Bobbili[1], MM Rich[2], CJ Padilla[1], ME Harrian[1], H Harris[1], JM Schwab[1], SB Rutkove[3], BC Clark[4] (1. Department of Neurology, The Ohio State University, Columbus, OH, USA; 2. Department of Neuroscience, Cell Biology, and Physiology Wright State University, Dayton, OH, USA; 3. Department of Neurology, Beth Israel Deaconess, Harvard Medical School, Boston, MA, USA; 4. Ohio Musculoskeletal and Neurological Institute, Ohio University, Athens, OH, USA)

Pathological age-related loss of skeletal muscle strength, the key characteristic of sarcopenia, contribute to impaired physical function in older adults. Factors that contribute to age-related weakness are not fully understood, impeding development of effective and specific diagnostic and therapeutic approaches. Inconclusive evidence across species suggests disruption of action potential signal transmission at the neuromuscular junction (NMJ), the crucial connection between the nervous and muscular systems, as a possible contributor to age-related muscle weakness. Here, data will

be presented from two recently published rodent (mice and rat) studies that investigated age-related loss of NMJ function using clinically relevant, electrophysiological measures (single-fiber electromyography (SFEMG) and repetitive nerve stimulation (RNS)) in aged versus young rodents. Measures of muscle function (e.g., grip strength, peak plantarflexion contractility torque) and mass were assessed for correlations with electrophysiological measures of NMJ transmission. Other outcomes also included plantarflexion muscle contractility tetanic torque fade during 1-s trains of stimulation as well as gastrocnemius motor unit size and number. Profiling NMJ function in aged rodents identified significant declines in NMJ transmission stability and reliability. Further, NMJ deficits were strongly correlated with hindlimb grip strength, gastrocnemius muscle weight, loss of peak contractility torque, degree of tetanic fade, and motor unit loss. Thus, these findings provide direct evidence for NMJ dysfunction as a potential mechanism of age-related muscle dysfunction pathogenesis and severity. These findings also suggest that NMJ transmission modulation may serve as a target for therapeutic development for age-related loss of physical function.

Communication 2: *Neuromuscular junction transmission failure is associated with weakness and impaired muscle quality in sarcopenic older adults,* Brian C. Clark[1], Leatha A. Clark[1], Thomas Skjærlund Grønnebæk[2], Jane Bold[2], Thomas Holm Pedersen[2], John Hutchison[2], W. David Arnold[3] (1. Ohio Musculoskeletal and Neurological Institute, Ohio University, Athens, OH, USA; 2. Pharma A/S, Aarhus, Denmark; 3. Department of Neurology, The Ohio State University, Columbus, OH, USA)

Enhancing physical function in older adults is a major public health priority and is urgently needed to reduce healthcare costs and improve quality of life. Sarcopenia, the pathological loss of muscle strength and size with advancing age, is a well-established determinant of physical limitations and poor health in older adults. According to the most recent consensus definitions, weakness, as compared to muscle mass, is the key characteristic of sarcopenia. The mechanisms of age-related weakness are multifactorial, with neurologic and skeletal muscle factors contributing. As the final nexus between the neurologic and skeletal muscle systems, integrity of the neuromuscular junction (NMJ) is necessary for dependable neural control of muscle force generation. Accordingly, the NMJ has long been a site of keen interest in the context of skeletal muscle function deficits in sarcopenia. In this study, we sought to determine whether older adults with clinically meaningful leg extensor weakness exhibited NMJ transmission failure. Here, we recruited ten older adults who self-reported physical limitations (mean age: 85.9$\pm$4.4 years). A control group of 8 young and middle-aged adults were tested for comparison (mean age: 29.5$\pm$8.7 years). For our primary interests, we assessed participants isokinetic leg extensor strength and obtained MRI's of the upper thigh that permitted us to accurately quantify fat-subtracted muscle volume. To further characterize the participants, we also quantified handgrip strength, physical function, and body composition using dual-energy x-ray absorptiometry scans to quantify lean mass. Then, we used stimulated single fiber electromyography (SFEMG) to quantify both jitter, which is the variability in the arrival time of action potentials to the recording electrode between consecutive electrical discharges, and intermittent impulse blocking (i.e., complete NMJ transmission failure) of the vastus lateralis. In performing SFEMG, a pair of needle stimulating electrodes were placed in the region of the vastus lateralis motor point, and a highly selective SFEMG needle recording electrode was inserted ~2-3 cm distally. Branches of the femoral nerve were supramaximally stimulated at 10 Hz, and jitter and blocking were assessed at each synapse following 50-100 consecutive stimulations. One of the older adults did not exhibit leg extensor weakness, whereas nine were classified as having leg extensor weakness based on previously published cut points. We should note that seven were also classified as having handgrip weakness based on the EWGSOP2 most recent consensus definition for sarcopenia, and that the older participants had low levels of physical performance as assessed by the short physical performance battery (e.g., 50% scored $\leq$8). Consistent with our prior rodent findings, we observed that, on average, the older adults with leg extensor weakness exhibited mean jitter values that were approximately 3 times longer than the controls. Moreover, many of the weak older adults exhibited prominent levels of blocking, and the degree of jitter and blocking were both associated with volitional muscle quality (i.e., leg extensor strength normalized to quadriceps muscle volume) (r=0.49-0.68). These findings provide direct evidence that NMJ transmission failure is prominent in weak older adults and that it is associated with impaired muscle quality.

Communication 3: *Investigating ClC-1 chloride channel inhibition as a therapeutic strategy for sarcopenia,* Thomas Holm Pedersen, Jeanette Jeppesen-Morgen, Martin Skov, Martin Broch-Lips (Pharma A/S, Aarhus, Denmark)

Neuromuscular junction (NMJ) transmission failure has been linked to age-related muscle weakness. Recently published findings showed that small molecule inhibition of the voltage dependent ClC-1 chloride channel can improve NMJ transmission and muscle function in ex vivo pharmacological models of NMJ transmission failure. Thus, we sought to examine whether ClC-1 inhibition, via a novel small molecule ClC-1 channel inhibitor, could improve NMJ transmission and muscle function in aged rats. We first confirmed that old rats demonstrated indices of NMJ transmission dysfunction on single fiber electromyography when compared to younger adult rats. We then initially conducted a single dose experiment that demonstrated that acute administration of a ClC-1 inhibitor significantly enhanced electrically-stimulated isometric force of old rats when compared to older rats given a vehicle and younger adult rats given a ClC-1 inhibitor. Subsequently, we conducted a 7-day multiple-dose, blinded study comparing grip strength across days between old rats given a ClC-1 inhibitor and old rats given vehicle. This study demonstrated increased grip strength across days in old rats given the ClC-1 inhibitor

compared to old rats given vehicle, and this effect was reversed with compound discontinuation. Collectively, these data suggest that ClC-1 inhibition could serve as a viable therapeutic target for enhancing NMJ transmission and muscle function in the context of sarcopenia.

S5- ADVANCES IN SKELETAL MUSCLE ULTRASOUND IN THE ASSESSMENT OF SARCOPENIA.

Marco Narici *(Department of Biomedical Sciences, University of Padova, Italy)*

Communication 1: *Standardisation of ultrasound measures for muscle assessment of sarcopenia: results of the sarcus study,* Stany Perkisas (Department of Geriatrics, University of Antwerp, Antwerp, Belgium)

Background: In the battle against sarcopenia, the main concern in clinical practice remains the routine measurement of muscle mass. As MRI, CT, DEXA and BIA are not easily available bed-side, ultrasonography could prove to be an interesting alternative. Recent efforts of the SARCUS working group of the EuGMS have standardised the measurements of muscle assessment. The next step is the implementation in clinical practice. This study investigates the relation between the ultrasonographic assessment of the biceps muscle with other muscle parameters. **Methods:** Ultrasonographic measurements of the biceps muscle of the dominant arm were taken according to the guidelines described in the 2020 SARCUS article. Muscle thickness, cross-sectional area, pennation angle and shear-wave elastography were measured in healthy volunteers of different age groups. Also, bio-impedancemetry (BIA) and hand grip strength were taken. **Results:** In total, 123 individuals (51 men, 72 women) between 18 and 69 years were included. First, normal values for different muscle parameters will be presented. In both men and women, a decrease of hand grip strength was correlated with a decrease in global phase angle and muscle stifness, and an increase in fat mass and pennation angle. Total muscle mass, phase angle (BIA) and hand grip strength also correlated positiviely with muscle thickness and cross-sectinoal area. **Conclusions:** Sarcopenia is not only dependent upon muscle volume, but also upon muscle quality. Data on muscle assessment of the biceps msucle by ultrasound and BIA is strongly correlated. Ultrasonograpic assessment of muscles is a painless, non-invasive, cheap instrument that is available bed-side. More studies in other muscles are needed to provide further prove of concept.

Communication 2: *Age-related alterations in muscle architecture are a signature of sarcopenia: the ultrasound sarcopenia index,* Marco Narici[1,2], Jamie McPhee[3], Maria Conte[4], Martino V Franchi[1], Kyle Mitchell[5], Sara Tagliaferri[6], Elena Monti[1], Giuseppe Marcolin[1], Philip J Atherton[7], Kenneth Smith[7], Bethan Phillips[7], Jonathan Lund[8], Claudio Franceschi[4], Marcello Maggio[9], Gillian S Butler-Browne[10] (1. Department of Biomedical Sciences, University of Padova, Pa.dova, Italy; 2. CIR-MYO Myology Center, University of Padua, Padua, Italy; 3. Department of Sport and Exercise Sciences, Manchester Metropolitan University, Manchester, UK; 4. Department of Experimental, Diagnostic and Specialty Medicine, University of Bologna, Bologna, Italy; 5. Dorsey County Hospital NHS Foundation Trust, Dorchester, UK; 6. Department of Medicine and Surgery, University of Parma, Parma, Italy; 7. MRC/Versus Arthritis Centre for Musculoskeletal Ageing Research and National Institute for Health Research Nottingham Biomedical Research Centre, University of Nottingham, Derby, UK; 8. Department of Surgery and University of Nottingham School of Medicine, Royal Derby Hospital, Derby, UK; 9. Department of Internal Medicine and Biomedical Sciences, Section of Geriatrics, University of Parma, Parma, Italy; 10. Center for Research in Myology UMRS974, Sorbonne Université, INSERM, Myology Institute, Paris, France)

Background: The assessment of muscle mass is a key determinant of the diagnosis of sarcopenia. We introduce here an ultrasound imaging method for diagnosing sarcopenia based on changes in muscle architecture. **Methods:** Vastus lateralis muscle fascicle length (Lf) and thickness (Tm) were measured at 35% distal femur length by ultrasonography in a population of 219 elderly individuals classified as moderately active (MAE), sedentary (SE) (n = 109), mobility impaired (MIE) (n = 43), and in 60 adult young controls (YC). The ratio of Lf/Tm was used an index of muscle sarcopenia (USI). In a subsample of elderly male individuals (52 MAE and 24 SE) DXA-derived skeletal muscle index (SMI, appendicular limb mass/height^2) was compared with corresponding USI values. **Results:** In all participants, USI values were found to be independent of sex, height and body mass. USI values were 3.70 ± 0.52 for YC, 4.50 ± 0.72 for the MAE, 5.05 ± 1.11 for the SE and 6.31 ± 1.38 for the MIE ($P < 0.0001$, between each population). Based on the USI Z-scores, with YC as reference, elderly participants were stratified according to their muscle sarcopenic status. Individuals with USI values ranging between 3.70 < USI >= 4.23 were classified as non-sarcopenic (prevalence 23.7%), those with USI values within 4.23 < USI >= 4.76 as pre-sarcopenic (prevalence 23.7%), those with USI values within 4.76 < USI >= 5.29 as moderately sarcopenic (prevalence 15.1%), those with USI values within range 5.29 < USI >= 5.82 as sarcopenic (prevalence 27.9%), and those with USI values >5.82 as severely sarcopenic (prevalence 9.6%). The DXA-derived SMI significantly correlated with USI ($r = 0.61$, $P < 0.0001$). **Conclusions:** We propose a novel, practical, and inexpensive imaging marker of muscle sarcopenia, called the ultrasound sarcopenic index (USI), based on changes in muscle geometric proportions. These changes provide a useful 'signature of sarcopenia' and allow the stratification of individuals according to the presence and severity of muscle sarcopenia. We are convinced that the USI will be a useful clinical tool for confirming the diagnosis of sarcopenia, of which the assessment of muscle mass is a key-component. Funding by PRIN project 'NeuAge' (2017CBF8NJ_001, Narici, is acknowledged.

Communication 3: *Use of second order texture features and computational approaches to aid ultrasound estimates of muscle quality across clinical settings,* Michael O. Harris-Love[1,2], Tomas Gonzales[3] (1. Muscle Morphology, Mechanics, and Performance Laboratory, Rocky Mountain Regional Veterans Affairs Medical Center, Aurora, CO, USA; 2. Department of Physical Medicine & Rehabilitation, The University of Colorado Anschutz Medical Center, Aurora, CO, USA; 3. MRC Epidemiology Unit, University of Cambridge School of Clinical Medicine, Institute of Metabolic Science, Cambridge Biomedical Campus, Cambridge, UK)

Background: First order ultrasound (US) imaging features such as echogenicity have been used to characterize muscle quality. However, the clinical utility of this measure is limited by variation in imaging parameters and machine capabilities across clinical settings. Second order texture features and computational approaches are presumed to be intensity invariant and may allow for the comparison of muscle quality between US machines. We present our findings concerning the utility of histogram dispersion modelling and gray level of co-occurrence matrix (GLCM) analysis using 3 different US machines. **Methods:** B-mode images were acquired using the SonoSite 180 Plus, Hitachi-Aloka Noblus, and Phillips EPIQ 7 US machines. Image analysis of 360 scans were obtained by a single examiner from 6 muscle groups (rectus femoris, lower-trapezius, brachioradialis, tibialis anterior, middle deltoid, and pectoralis major) from 20 older community-dwelling veteran participants. Computational approaches included luminosity ratio (LR, muscle/subcutaneous fat luminosity) and the negative binomial distribution (k). GLCM features included angular second moment (ASM), entropy (ENT), inverse difference moment (IDM), correlation (COR), and contrast (CON) using MIPAV (Ver. 11.0.3). Physical performance testing included grip strength, habitual walking speed (10 m), and the Short Physical Performance Battery. **Results:** Concurrent validity of the muscle quality measures for all muscle groups was strongest using unadjusted echogenicity ($R2 = .56 - .74$, $p < .05$), with the most measurement concordance observed between the Sonosite and Phillips machines. Individual muscle groups with the strongest relationships using this device pair were the deltoid ($R2 = .90$, $p < .01$) and the rectus femoris ($R2 = .73$, $p < .01$). In contrast, GLCM features were more strongly associated (using Spearman's rho) with performance measures in comparison to echogenicity (grip strength: COR-Deltoid, rho = .48, $p < .05$; CON-Deltoid, rho = -.58, $p < .01$). **Conclusions:** Echogenicity demonstrated moderate inter-machine measurement concordance and exhibited greater utility than the LR, the negative binomial distribution (k), and GLCM features across the 3 devices. However, GLCM features may reflect muscle tissue characteristics better than echogenicity and other measures derived from image luminosity given the relationship of grip strength with COR and CON. Proprietary image correction algorithms and non-linear soundwave attenuation are associated with the commercial US machines used in this study. These constraints will require additional approaches to facilitate consistent US image analysis and muscle quality estimates across clinical settings.

S6- EFFECTS OF 12 WEEKS EXERCISE INTERVENTIONS IN OBESE OLDER ADULTS: FROM CLINICAL TO BIOLOGICAL PERSPECTIVES.

Aubertin-Leheudre Mylene *(Faculté des Sciences, Département des sciences de l'activité physique, UQAM & Centre de recherche de l'institut Universitaire de Gériatrie de Montréal, Montreal, Qc-Canada)*

Communication 1: *Effects of 12-weeks aerobic exercise interventions on physical and functional parameters in obese older adults,* Mylène Aubertin-Leheudre[1,2,3], Vincent Marcangeli[2,4], Livia P Carvalho[1,5,6], Maude Dulac[2,4], Guy Hajj-Boutros[2,7], Layale Youssef[3,8], Pascale Mauriège[9], José A Morais[2,7], Pierrette Gaudreau[10], Gilles Gouspillou[1,2,3], Philippe Noirez[1,2,11] (1. Département des sciences de l'activité physique, Faculté des Sciences, UQAM, Montréal, Québec, Canada; 2. Groupe de recherche en Activité Physique Adaptée, Montréal, Québec, Canada; 3. Centre de Recherche de l'Institut Universitaire de Gériatrie de Montréal, Montréal, Québec, Canada; 4. Département des sciences biologiques, Faculté des Sciences, UQAM, Montréal, Québec, Canada; 5. École de Réadaptation, Faculté de médecine et des sciences de la santé, Université de Sherbrooke, Sherbrooke, Québec, Canada; 6. Centre de Recherche sur le Vieillissement du Centre intégré universitaire de santé et services sociaux de l'Estrie-CHUS, Sherbrooke, Québec, Canada; 7. Research Institute of the McGill University Health Centre; Department of Medicine, Montréal, Québec, Canada; 8. École de Kinésiologie et des Sciences de l'activité physique, U Montreal, Montréal, Québec, Canada; 9. Département de kinésiologie, Université Laval, Québec, Québec, Canada; 10. Département de Médecine de l'Université de Montréal, Centre de Recherche du Centre Hospitalier Universitaire de Montréal (CRCHUM), Université de Montréal, Montréal, Québec, Canada; 11. UFR STAPS, Université de Reims Champagne-Ardenne, Reims, France)

Introduction: Older adults are at risk of developing obesity, which leads, in addition to metabolic disorders, to physical and functional declines. Older adults are also mainly inactive and one of the main barriers is the lack of time. High-intensity interval training (HIIT) has been shown to improve metabolic health, cardiorespiratory fitness, exercise and body composition when compared to continuous aerobic training, in an adult population. It has been demonstrated that fat mass loss is similar for both moderate-intensity continuous training (MICT) and HIIT in obese adults. Moreover, it has been shown that obese adults had similar levels of enjoyment and adherence while performing HIIT or MICT. Thus, HIIT appears to be an interesting time-efficient intervention compared MICT. However, the potential effectiveness of HIIT in older obese population is still unknown. **Aim:** To verify whether a HIIT, in comparison to a MICT , leads to higher improvements in physical function and body composition among obese older adults. **Methods:** Seventy-one obese (FM: men > 27% and women > 35%) older adults completed exercise interventions. Participants were randomized to a supervised 12-weeks intervention (3 times/week): elliptical HIIT program (n=36;

30min/session; cycle: 30 sec at Borg scale>17 & 90 sec at Borg scale13-16) or a treadmill MCIT (n=35; 60min/session; borg scale at 13-16). Body composition (DXA), muscle composition (QPCT), functional capacities (balance, chair test, walking speed, TUG), muscle function (strength, power and quality) and aerobic capacity (6min walking test) were assessed pre and post intervention. **Results:** Both HIIT and MICT interventions improved functional capacities (chair test, walking speed, TUG) and aerobic capacity in our population. These interventions also increased lean leg mass and decreased appendicular fat mass as well as waist circumference. **Conclusion:** HIIT is as effective as MICT for body composition and physical performance improvements in obese older adults. Thus, HIIT appears to be a more time-efficient exercise intervention than MICT. Biological adaptations and mechanisms underlying these results need to be explored.

Communication 2: *Effects of 12-weeks aerobic exercise interventions on biological parameters in obese older adults,* Philippe Noirez[1,2,3], Vincent Marcangeli[3,4], Livia P Carvalho[3,5,6], Maude Dulac[3,4], Guy Hajj-Boutros[3,7], Layale Youssef[8,9], Pascale Mauriège[10], José A Morais[2,7], Pierrette Gaudreau[11], Gilles Gouspillou[2,3,9], Mylène Aubertin-Leheudre[2,3,9] (1. UFR STAPS, Performance Santé Métrologie Société (EA-7507), Université de Reims Champagne-Ardenne, Reims, France; 2. Département des sciences de l'activité physique, Faculté des Sciences, UQAM, Montréal, Québec, Canada; 3. Groupe de recherche en Activité Physique Adaptée, Montréal, Québec, Canada; 4. Département des sciences biologiques, Faculté des Sciences, UQAM, Montréal, Québec, Canada; 5. École de Réadaptation, Faculté de médecine et des sciences de la santé, Université de Sherbrooke, Sherbrooke, Québec, Canada; 6. Centre de Recherche sur le Vieillissement du Centre intégré universitaire de santé et services sociaux de l'Estrie-CHUS, Sherbrooke, Québec, Canada; 7. Research Institute of the McGill University Health Centre; Department of Medicine, Montréal, Québec, Canada; 8. École de Kinésiologie et des Sciences de l'activité physique, U Montreal, Montréal, Québec, Canada; 9. Centre de Recherche de l'Institut Universitaire de Gériatrie de Montréal, Montréal, Québec, Canada; 10. Département de kinésiologie, Université Laval, Québec, Québec, Canada; 11. Département de Médecine de l'Université de Montréal, Centre de Recherche du Centre Hospitalier Universitaire de Montréal (CRCHUM), Université de Montréal, Montréal, Québec, Canada)

Introduction: 12-weeks of High-Intensity Interval Training (HIIT) and moderate-intensity continuous training (MICT) lead to body composition and physical performance improvements in obese older adults. Biological adaptations and mechanisms underlying exercise interventions need to be explored in order to prescribe a sufficient dose of exercise to achieve health benefits. **Objective:** To explore biological adaptations following a HIIT and MCIT in obese older adults. **Methods:** Blood samples (15mL) were collected in the morning after an overnight fast (12h) to assess serum levels of biochemical and hormonal markers of the participants, who completed the 12-weeks exercise interventions (HIIT: n=36; MCIT: n=35). A subset of these participants underwent a skeletal muscle biopsy [HIIT: n=13 (women:9; men:4) vs MICT: n=14 (women:6; men:9)] and an abdominal adipose tissue (AT) biopsy [HIIT: n=21 (women:10; men:11); MICT n=15 (women:9; men:6)]. Abdominal subcutaneous AT was collected at the peri-umbilical region using a 12-gauge Yale needle, whereas muscle sample was obtained from the vastus lateralis muscle using Bergstrom needle biopsy. Mitochondrial biogenesis, fusion, fission and mitophagy were determined in muscle homogenates by immunoblotting. Expression of key genes involved in adipose tissue lipid metabolism was analyzed. **Results:** We observed a decrease in TG and ferritin levels in HIIT only. The expression of UCP-1 mRNA in AT increased significantly in MCIT only. TFAM expression was significantly increased in both groups. An increase in TOM20, Parkin and MFN2 expression was observed in HIIT only. All other measured parameters in blood, AT and muscle were not influenced by our interventions. **Conclusion:** HIIT seems to be more effective than MICT to stimulate mitochondrial adaptations in muscle. In AT, the increase in UCP-1 mRNA expression in MICT may contribute to explain the fat mass loss observed in this group. The changes in TG and ferritin blood levels may be explained by a higher basal level of HIIT participants. In order to gain an in-depth understanding of the biological adaptations of exercise interventions, omic analyses should be undertaken.

Communication 3: *Are metabolomic adaptations following 12-weeks aerobic exercise interventions related to physical improvements in obese older adults?* Layale Youssef[1,2,3], Sylvère Durand[4,5], Fanny Aprahamian[4,5], Deborah Lefevre[4,5], Melanie Bourgin[4,5], Maria Chiara Maiuri[4,5], Maude Dulac[3,6,7], Guy Hajj-Boutros[6,8], Vincent Marcangeli[3,6,7], José A Morais[8], Pierrette Gaudreau[9,10], Gilles Gouspillou[3,6,11], Guido Kroemer[4,5], Mylène Aubertin-Leheudre[3,6,11], Philippe Noirez[1,6,11,12] (1. INSERM U1124, Université de Paris, Paris, France; 2. École de Kinésiologie et des Sciences de l'Activité Physique (EKSAP), Université de Montréal, Montréal (QC), Canada; 3. Centre de Recherche de l'Institut Universitaire de Gériatrie de Montréal, Montréal, Canada; 4. INSERM U1138, Centre de Recherche des Cordeliers, Sorbonne Université, Université de Paris, Paris, France; 5. Metabolomics and Cell Biology Platforms, Gustave Roussy Cancer Campus, AMMICa US23/ CNRS UMS3655, Villejuif, France; 6. Groupe de Recherche en Activité Physique Adaptée, Université du Québec à Montréal, Montréal, Canada; 7. Département de biologie, Université du Québec à Montréal, Montréal, Canada; 8. Research Institute of the McGill University Health Center (MUHC), Montréal (QC), Canada; 9. Centre de Recherche du Centre Hospitalier de l'Université de Montréal, Université de Montréal, Montréal (QC), Canada; 10. Department of Medicine, University of Montreal, Montréal (QC), Canada; 11. Département des sciences de l'activité physique, Université du Québec à Montréal, Montréal, Canada; 12. UFR STAPS, Performance Santé Métrologie Société (EA-7507), Université de Reims Champagne Ardenne, Reims, France)

Introduction: Ageing and obesity became major public health issues. Older adults are becoming increasingly aware of

the importance of exercising for a healthy lifestyle. It has been shown that the metabolome can be affected by exercising. It would be inter-esting to evaluate if the metabolome adaptations are related to clinical adaptations following exercise interventions. **Objective:** To evaluate if the serum metabolomic adaptations following a High-Intensity Interval Training (HIIT) and a Continuous Training (MICT) in obese older adults are cor-related with the clinical adaptations observed to each type of training. **Methods:** Seventy-one obese, sedentary elderly men and women participated in this randomized, double-blind interventional study: a 12-week HIIT training program or a 12-week MICT training program. Serum samples were collected before and after the intervention to obtain the metabolomic profile through 4 spectrometers: 1) UHPLC/q-Extractive (Thermo Scientific); 2) LC/QTRAP 6500+ (AB Sciex); 3) LC/QQQQ 6410 (Agilent); 4) GC/7000C (Agilent)) coupled with different liquid or gas chromatography methods. Among 364 identified metabolites, only those with a significant training effect were selected. Pearson correlations were performed using delta change values from clinical parameters and selected metabolites. Only correlations with $r > 0.60$ and $p \leq 0.01$ were reported. **Results:** Following HIIT, we observed correlations between cholinephosphate and fat parameters (leg and trunk fat masses; total cholesterol) or muscle function (calf circumference, muscle leg power; gynoid lean mass and IGF-1). Following MCIT, we observed correlations between pyruvic acid/oxaloacetic acid and muscle function (muscle leg power and gynoid lean mass). We also found correlations between cholesterol profile (total and LDL cholesterol) and xylitol or TG(18:3/18:3/22:0). In both interventions, we observed other relationships between clinical parameters and other metabolites (not reported since $r < 0.59$ or isolated). **Conclusion:** Interestingly, the metabolites related to muscle function or fat metabolism changes are different following 2 aerobic exercise interventions (HIIT: cholinephosphate vs. MCIT: xylitol or pyruvic acid). Further studies are needed to confirm these findings and to understand whether the mechanisms are specific to aerobic training or also influenced by age or obesity status.

S7- ORAL HEALTH AND FRAILTY. Luis Miguel Gutiérrez-Robledo *(Instituto Nacional de Geriatría, National Institutes of Health, Health Ministry, Mexico)*

Communication 1: *The available evidence: Methodological details and results,* Luísa Helena do Nascimento Tôrres (Federal University of Santa Maria (UFSM), Graduate Program in Dental Sciences, Brazil)

Several manuscripts addressing the association between oral conditions and frailty have been published during the last four years. These manuscripts have used about 18 different strategies to evaluate older people's frailty status and various strategies for measuring participants' oral health characteristics and functionality. The various manuscripts report the association between frailty and a set of composite oral health measurements; one focused on self-reported data, the other focused on clinical data, and two of them combined subjective and objective measurements. A recent review listed the 12 oral conditions associated with frailty and suggested that the number of teeth could be a marker for general health. This presentation describes and discusses the methodological details and results reported on the association between oral health and frailty during the last years.

Communication 2: *Integrating the available evidence,* Faisal Hakeem (Centre for Epidemiology Versus Arthritis, The University of Manchester, Manchester, UK)

This presentation aims to elaborate on the integration and interpretation of the available evidence to identify and interpret the potential paths linking oral conditions and older people's frailty status and offer a sound theoretical background to keep the topic growing. This is a small part of a larger picture despite identifying a collection of oral characteristics cross-sectionally and prospectively associated with frailty. Reviewing this evidence with a wider lens could help to discover additional layers of knowledge.

Communication 3: *Implications, gaps and next steps,* Roberto Carlos Castrejón-Pérez (Instituto Nacional de Geriatría, National Institutes of Health, Health Ministry, Mexico)

The evidence available results from two main questions: 1) Is there a cross-sectional association between oral conditions and older people's frailty status? 2) Is there a prospective association between oral conditions and older people's frailty status? And the answer to these questions is not entirely satisfactory. The manuscripts addressing these two questions used a variety of strategies to achieve results, and the results make evident a set of gaps that need to be addressed in health research. This presentation aims to discuss the implications inherent to the potential association between oral conditions and frailty, present some new questions to address, and suggest some of the next steps to move forward with the topic.

ONLINE SYMPOSIUM- IMPROVING PROTEIN INTAKE OF OLDER ADULTS: METABOLIC ASPECTS AND IMPACT ON APPETITE AND PHYSICAL FUNCTIONING. Marjolein Visser *(Department of Health Sciences, Vrije Universiteit Amsterdam, The netherlands)*

Communication 1: *Optimization of protein intake in the elderly beyond the amino acid composition: what is the positioning of plant proteins and under what conditions?* Dominique Dardevet, Isabelle Savary-Auzeloux, Laurent Mosoni, Marie-Agnès Peyron, sergio Polakof, Didier Rémond (Université Clermont Auvergne, INRAE, UMR1019, Unité Nutrition Humaine, Clermont-Ferrand 63000, France)

There seems to be a consensus that the need for proteins is increased in the elderly to maintain optimal all the body functions. In several countries, the RDA for proteins has recently been increased to 1g/kg/d for adults over 65 years of age with dietary proteins of good quality. Apart from the

quantity to be ingested, which can still remain a problem to reach for this population, the quality of the proteins ingested is essential and involves much more than just the composition of amino acids. The lower the quality of these proteins, the more the quantity to be ingested to meet the AA requirement will be important and therefore difficult to achieve. The quality of a dietary protein is related to its amino acids composition (AA) but also to several other determinants including the speed of digestion, the presence of specific AAs, the food matrix in which the dietary proteins are included and the processes involved in the production of food products (gelation, cooking temperature). The search for alternative protein sources and transitioning towards more sustainable, plantbased nutrition has received much attention in the past decade. But, is this transition compatible with optimal protein nutrition in the elderly? Plant proteins are mostly of low quality in terms of AA composition, digestibility and the presence of anti-nutritional factors. The maintenance of 30% of animal proteins should be considered in the diet to limit the increase of total proteins ingested to 25% above the 1g/kg/d. However, with the increasing number of commercially available proteins isolates, it is now possible to elaborate plant blends competing with animal proteins in terms of nutritional quality. Finally, due to the different life trajectories, inter-individual variability in the response to food intake is high in the elderly and should be studied in order to propose tailored strategies to each older adults phenotype.

Communication 2: *Innovative plant protein fibre and physical activity solutions to address poor appetite and prevent undernutrition in older adults – the APPETITE project,* Dorothee Volkert[1], Clare A Corish[2], Dominique Dardevet[3], Giuseppe De Vito[4], Christelle Guillet[3], Katy Horner[2], Stephanie Bader-Mittermaier[5], Susanne Naumann[5], Sian Robinson[6,7], Helen M Roche[2,8], Avan A Sayer[6,7], Marjolein Visser[9] for all APPETITE partners (1. Institute for Biomedicine of Aging, Friedrich-Alexander-Universität Erlangen-Nürnberg, Nuremberg, Germany; 2. School of Public Health, Physiotherapy and Sports Science and University College Dublin Institute of Food and Health, Dublin, Ireland; 3. Institut National de Recherche pour l'Agriculture, l'Alimentation et l'Environnement, Saint Genès Champanelle, France; 4. Department of Biomedical Science, University of Padua, Italy; 5. Fraunhofer Institute for Process Engineering and Packaging, Freising, Germany; 6. AGE Research Group, Translational and Clinical Research Institute, Newcastle University, United Kingdom; 7. NIHR Newcastle Biomedical Research Centre, Newcastle upon Tyne Hospitals NHS Foundation Trust and Newcastle University, Newcastle upon Tyne, UK; 8. University College Dublin Conway Institute, Dublin, Ireland; 9. Department of Health Sciences, Vrije Universiteit Amsterdam, the Netherlands)

Appetite is a key driver of food intake, which is however often reduced in older persons for a variety of reasons, leading to poor food intake including poor protein intake. Strategies to improve appetite and protein intake are vital to preventing malnutrition, sarcopenia and frailty. In APPETITE, a transdisciplinary consortium of experts from eight institutions in six European countries will collaborate to design potentially effective interventions to enhance protein intake and appetite of community-dwelling older adults with poor appetite, thereby addressing malnutrition through a targeted nutrition- and physical activity-based strategy. Older adults with poor appetite will first be evaluated using a mixed-methods approach to gain insights into their nutritional and behavioral preferences. Working with this target group, innovative, acceptable, and affordable plant-based food products will be developed that combine several domestic plant proteins and dietary fibres which are also often not consumed in sufficient quantities. Mechanistic insights will be gained by examining the impact of selected products and physical activity on digestibility, amino acid bioavailability and whole-body protein metabolism. In a multi-country randomized controlled intervention trial, the impact of two new food products, provided as part of a personalized diet, a physical activity program, and their combination will be determined regarding appetite, dietary intake, nutritional status, anabolic response, metabolic parameters and physical function. APPETITE will improve our understanding about plant-based protein and fiber products and their metabolic and clinical effects. It will create new knowledge about how plant-protein products can be combined in a whole-diet approach, together with physical activity and regular social contacts, to improve appetite and maintain muscle mass and physical function and avoid malnutrition, sarcopenia and frailty.

Communication 3: *The effectiveness of personalized dietary advice to increase protein intake on change in physical functioning in community-dwelling older adults,* Marjolein Visser[1], Ilse Reinders[1], Satu K. Jyväkorpi[2], Riikka T. Niskanen[2], Ingeborg A. Brouwer[1], Margreet R. Olthof[1], P Caserotti[3], Angela Jornada[1], Kaisu H. Pitkälä[2], Merja H. Suominen[2], Hanneke A.H. Wijnhoven[1] (1. Department of Health Sciences, Vrije Universiteit Amsterdam, the Netherlands; 2. University of Helsinki, Department of General Practice and Primary Health Care, and Helsinki University Central Hospital, Unit of Primary Health Care, Finland; 3. Department of Sports Science and Clinical Biomechanics, Center for Active and Healthy Ageing, University of Southern Denmark, Odense, Denmark)

Aim of this multicenter randomized controlled trial was to examine the effectiveness of dietary advice to increase protein intake on 6-month change in physical functioning among older adults. A total of 276 community-dwelling older adults with a habitual protein intake < 1.0 g/kg adjusted body weight (aBW)/d were randomly assigned to either Intervention 1; advice to increase protein intake to ≥ 1.2 g/kg aBW/d (PROT, n = 96), Intervention 2; similar advice and in addition advice to consume protein (en)rich(ed) foods within half an hour after usual physical activity (PROT + TIMING, n = 89), or continue the habitual diet with no advice (CON, n = 91). Primary outcome was 6-month change in 400-m walk time. Secondary outcomes were 6-month change in physical

performance (SPPB), leg extension strength, grip strength, body composition, self-reported mobility limitations and quality of life. Compared to CON, a positive effect on walk time was observed for PROT; – 12.4 s (95%CI, – 21.8 to – 2.9), and for PROT + TIMING; – 4.9 s (– 14.5 to 4.7). Leg extension strength significantly increased in PROT (+ 32.6 N (10.6–54.5)) and PROT + TIMING (+ 24.3 N (0.2–48.5)) compared to CON. No significant intervention effects were observed for the other secondary outcomes, including SPPB score and repeated chair stands time. The intervention effect was greater for those with a slower baseline 400-m walk time (>294 s, representing a gait speed <1.36 m/s), with no effect in faster walkers. Recent post-hoc analyses showed no effect modification for the baseline characteristics protein intake (<0.9 versus 0.9-1.0 g/kg aBW/d), sex, BMI (<28 vs ≥28 kg/m2), total daily step count, and time in activity behavior (min/d). In conclusion, dietary advice to increase protein intake to ≥ 1.2 g/kg aBW/d improved 400-m walk time and leg strength among older adults with a lower habitual protein intake. Trial Identifier: NCT03712306.

Oral Communications

OC1- BIOMARKER RESULTS FROM A PHASE 2B CLINICAL TRIAL ASSESSING LOMECEL-B INFUSION IN OLDER ADULTS WITH FRAILTY. Kevin N. Ramdas, Danial Mehranfard, Geoff Green, L. McClain-Moss, Dan Gincel, Joshua M. Hare, Anthony A. Oliva *(Longeveron Inc., Miami, USA)*

Backgrounds: Aging Frailty(AF) is an age-related multidimensional syndrome that manifests with heterogeneous physical and cognitive symptoms rendering affected older adults at higher risk for adverse health outcomes. Mechanistically, inflammaging, which is an age-associated low-grade chronic inflammatory state, vascular endothelial dysfunction, and reduced regenerative capacity plays a crucial role in AF pathophysiology. Lomecel-B, an allogeneic bone-marrow-derived product featuring medicinal signaling cells(MSCs) has pleiotropic immunomodulatory activities and can potentially ameliorate the AF pathology. **Objectives:** This Phase 2b study was conducted to assess the safety and preliminary efficacy of Lomecel-B in individuals with AF. **Methods:** This was a randomized, double-blinded, placebo-controlled trial evaluating the safety and dose-range effects of Lomecel-B in subjects aged 70–85 years with mild-to-moderate frailty per Canadian Study of Health and Aging Clinical Frailty Scale, a six-minute walk test(6MWT) of 200-400m, a mini-mental examination score>24, and a Tumor Necrosis Factor-α ≥2.5pg/mL. 143 subjects were randomized to receive a single intravenous infusion of placebo, or Lomecel-B at doses of 25M(N=35), 50M(N=30), 100M(N=33), and 200M(N=16). Safety and efficacy assessments were conducted at 1, 3, 6, and 9 months, with a safety follow-up call at 12-months post-infusion. **Results:** Soluble Tie2(sTie2) was significantly reduced after Lomecel-B treatment at 9 months, in the 50M, 100M, and 200M arms, with 200M displaying the largest effect size, whereas the placebo group showed an increasing trend. Reduced levels of sTie2 indicate decreased Tie2 proteolytic cleavage by Lomecel-B which can promote pro-vascular signaling in endothelial cells. In parallel with reduced sTie2 levels, at 9 months, 200M Lomecel-B increased circulating levels of vascular endothelial growth factor-D, a mitogen for endothelial cells which is shown to promote endothelial differentiation of MSCs. Additionally, circulating Transforming Growth Factor-β levels, a major pro-fibrotic biomarker, showed an increasing trend in the placebo arm, and a reduction trend in 200M Lomecel-B arm. **Conclusion:** These findings support improved endothelial function, vascular stabilization, and reduced inflammation in a dose-response manner via Angpt1/Tie2 and VEGF pathways as potential underlying mechanism of actions for the benefits of Lomecel-B. Based on the mechanistic findings Longeveron is aiming to develop a potency assay which is required to enter a pivotal trial.

OC2- EFFECTS OF VITAMIN D, OMEGA-3 FATTY ACIDS AND A SIMPLE HOME EXERCISE PROGRAM ON PRE-FRAILTY PREVENTION AMONG GENERALLY HEALTHY AND ROBUST ADULTS AGE 70 AND OLDER: THE DO-HEALTH RANDOMIZED CLINICAL TRIAL. Michael Gagesch[1,2], Maud Wieczorek[1,2], Bruno Vellas[3], Reto W. Kressig[4], René Rizzoli[5], John Kanis[6,7], Walter C Willett[8,9], Andreas Egli[2], Wei Lang[1,2], E. John Orav[10], Heike A. Bischoff-Ferrari[1,2,11] *(1. Department of Aging Medicine, University Hospital Zurich, Zurich, Switzerland; 2. Centre on Aging and Mobility, University Hospital Zurich and University of Zurich, Zurich, Switzerland; 3. Gérontopôle, Toulouse University Hospital, University of Toulouse, UMR INSERM 1295, Toulouse, France; 4. University Department of Geriatric Medicine FELIX PLATTER, Basel, Switzerland; 5. Service of Bone Diseases, Geneva University Hospitals and Faculty of Medicine, Geneva, Switzerland; 6. Mary McKillop Institute for Health Research, Australian Catholic University, Melbourne, Australia; 7. Centre for Metabolic Bone Diseases, University of Sheffield Medical School, Sheffield, UK; 8. Department of Epidemiology, Harvard T. H. Chan School of Public Health, Boston, USA; 9. Department of Nutrition, Harvard T. H. Chan School of Public Health, Boston, USA; 10. Department of Biostatistics, Harvard T. H. Chan School of Public Health, Boston, USA; 11. University Clinic for Aging Medicine, City Hospital Zurich, Zurich, Switzerland)*

Backgrounds: The benefits of supplemental vitamin D, marine omega-3 fatty acids, and a simple home exercise program (SHEP) on frailty prevention in generally healthy community-dwelling older adults are unclear. **Objectives:** To test the effect of vitamin D, omega-3s, and a SHEP, alone or in combination on incident pre-frailty and frailty in robust older adults over a follow-up of 36 months. **Methods:** DO-HEALTH is a multi-center, double-blind, placebo-controlled, 2x2x2 factorial randomized clinical trial among generally healthy European adults aged 70 years or older, who had no major health events in the 5 years prior to enrollment, sufficient mobility and intact cognitive function. As a secondary outcome

of the DO-HEALTH trial, among the subset of participants who were robust at baseline, we tested the individual and combined benefits of supplemental 2,000 IU/day of vitamin D3, 1 g/day of marine omega-3s, and a SHEP on the odds of being pre-frail and frail over 3 years of follow up. **Results:** At baseline 1,137 out of 2,157 participants were robust (mean age, 74.3 years; 56.5% women, mean gait speed 1.18 m/s). Over a median follow-up of 2.99 years, 696 (61.2%) became pre-frail and 29 (2.6%) frail. Odds ratios (OR) (95% CI) for becoming pre-frail were 0.81 (0.62-1.07; p=0.13) for vitamin D3 compared to no vitamin D3, 0.84 (0.64-1.11; p=0.22) for omega-3s compared to no omega-3s, 0.89 (0.67-1.16; p=0.38) for SHEP compared to control exercise, and 0.61 (0.38-0.98; p=0.04) for all 3 treatments combined compared to control (placebo for the supplements and control exercise). None of the individual treatments or their combination significantly reduced the odds of becoming frail. **Conclusions:** Robust, generally healthy and active older adults without major comorbidities, may benefit by a combination of high-dose supplemental vitamin D3, marine omega-3s, and SHEP with regard to the risk of becoming pre-frail over 3 years.

OC3- EFFECTS OF A 2-YEAR EXERCISE TRAINING ON THE NEUROMUSCULAR SYSTEM HEALTH IN OLDER INDIVIDUALS WITH LOW MUSCLE FUNCTION. M.V. Narici[1,6], E. Monti[1], S. Tagliaferri[2], S. Zampieri[1,3], F. Sarto[1], M.V. Franchi[1], G. Sirago[1], A. Ticinesi[4], Y. Longobucco[2], F. Lauretani, M. Maggio[2,5] *(1. Department of Biomedical Sciences, University of Padova, Padova, Italy; 2. Department of Medicine and Surgery, University of Parma, Parma, Italy; 3. Department of Surgery, Oncology, and Gastroenterology, University of Padova, Padova, Italy; 4. Geriatric-Rehabilitation Department, University Hospital of Parma, Parma, Italy; 5. Clinical Geriatric Unit, University Hospital of Parma, Parma, Italy; 6. CIR-MYO Myology Center, University of Padua, Italy)*

Backgrounds: Aging is accompanied by a progressive loss of skeletal muscle mass and strength, leading to the clinical syndrome of sarcopenia. Evidence suggests that motoneurons and neuromuscular junction (NMJ) degeneration contribute to sarcopenia pathogenesis. **Objectives:** Seeking for solutions to slow down sarcopenia insurgence and progression, we investigated whether a two-year mixed aerobic, strength and balance training would be effective for improving or preserving motoneuron health, NMJ stability, muscle mass, strength and functionality in an old, sarcopenic population. **Methods:** 46 sarcopenic elderly (35 females; 11 males) with low DXA lean mass and Short Physical Performance Battery (SPPB) score < 9, were randomly assigned either to a control group (Healthy Aging Lifestyle Education -HALE-, n=22) or an intervention group (MultiComponent Intervention -MCI-, n=24). MCI trained 3 times/week for 2 years. Before and after the intervention, ultrasound scans of the vastus lateralis (VL), SPPB and a blood sample were obtained. VL architecture (pennation angle, PA, and fascicle length, Lf) were measured. As biomarkers of neuronal health and NMJ stability, Neurofilament Light Chain (NfL) and C-terminal agrin fragment (CAF) concentration were measured in serum. Statistical significance of differences between baseline and follow-up measurements were tested with 2-way repeated measures ANOVA or Wilcoxon test and between parameters using multivariate analysis. **Results:** At follow-up, MCI showed preserved VL architecture (PA, Lf), maintained CAF concentration, and improved SPPB performance (from 7.6 to 9.3, p=0.007), while HALE showed a significant decrease in muscle cross-sectional area (-13%, p<0.001), PA and Lf (-5.3%, p<0.001), together with an 7.8% increase in CAF (p=0.003). NfL concentration increased in both MCI and HALE (+20.4%, p<0.001, and +30.4%, p=0.026, respectively). A negative relationship between changes in CAF concentration and SPPB gait score was found in MCI (β=-0.001, p=0.028), while in HALE, NfL changes were negatively correlated with SPPB gait speed, chair stand and total score variations. **Conclusions:** The present findings suggest that our 2-year mixed-aerobic, strength and balance training, despite being unable to fully protect from sarcopenia-associated motoneuron degeneration, was effective in preventing furthe increases in CAF concentration, potentially promoting reinnervation capacity in old sarcopenic individuals, preserving muscle structure while improving physical performance.

OC4- IMPACT OF UROLITHIN A VS PLACEBO SUPPLEMENTATION ON MUSCLE ENDURANCE AND MITOCHONDRIAL HEALTH IN OLDER ADULTS: A RANDOMIZED CLINICAL TRIAL. Sophia Liu[1], Davide D'Amico[2], Eric Shankland[1], Saakshi Bhayana[1], Jose M Garcia[3], Patrick Aebischer[4], Chris Rinsch[2], Kevin E. Conley[1], Anurag Singh[2], David J. Marcinek[1] *(1. Dept. of Radiology, University of Washington Medical Center, Seattle, WA, USA; 2. Amazentis SA, EPFL Innovation Park, Ecublens, Switzerland ; 3. GRECC, Puget Sound VA and Div. of Geriatrics, Dept. of Medicine, University of Washington Medical Center, Seattle, WA, USA; 4. Ecole Polytechnique Fédérale de Lausanne, Lausanne, Switzerland)*

Backgrounds: Aging is associated with a decline in mitochondrial function and reduced exercise capacity. This warrants the development of new nutritional interventions to promote healthy aging and address health burdens in an aging population. Urolithin A (UA) is a natural food metabolite that has been shown to stimulate mitophagy and improve muscle function in aged animals and induce mitochondrial gene expression in the older adults. Objectives: Investigate if oral administration of UA improved 6-minute walking distance (6MWD), muscle endurance in hand and leg muscles, and biomarkers linked to improved mitochondrial and cellular health. **Methods:** A randomized, double-blind, placebo-controlled study in older adults (65-89 yrs.) was conducted. 128 subjects were screened and 66 were randomized (n=33/arm) between March 2018 and March 2020. Muscle fatigue and plasma biomarkers were assessed at baseline, 2 and 4 months. 6MWD and ATPmax via magnetic resonance spectroscopy (MRS) were assessed at baseline and at

the end of study. The primary endpoint was change from baseline in the 6MWD and ATPmax in the hand skeletal muscle at 4 months. Key secondary endpoints were change in skeletal muscle endurance in the hand and leg. Cellular health biomarkers were investigated via plasma metabolomics. **Results:** UA significantly improved muscle endurance in two different skeletal muscles ($p<0.05$) compared with placebo at 2 months. Plasma levels of several acylcarnitines, ceramides and C-reactive-protein (CRP) were decreased by UA at the end of study ($p<0.05$). An increase in 6MWD distance (PL 42.5 73.3 m, UA 60.8 67.2 m) and ATPmax (PL 13.7 31.4%, UA19.4 56.8%) was observed in both groups compared to baseline with no significant improvement with UA supplementation compared to placebo. UA oral administration was safe and well-tolerated with no statistical differences in adverse events observed between groups. **Conclusion:** Long-term UA supplementation is safe in the tested population. Results for the primary outcome were negative, but supportive results were obtained for secondary outcomes of muscle endurance and plasma biomarkers. This work suggests UA may hold promise to positively impact muscle health in older adults; however, future work is needed to confirm. The study is registered in clinicaltrials.gov as: NCT03283462.

OC5- ASSOCIATION OF D3CR MUSCLE MASS WITH MRI-BASED MEASURES OF MUSCLE SIZE AND FAT INFILTRATION; STRENGTH; AND WALKING SPEED IN OLDER MEN AND WOMEN: PRELIMINARY DATA FROM THE SOMMA STUDY. Peggy M. Cawthon[1,2], Stephen B. Kritchevsky[3], Anne B. Newman[4], Russell T. Hepple[5], Paul M. Coen[6], Bret H. Goodpaster[7], Adam J. Santanasto[4], Kate Duchowny[2], Theresa Mau[3], William J. Evans[7], Steven R. Cummings[1,2] *(1. Research Institute, California Pacific Medical Center, San Francisco, CA, USA; 2. Department of Epidemiology and Biostatistics, University of California, San Francisco, CA, USA; 3. Department of Internal Medicine: Gerontology & Geriatric Medicine and The Sticht Center for Healthy Aging and Alzheimer's Prevention, Wake Forest School of Medicine, Winston-Salem, NC, USA; 4. Department of Epidemiology, University of Pittsburgh, Pittsburgh, PA USA; 5. Department of Physical Therapy, University of Florida, Gainesville, FL USA; 6. Research Institute, AdventHealth, Orlando, FL, USA; 7. Department of Nutritional Sciences and Toxicology, University of California, Berkeley, CA, USA)*

Backgrounds: D3-creatine (D3Cr) dilution provides a measurement of whole-body muscle mass that is associated with slowness, disability, and death in older men. However, the relation between D3Cr muscle mass and measures of components of muscle size and muscle fat infiltration by MRI in older men and women is not clear. Further, the relation between D3Cr muscle mass with strength and physical performance with aging has not been widely reported in women. **Objectives:** Data were from the first 42% of participants enrolled in the Study of Muscle, Mobility, and Aging (SOMMA, 158 men and 213 women) aged ≥70 years. We describe the association of D3Cr muscle mass with MRI-based measures muscle size and fat infiltration, and with measures of strength and physical performance. **Methods:** D3Cr muscle mass was measured by D3-creatine dilution, and total thigh muscle volume and thigh muscle fat infiltration (proton density fat fraction) by whole body MRI (AMRA medical). Grip strength, leg extension 1-rm max (Keiser), and walking speed (400m usual walk) used standardized protocols. We calculated sex-stratified unadjusted Pearson correlation coefficients, and partial Pearson correlation coefficient adjusted for body size (height, weight). **Results:** D3Cr muscle mass was correlated with weight (men: unadjusted $r=0.44$, $p<.001$; women: unadjusted $r=0.44$, $p<.001$); and total thigh muscle volume (men: unadjusted $r=0.67$, $p<0.001$; women: unadjusted $r=0.65$; $p<.001$). Results suggest a modest correlation between D3Cr muscle mass and muscle fat infiltration (men: unadjusted $r=-0.14$, $p=0.08$; women: unadjusted $r=-0.06$, $p=0.41$). D3Cr muscle mass was positively correlated with grip strength (men: unadjusted $r=0.28$, $p<.001$; women: unadjusted $r=0.16$, $p=0.02$) and leg extension strength (men: unadjusted $r=0.44$, $p<.001$; women: unadjusted $r=0.31$, $p<.001$). D3Cr muscle mass was correlated with 400-m walk speed only after adjustment for body size among both men (partial $r=0.29$, $p<.001$) and women (partial $r=0.16$, $p=0.02$). Associations of total thigh muscle volume with strength and walking speed were of similar magnitude to the associations between D3Cr muscle mass with strength and walking speed. **Conclusions:** In older adults, D3Cr muscle mass and total thigh muscle volume are correlated with each other; and lower levels of each are associated with lower strength, and, after adjusting for body size, slower walking speed.

OC6- DEVELOPMENT OF A SMALL MOLECULE APELIN MIMETIC (BGE-105) TO PREVENT SKELETAL MUSCLE ATROPHY, SARCOPENIA, AND FRAILTY IN OLDER ADULTS. Kyra Silbernagel, Jen Otto, Allan Gordon, Patrick Martin, Robert E. Hughes, Justin Rebo, Ann Neale, Eric Morgen, Kristen Fortney, Paul Rubin, Carrie-Lynn L. Furr *(BioAge Labs, Richmond, CA, USA)*

Backgrounds: BioAge Labs' human-centric platform is a genomics-driven discovery engine for building a portfolio of drugs for aging. The platform reveals that the apelin–APJ signaling pathway regulates multiple aspects of muscle metabolism, growth, and repair to preserve muscle function; higher levels of apelin signaling in older people are associated with increased lifespan and reduced symptoms of frailty. As validated in preclinical experiments, the apelin-like drug BGE-105 significantly rescued muscle atrophy during disuse in aged animals, suggesting that BGE-105 may be a promising candidate for the treatment of frailty and sarcopenia. We hypothesize that BGE-105 could recapitulate these positive effects to improve frailty and skeletal muscle function in older adults. Building on existing clinical data, apelin-like effects of BGE-105 will be assessed further in a Phase 1b study in adults with skeletal muscle atrophy induced by 6 days of bed rest. The results of this clinical trial will inform subsequent development

activities to prevent skeletal muscle atrophy, sarcopenia, and ultimately, frailty. **Objective:** In addition to evaluating safety, tolerability, pharmacokinetics, and pharmacodynamics, the pharmacokinetic/pharmacodynamic relationships of BGE-105 will be characterized on predefined biomarkers and pharmacodynamic variables after 6 days of bed rest. **Methods:** A Phase 1b, randomized, double-blind, placebo-controlled, single- and multiple ascending dose study will assess the safety, tolerability, pharmacokinetics, and pharmacodynamics of BGE-105 in healthy adults. Skeletal muscle atrophy induced by 6 days of bedrest will be characterized by skeletal muscle protein synthesis rate and skeletal muscle circumference, cross-sectional area, color flow analysis, AP diameter, and echo density assessed by ultrasound of the vastus lateralis and gastrocnemius. **Results:** The clinical trial will be ongoing at the time of the conference. **Conclusions:** Findings from this study will inform subsequent drug development activities to prevent skeletal muscle atrophy, sarcopenia, and ultimately, frailty.

OC7- SEX DIFFERENCES IN THE ASSOCIATION OF THIGH MUSCLE STRENGTH, AREA, AND SPECIFIC FORCE WITH LOWER URINARY TRACT SYMPTOMS: THE BALTIMORE LONGITUDINAL STUDY OF AGING.

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Backgrounds: Lower urinary tract symptoms (LUTS) are associated with increased risk of mobility impairment in older adults. Muscle health is critical for maintaining mobility in older age. Therefore, age-related muscle changes are potential, yet unexplored, shared mechanisms of both LUTS and mobility impairment. **Objectives:** To evaluate the cross-sectional association of thigh muscle strength, area, and specific force with LUTS severity in older adults. **Methods:** This analysis includes 343 women and 295 men enrolled in the Baltimore Longitudinal Study of Aging. We restricted the analysis to participants age ≥60 years with no history of stroke or Parkinson's disease and no missing LUTS or muscle measures seen between February 2011 and September 2015. LUTS severity was assessed using the American Urologic Association Symptom Index (AUASI; ≥8 moderate-to-severe LUTS). Thigh muscle strength (Nm) was defined as maximum concentric 30 /s knee extensor torque. Thigh muscle area (cm2) was estimated using mid-femur cross-sectional 10-mm CT images. Thigh specific force (Nm/cm2) was defined as thigh muscle strength divided by area. We used multivariable linear regression to model associations between muscle measures (per SD increment) and AUASI. Associations were adjusted for age, sex, race, height, weight, height*weight, health-related behaviors, and comorbidities. We tested for effect modification by sex using cross-product terms. **Results:** Moderate-to-severe LUTS was present in 31% of women and 48% of men. Among men, each SD increment in thigh specific force was associated with a 0.78 lower AUASI score (95%CI -1.51,-0.06) and each SD increment in thigh muscle strength was associated with a 0.84 lower AUASI score (95%CI -1.64,-0.03), whereas thigh muscle area was not significantly associated with AUASI score (β=-0.14, 95%CI -1.18,0.89). No associations were observed among women (P>0.05 for all). We observed effect modification by sex for thigh specific force (P=0.03) and a suggestion of effect modification by sex for thigh muscle strength (P=0.07), but not for thigh muscle area (0.74). **Conclusion:** Thigh muscle strength and specific force were inversely associated with LUTS severity in older men but not women. Thigh muscle area was not associated with LUTS. Age-related changes in thigh muscle strength represent novel non-urologic LUTS mechanisms that warrant further exploration. Source of Funding: This research was supported by the Intramural Research Program of the NIH and National Institute on Aging as well as grants to SRB from the National Institute on Aging (grant numbers 1R03AG067937 and 1K76AG074903) and the UCSF Claude D. Pepper Older Americans Independence Center funded by National Institute on Aging (grant number P30 AG044281 to KC).

OC8- LOMECEL-B AS A GEROSCIENCE THERAPEUTIC CANDIDATE FOR COGNITIVE FRAILTY.

Anthony A. Oliva *(Longeveron Inc., Miami, FL, USA)*

Backgrounds: Lomecel-B is a formulation of allogeneic medicinal signaling cells (MSCs) under clinical investigation for Alzheimer's disease (AD). The promise of Lomecel-B resides in pleiotropic mechanisms of action (MOAs) can potentially target multiple pathophysiological features of this devastating disease simultaneously. **Objectives:** We report here on the progress of our clinical program using Lomecel-B for Alzheimer's disease and other aging-related indications. This includes results from a double-blinded, randomized, placebo-controlled phase 1 AD trial, and progress of our actively enrolling phase 2 AD trial. **Methods:** We have completed a double-blinded, randomized, placebo-controlled trial using Lomecel-B for AD (ClinicalTrials.gov: NCT02600130). Mild AD patients received a single infusion of Lomecel-B at 20 (N=15) or 100 million cell dosages (N=10), or placebo (N=8), and were followed for a year thereafter. Eligibility

included clinical evaluation, blood work, MRI to exclude other etiologies, and beta-amyloid tracer PET to confirm AD. Pre-specified endpoints included neurocognitive, quality-of-life (QOL), activities of daily living (ADL), and biomarker assessments. We have now begun a phase 2 trial evaluating the effects of multiple doses of Lomecel-B in patients with mild AD. **Results:** Lomecel-B has been well-tolerated and has not led to any serious adverse events, and met the primary endpoint of the phase 1 trial. In addition, exploratory biomarker endpoints provided preliminary evidence for multiple mechanisms of action (MOAs), including anti-inflammatory (IL-10, IL-12, sIL-2Rα) and pro-vascular (VEGF, IL-4, IL-6) activities. There were also significant improvements in the Lomecel-B arms relative to placebo in multiple clinical endpoint domains, including significantly decreased decline in the neurocognitive assessment, Mini Mental State Exam (MMSE). Informed by these phase 1 results, we are now conducting a phase 2a study as a next-step in this clinical program, which is FDA cleared, IRB- approved, and actively enrolling. **Conclusion:** Our results support the geroscience potential of Lomecel-B to improve clinical outcomes in AD and other aging-related indications. We anticipate that given the potential pleiotropic MOAs, Lomecel-B has potential as a novel therapeutic candidate for a variety of conditions related to cognitive frailty.

OC9- NICOTINAMIDE N-METHYLTRANSFERASE INHIBITOR TREATMENT COMBINED WITH EXERCISE IMPROVES MUSCLE STRENGTH AND RUNNING CAPACITY IN AGED MICE. Harshini Neelakantan *(Ridgeline Therapeutics, Houston, USA)*

Background: Sarcopenia is a prevalent aging condition marked by significant decline in muscle mass and strength. Current best practices for preserving muscle strength among the elderly include resistance exercise and high protein diets. However, these interventions only marginally enhance skeletal muscle strength and clinical trials of potential pharmacotherapies for sarcopenia have been largely unsuccessful in improving muscle strength and physical function. Nicotinamide N-methyltransferase (NNMT) is an enzyme that regulates the nicotinamide adenine dinucleotide (NAD) salvage pathway and methionine cycle that are critical for skeletal muscle energy metabolism. NNMT is a dominant component of a gene expression signature for sarcopenia and is highly upregulated in both aging skeletal muscle and aging muscle satellite cells. Therapeutics targeting NNMT for sarcopenia are emerging. **Objective:** Evaluate the efficacy of a novel nicotinamide N-methyltransferase small molecule inhibitor (NNMTi) drug to improve grip strength, muscle torque measurement, and running capacity both alone and in combination with resistance exercise training in aged mice. **Methods:** Aged mice (22-mo-old) were randomized into sedentary (normal cage activity, no wheel access) and exercise (Progressive Weighted-Wheel Running, i.e., PoWeR) groups with control (saline, subcutaneous, once-daily) and treatment (NNMTi, 10 mg/kg/day) arms included in both conditions. Treatment was continued for 8 weeks, with running distance measured weekly, grip strength recorded at 6 weeks-post treatment, and in vivo muscle torque and muscle wet weights recorded terminally. Collected muscle samples were processed ex vivo for fiber cross sectional area, fiber type, and proteomic analyses. **Results:** Relative to exercise alone (PoWeR controls), NNMTi treatment significantly increased grip strength ($p<0.05$), preserved running capacity during weeks 7-8 of the study ($p<0.01$), and increased pooled gastroc muscle and type IIb fiber cross-sectional areas ($p<0.001$) in the PoWeR group. NNMTi treatment also tended to increase grip strength in the sedentary mice, recapitulating muscle protein profile like differentially expressed proteins observed in the exercise alone group. **Conclusion:** We have validated the effects of NNMTi treatment alone and in combination with exercise in a translationally-relevant murine model of sarcopenia. Our data holds promise for continued development of NNMTi as a transformative therapeutic to address muscle strength decline in sarcopenia.

OC9bis- RJX-01 INTO THE CLINIC: A FIRST-OF-ITS KIND MUSCLE DISUSE STUDY. Ann Belien *(Rejuvenate Biomed, Heusden-Zolder, Belgium)*

No abstract

OC10- ASSOCIATION OF FRAILTY WITH BREAKTHROUGH COVID INFECTION AFTER VACCINATION IN PATIENTS WITH CANCER AND FRAILTY, A NATIONWIDE US VA STUDY. Natasha M. Resendes[1,2], Fei Tang[1], Jorge G. Ruiz[1,2] *(1. Miami Geriatric Research Education Clinical Center, Miami VAHS, Miami FL, USA; 2. University of Miami Miller School of Medicine, Miami, FL, USA)*

Backgrounds: Frailty and cancer are common conditions that often coexist. Patients with cancer and frailty have poor COVID-10 related clinical outcomes. Recent evidence shows that certain cancer patients may still benefit from vaccination. Frailty may decrease response to COVID vaccines in cancer patients through age-related changes in cellular and humoral immunity known also as immunosenescence. The role of frailty on COVID-19 vaccine protection in cancer patients is unclear. **Objectives:** In veterans with cancer who had full immunization with US FDA approved COVID 19 vaccines, determine the association of frailty with breakthrough Infection. **Methods:** This was a nationwide, retrospective cohort study of SARS-CoV-2 vaccination and infection among patients with cancer in the VA Health Care System from January 1,2021 to November 1, 2021. All patients with > 1 negative Covid-19 test and > 1 cancer diagnosis in the previous two years were eligible for inclusion. Patients who tested positive for COVID-19 after 01/01/2021 but before full vaccination were excluded. We defined frailty as >0.21 on a 30-item VA Frailty Index (VA-FI, excluding the cancer variable), robust (<0.10) and prefrail (0.10-0.21). The primary outcome was polymerase chain reaction or antigen-confirmed SARS-CoV-2

infection in vaccinated versus unvaccinated patients stratified by frailty. We performed logistic regression adjusting for age, BMI, race, ethnicity, sex, smoking status, VA facility, and rurality. **Results:** 279,603 Veterans with Cancer were included, mean age years 69.0 years (SD=10.6), 93.3% male, 70.4% White, 90.3% Non-Hispanic, and 74.0% were from Urban areas. The cohort included 18.3% robust, 30.0% pre-frail and 51.1% with frailty. Patients with frailty were older compared to the non-frail. Vaccinated patients had lower levels of infection compared with unvaccinated: 22382 (10.9%) vs. 14254 (19.0%), HR:.0.53 (95%CI:0.51-0.54), p<0.01. Patients with frailty displayed lower levels of vaccine protection against breakthrough infection adjusted OR: 0.63(95%CI:0.61-0.66) than prefrail 0.44 (95%CI:0.42-0.46) and robust 0.46(95%CI:0.44-0.49). **Conclusions:** In patients with cancer and frailty, COVID-19 vaccination offers decreased protection against infection compared to their vaccinated non-frail counterparts. Frailty is a factor to consider when developing and evaluating COVID Vaccines for patients with cancer.

OC11- ICOPE IMPLEMENTATION IN CLINICAL PRACTICE : DATA FROM 17,000 SENIORS PART OF THE ICOPE MONITOR DIGITAL PROGRAM TO MAINTAIN FUNCTION AND PREVENT DEPENDENCY IN FRANCE.

Bruno Vellas *(Toulouse, France)*

No abstract

OC12- ASSOCIATION BETWEEN PHYSICAL FRAILTY AND QUALITY OF LIFE: NATIONAL HEALTH AND AGING TREND STUDY (NHATS) 2011-2020.

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Introduction: Physical frailty is a state of decreased physiological reserve that increases vulnerability to adverse outcomes such as hospitalization, functional decline, and institutionalization when exposed to stressors. These outcomes are strongly associated with reduced quality of life in older adults. **Objective:** Our objective was to investigate the impact of the five individual components of the Fried frailty phenotype on specific health-related quality of life measures in community-dwelling older adults. **Methods:** We conducted a cross-sectional analysis of all data from the nine waves of the National Health and Aging Trend Study (NHATS) from 2011-2020 in adults aged ≥ 65 years. We identified the five individual components of Fried's phenotype: weakness, slow gait speed, low physical activity, exhaustion, and weight loss. Health-related quality of life (HRQoL) was examined using validated measures that mapped directly onto five SF-12 subscales: depression, anxiety, overall health, pain, and functional limitations. Separate regression analyses assessed the impact of each individual component on measures of HRQoL. **Results:** We included 42583 observations (57.2% female, median age category: 75-79). Percentage of observations that fulfilled criteria for the individual components of Fried's phenotype was as follows: weakness 36.96%, slow gait 21.98%, low activity 31.45%, exhaustion 30.25% and weight loss 16.1%, There was a strong relationship between individual frailty components on each of the five measures of HRQoL. Self-reported exhaustion appeared to have the most consistent associatioin with each of the five individual components of HRQoL:(depression: b= 1.39 +- 0.027; anxiety: 1.14 +- 0.026; overall health: b= 1.39 +- 0.03; pain: b= 1.19 +- 0.029; functional limitations: b= 1.28 +- 0.028). **Conclusion:** In this cross-sectional analysis of a prospective cohort study, we found that all components of Fried's physical frailty phenotype were associated with reduced HRQoL in community-dwelling older adults.

	Depression	Anxiety	Overall Health	Pain	Functional limitation
Grip strength	-0.12 +- .012, pval = 0.000	-0.12 +- 0.012, pval = 0.000	-0.15 +- 0.014, pval = 0.000	-0.17 +- 0.012, pval = 0.000	-0.25 +- 0.014, pval = 0.000
Gait speed	-0.22 +- 0.011, pval = 0.000	-0.08 +- 0.011, pval = 0.000	-0.44 +- 0.013, pval = 0.000	-0.11 +- 0.011, pval = 0.000	-0.55 +- 0.013, pval = 0.000
Activity	0.19 +- 0.027, pval = 0.000	-0.019 +- 0.027, pval = 0.470	0.42 +- 0.031, pval = 0.000	0.14 +- 0.027, pval = 0.000	0.22 +- 0.029, pval = 0.000
Exhaustion	1.39 +- 0.027, pval = 0.000	1.14 +- 0.026, pval = 0.000	1.39 +- 0.03, pval = 0.000	1.19 +- 0.029, pval = 0.000	1.28 +- 0.028, pval = 0.000
Weight loss	0.39 +- 0.034, pval = 0.000	0.29 +- 0.032, pval = 0.000	0.55 +- 0.036, pval = 0.000	0.20 +- 0.033, pval = 0.000	0.21 +- 0.035, pval = 0.000

OC13- RELATIONSHIP BETWEEN SEVERITY AND LATERALITY OF AGE-RELATED SENSORY DECLINE AND FRAILTY IN MULTI-ETHNIC ELDERLY ASIANS.

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Background: The contribution of vision, hearing, or both to frailty remains unclear in the elderly. **Objectives:** To investigate the relationship of the severity and laterality (i.e., unilateral or bilateral) of vision, hearing, and dual sensory impairments (VI, HI and DSI, respectively) with frailty in older Asians. **Methods:** We included individuals from The PopulatION HEalth and Age-Related SEnsory Decline PRofilE (PIONEER), a population-based study of multi-ethnic Singaporeans aged ≥60 years. Visual acuity (VA) was assessed using a LogMAR chart, and a hearing test using a portable audiometer. The Fried frailty phenotype was used to assess frailty, defined as meeting at least three out of five criteria comprising unintentional shrinking (BMI<18.5 kg/m2); slowness (≤0.8m/s on 4m-gait speed); weakness (strength <30 kg (men) and <20 kg (women)); exhaustion (via vitality domain of the SF-12); and low self-reported physical activity. Any, mild and ≥ moderate VI was defined as distance VA >0.3 logMAR; 0.3< VA ≤0.48 logMAR; and VA >0.48 logMAR, respectively; and any, mild and ≥ moderate HI as an average threshold of ≥40 dB, 40≤ hearing loss <60 dB; and hearing loss ≥60 dB, respectively. **Results:** Of the 1,510 adults (mean±SD age 72.1 ±7.9yr), 44.0%, 43.7% and 23.1% had any VI, HI and DSI, respectively. Of these, 34.0% had bilateral VI only; 64.7% had bilateral HI only, and 18.3% had DSI+ comprising

(a) bilateral VI/HI and unilateral HI/VI; or (b) bilateral VI and bilateral HI). Notably, 33.9% of participants were frail. In multivariable-adjusted analyses, bilateral VI or HI (any severity) was independently associated with almost twice the odds of having frailty (odds ratio [OR]: 1.82, 95% confidence interval [CI]: 1.25, 2.44; for VI; OR: 1.84, 95% CI: 1.32, 2.57; for HI) compared to those with no sensory impairment. Critically, those with DSI+ had even higher odds of being frail (ORs between 2.15-3.35). Unilateral VI, HI and DSI (i.e., unilateral VI and HI) of any severity were not associated with frailty. **Conclusions:** Elderly Singaporeans with bilateral VI or HI of any severity; and DSI comprising any bilateral impairment are at high risk of frailty. Strategies to prevent and delay progression to bilateral sensory losses are warranted to reduce frailty in our ageing society.

OC14- CAN RANKL INHIBITION AMELIORATE SARCOPENIA? John Gostage[1,2], Katarzyna Goljanek-Whysall[2,3], Ilaria Bellantuono[1], Eugene McCloskey[1] *(1. Department of Oncology and Metabolism, The Mellanby Centre For Musculoskeletal Research, Healthy Lifespan Institute and The Centre for Integrated research in Musculoskeletal Ageing (CIMA). University of Sheffield, Sheffield, United Kingdom; 2. Discipline of Physiology, School of Medicine, National University of Ireland Galway, University Road, Galway, Ireland; 3. Institute of Ageing and Chronic Disease and The Centre for Integrated research in Musculoskeletal Ageing (CIMA), University of Liverpool, Liverpool, United Kingdom)*

Background: Osteoprotegerin (OPG) and denosumab bind and inhibit RANKL, a major regulator of osteoclastic bone resorption. As well as reducing fracture risk and increasing bone mineral density, denosumab has also shown to significantly reduce fall incidence in placebo-controlled trials, suggesting RANKL inhibition influences skeletal muscle. OPG appears to induce beneficial effects on muscle function in mouse models (muscular dystrophy and cardiotoxin-induced muscle injury), and previous work from our group has shown a pro-myogenic effect of OPG in vitro - OPG significantly improved the viability of primary mouse myotubes, induced the formation of hypertrophic myotubes and improved myogenic phenotype (myotube fusion index and diameter). Taken collectively, we hypothesise RANKL inhibition benefits muscle. **Objectives:** Explore the effects of OPG and denosumab on myogenesis, specifically looking at their influence on viability and myogenic phenotype, in mouse and human myoblasts in vitro. **Methods:** Immortalised human myoblasts, derived from young (AB1709) and old (KM670) donors by Dr. Vincent Mouly's lab (Institute of Myology, France), were treated with human recombinant OPG or denosumab (fully human monoclonal RANKL antibody), at different stages of in vitro myogenesis. MTT was used to determine their effects on viability/cytotoxicity, and MF20 immunohistochemistry characterised myotube phenotype. RT-qPCR examined the effect of OPG on atrophy markers in primary mouse myo-blasts/tubes. **Results:** Atrophy markers MuRF1 ($p<0.01$) and Atrogin-1 were downregulated in mouse myotubes treated with OPG 10ng/ml. OPG significantly improved the viability of AB1709 and KM670 myotubes (20ng/ml: $p<0.001$). Denosumab significantly improved viability in differentiating AB1709 myoblasts and KM670 myotubes. Significant improvements in AB1709 myotube diameter were seen after 10 days of OPG (20ng/ml: $p<0.01$) and denosumab (1μg/ml: $p<0.05$). **Conclusion:** Both OPG and denosumab exert beneficial effects on muscle in vitro, most noticeably at later stages of myogenesis. The beneficial effect of OPG on mouse myotube phenotype may be mediated by decreased expression of atrophy regulators. Both treatments benefited viability and the phenotype of AB1709 myotubes (similar observations were noted between human and mouse myotubes). Future studies exploring the mechanisms of these OPG and denosumab effects could provide new insights in developing treatment options for muscle wasting and sarcopenia.

OC15- HIGHER DIETARY PROTEIN INTAKE IS ASSOCIATED WITH SARCOPENIA IN OLDER BRITISH TWINS: A TWINSUK STUDY. Mary Ni Lochlainn[1], Ruth C. E. Bowyer[1], Ailsa A. Welch[2], Kevin Whelan[3], Claire J. Steves[1,] *(1. King's College London, Department of Twin Research and Genetic Epidemiology, London, United Kingdom; 2. University of East Anglia, Norwich Medical School, Norwich, Norfolk, United Kingdom; 3. King's College London, Department of Nutritional Sciences, Franklin Wilkins Building, London, Unitd Kingdom)*

Background: Muscle loss occurs with age; however, some older adults develop sarcopenia, an accelerated loss of muscle mass and function. **Objectives:** The aim of this study was to evaluate protein intake and other factors associated with low muscle strength and sarcopenia. **Methods:** This study used data from a longitudinal study of community dwelling adult twins aged ≥60 years from the TwinsUK Registry. Data on socio-demography, diet, anthropometry, frailty status, appetite, physical activity, and gut microbiota diversity were collected. Muscle mass was measured using DXA scans and muscle strength was measured using hand gripstrength and/or chair rise time. Sarcopenia was defined using the European Working Group on Sarcopenia in Older People (EWGSOP2) criteria. Low muscle strength was defined as meeting the EWGSOP cut off for either grip strength (<27kg males; <16kg females) or chair rise time (>15 seconds for 5 rises). **Results:** Participants (n=3326) were 89% female (n=2944), with an average age of 72 (±7) years, and comprised of 869 (54%) monozygotic, 717 (46%) dizygotic twin pairs and 154 individual lone twins. The prevalence of low muscle strength and sarcopenia was 12.1% (n=401) and 4.3% (n=129), respectively. There was no significant association between protein intake and low muscle strength (OR 0.95; 95% CI 0.82-1.09; p=0.430), or between low protein intake and sarcopenia (OR 0.7; 95% CI 0.39-1.25; p=0.229) in unadjusted models. High protein intake was associated with sarcopenia (OR 2.04; 95% CI 1.21-3.44; p=0.008), and this association was robust to adjustment for age, sex, smoking, income, education, height, frailty index, physical

activity, energy intake, diet, appetite, and gut microbiome diversity. Regressions fitted to include coefficients for within-twin-pair and between-pair effects revealed that the observed association between muscle strength and income, education, frailty, and physical activity, can be accounted for by shared twin factors, whereas for weight, BMI, healthy eating index, protein intake, and microbiome diversity, the association is independent of shared twin factors. This tentatively suggests that such factors may be more modifiable in future studies aiming to prevent and/or treat reduced muscle strength and sarcopenia. **Conclusion:** High protein intake is associated with increased risk of sarcopenia in a cohort of healthy volunteer older British twins.

OC16- DEATH-SEQ IDENTIFIES REGULATORS OF CELL DEATH AND SENOLYTIC THERAPIES. Alex Colville[1,2], Jie-Yu Liu[1], Samantha Thomas[1], Heather D. Ishak[1], Ronghao Zhou[1,2], Julian D.D. Klein[1,5], David W. Morgens[2,6], Armon Goshayeshi[1], Jayesh S. Salvi[1], David Yao[2], Kaitlyn Spees[2], Michael C. Bassik[2,3], Thomas A. Rando[1,4] *(1. Paul F. Glenn Center for the Biology of Aging and Department of Neurology and Neurological Sciences, Stanford University School of Medicine, Stanford, CA, USA; 2. Department of Genetics, Stanford University, Stanford, CA, USA; 3. Chemistry, Engineering, and Medicine for Human Health (ChEM-H), Stanford University, Stanford, CA, USA; 4. Center for Tissue Regeneration, Repair, and Restoration, Veterans Affairs Palo Alto Health Care System, Palo Alto, CA, USA; 5. Present address: Molecular Medicine Research Institute, Sunnyvale, CA, USA; 6. Present address: Department of Molecular and Cell Biology, University of California, Berkeley, CA, USA)*

Background: Cellular senescence is a cell state triggered by various stresses and characterized by prolonged irreversible cell-cycle arrest with secretory features. Elimination of senescent cells extends median lifespan of mice and is being developed as a means to treat many age-related diseases and to restore tissue homeostasis in aging. Senolytics, drugs that selectively target senescent cells for death, hold promise for achieving those goals, however are limited to local administration due to the systemic toxicities of current senolytic targets. **Objectives:** While genetic screens could identify senolytics, current screens are underpowered for identifying genes that regulate cell death due to limitations in screen methodology. We sought to optimize screening methods to study cell death. **Methods:** To overcome these challenges and to increase the likelihood of uncovering targets in cell death pathways, we developed a method we termed "Death-seq" to positively select dying cells in response to genetic or pharmacologic interventions. Death-seq, a positive selection CRISPR screen, is optimized to identify enhancers and mechanisms of cell death. **Results:** Our screens identified synergistic enhancers and regulators of cell death induced by several senolytic drugs as well as gene targets to induce selective cell death in senescent cells. **Conclusions:** Death-seq enables the systematic screening of cell death pathways to uncover molecular mechanisms of regulated cell death subroutines and identify drug targets for diverse pathological states such as senescence, cancer, and neurodegeneration.

OC17- PHYSICAL FRAILTY AND COGNITIVE FUNCTION AMONG OLDER CHINESE ADULTS: THE MEDIATING ROLES OF ACTIVITY OF DAILY LIVING LIMITATIONS AND DEPRESSION. Changmin Peng[1], Jeffrey A. Burr[1], Yiyang Yuan[2], Kate L. Lapane[2] *(1. University of Massachusetts Boston, USA; 2. University of Massachusetts Chan Medical School, USA)*

Objectives: The study explored the association between physical frailty and the level and rate of change of cognitive function among community-dwelling Chinese older adults. We also examined whether activities of daily living (ADL) limitations and depressive symptoms mediate this relationship. **Methods:** Data were taken from four waves of the China Health and Retirement Longitudinal Study (2011-2018). Physical frailty was assessed with the physical frailty phenotype scale, which was based on measures of weakness, slowness, shrinking, exhaustion, and inactivity. Cognitive function was assessed with the Chinese version of the Telephone Interview for Cognitive Status instrument, including indicators of episodic memory, executive function, orientation, and visuospatial skills. Latent growth curve models were used to examine the associations among physical frailty, ADL limitations, depressive symptoms, and cognitive function. **Results:** Compared to non-frail older adults, pre-frail and frail older adults reported worse cognitive function at baseline. ADL limitations and depressive symptoms mediated the association between physical frailty and the level of cognitive function, but not for the association between physical frailty and the rate of cognitive decline. **Conclusions:** Intervention strategies that help maintain cognitive function may benefit from early screening and assessment of physical frailty. For pre-frail and frail older Chinese adults, programs designed to help improve or maintain activities of daily living and reduce number of depressive symptoms may contribute to better cognitive performance.

OC18- ASSOCIATION BETWEEN SARCOPENIA AND RISK OF ALL-CAUSE AND CARDIOVASCULAR DISEASE-SPECIFIC DEATH IN CANCER SURVIVORS AND COUNTERPARTS WITHOUT CANCER HISTORY. Dongyu Zhang[1,2], Kori A. Spiropoulos[1], Shama D. Karanth[2,3], Meghann Wheeler[1], Danting Yang[1], Robert T. Mankowski[3], Stephen Anton[3], Dejana Braithwaite[1,2,3] *(1. Department of Epidemiology, University of Florida College of Public Health and Health Professions, Gainesville, FL, USA; 2. University of Florida Health Cancer Center, Gainesville, FL, USA; 3. Department of Aging and Geriatric Research, University of Florida College of Medicine, Gainesville, FL, USA)*

Background: Prior studies suggest that 30 to 85 percent of people diagnosed with cancer experience malnutrition which usually leads to an increased risk of sarcopenia. Understanding the health impact of sarcopenia on cancer survivors may

improve their prognosis. **Objectives:** To determine how risk of all-cause and cardiovascular disease (CVD)-specific mortality differ by status of sarcopenia in cancer survivors and a matched cohort without cancer history. **Methods:** We used cohort data from the 1999-2006 and 2011-2014 National Health and Nutrition Examination Survey. Study participants included 946 adults surviving for at least 1 year since cancer diagnosis and a matched cohort without cancer history based on age, sex, and race (N=1,857). Sarcopenia was defined by appendicular lean mass and body height (males<7.26 kg/m2, females<5.45 kg/m2). Death was ascertained via the National Death Index and cause of death was assessed via ICD-10. Multivariable Cox proportional hazards models were used to estimate adjusted hazard ratio (aHR) and 95% confidence interval (CI) of sarcopenia in cancer survivors and the matched cohort, followed by restricted cubic splines depicting dose-response curves. **Results:** The mean age of cancer survivors and matched cohort was 60.6 (SD=15.0) and 60.2 (SD=14.9) years, respectively. The median follow-up was 10.5 years for survivors and 10.9 years for matched cohort. A total of 321 (33.9%) survivors and 495 (26.7%) participants in matched cohort died during follow-up. CVD-specific deaths were identified in 58 (6.1%) survivors and 122 (6.6%) participants in matched cohort. The multivariable Cox model suggested that sarcopenia was positively associated with all-cause (aHR=1.79, 95% CI=1.36, 2.36) and CVD-specific (aHR=2.17, 95% CI=1.16, 4.05) mortality in cancer survivors. Although the associations between sarcopenia and risk of all-cause (aHR=1.25, 95% CI=0.99, 1.59) and CVD-specific (aHR=1.27, 95% CI=0.80, 2.03) mortality were positive in the matched cohort, the magnitude was less substantial than cancer survivors and the estimates were non-significant. Dose-response analysis yielded similar pattern. **Conclusion:** Cancer survivors have a higher risk of all-cause and CVD-specific mortality if they have sarcopenia. Such relative increase is larger than risk increase in counterparts without cancer history.

OC19- HEALTH TRAJECTORIES OF ELDERLY LIVING IN SENIOR HOUSING: A LONGITUDINAL PERSPECTIVE Maturin Tabue-Teguo[1,2,3], Denis Boucaud-Maitre[1,2], Céline Meillon[3], Luc Leteneur[3], Roxane Villeneuve[1], Jean-François Dartigues[3], Hélène Amieva[3] *(1. University Hospital of Guadeloupe, Pointe-à-Pitre, France; 2. Team LAMIA, University of West Indies, Guadeloupe, France; 3. Inserm U1219 Bordeaux Population Health Center, University of Bordeaux, Bordeaux, France)*

Background: With the aging of the population, increasing demand for long-term services and supports is expected. Senior housing could be a transition or an alternative between home care and nursing homes. **Objectives:** The main objective of this study was to compare risks of mortality and of nursing homes admission between older adults who did or did not move to senior housing over time. **Methods:** Data came from the French longitudinal cohorts of 3C Study (n=2104 people aged 65 years and over, 17 years of follow-up) and PAQUID study (n=3777, 27 years of follow-up) living at home at baseline. A hazard model that accounts for the competing risk of mortality and nursing homes admission was used to compare older adults who did and did not move to senior housing. Cox models were then performed to estimate the risks of hospitalizations, falls, and frailty, using the 3C data. **Results:** In the 3C study, 143 (6.8%) participants moved into a senior housing facility during the follow-up. This move was associated with a lower risk of mortality (hazard ratio (HR): 0.64; 95% confidence interval (CI) 0.46 to 0.77) and a higher risk of nursing home admissions (HR: 1.54 (1.10-2.15)) compared to older adults living at home initially who do not move to senior housing over time. The risks of hospitalizations (HR: 0.54 (0.40-0.73)) and falls (HR: 0.63 (0.50 to 0.79)) were lower. In the PAQUID study, 161 (4.3%) participants moved into a senior housing facility. This move was also associated with a lower mortality risk (HR: 0.72 (0.58 to 0.88)) and a higher risk of nursing home admissions (HR: 1.39 (1.05-1.86)). **Conclusions:** Our results showing lower risks of mortality suggest that senior housing may be a relevant care model for vulnerable older adults. More studies are needed to confirm these results and better characterize those older adults who would most benefit from this type of facility.

OC20- MICRORNAS IN WOMEN WITH DYNAPENIA AND DYNAPENIC ABDOMINAL OBESITY. Lisa Dowling[1], Jennifer S Walsh[1], Katarzyna Goljanek-Whysall[2,3] *(1. The University of Sheffield, United Kingdom; 2. The University of Liverpool, United Kingdom; 3. National University of Ireland, Galway, College of Medicine, Nursing and Health Sciences, School of Medicine, Department of Physiology, United Kingdom)*

Background: Dynapenic abdominal obesity (DAO) is a distinct condition of low muscle strength in the context of a high waist circumference, with the cumulative health risks of both phenotypes. MicroRNAs (miRNAs, miRs) are short non-coding RNAs which can regulate gene expression at the post-transcriptional level. The pathogenesis of DAO is not fully understood but miRNAs may play a role. To date, the miRNA profile of older adults with DAO has not been determined. **Objectives:** To determine whether a panel of miRNAs are differentially expressed in the serum of older women with DAO compared with normal weight, dynapenic or obese women. **Methods:** Samples (n=23) were obtained from healthy UK women who took part in the Fat and Bone Study (2011-2013). Dynapenia was defined as hand-grip strength <16kg and abdominal obesity as a waist circumference >88cm and body mass index ≥30kg/m2. Haemolysis was assessed (Nanodrop) and RNA extracted from fasted morning serum samples. RNA-seq was conducted with an Illumina HiSeq 2500. Quality was evaluated with fastQC v0.11.9 and multiQC v1.10. Significance was set at FDR <0.1. Functions and validated targets of selected miRNAs were determined from a literature search (PubMed). **Results:** Normal weight (n=7), dynapenic (n=6), obese (n=5) and DAO (n=5) women aged 59-70y were included. Compared with normal weight women, those with dynapenia had 13 over-expressed and 25 under-expressed miRNAs – the top 10 differentially expressed miRs

were all downregulated. A literature search found these miRs implicated in myogenesis (miR-487b-3p, miR-127-3p, miR-376c-3p, miR-543), insulin resistance (miR-127-3p, miR-409-3p), osteoporosis/osteogenesis (miR-654-3p, miR-487b-3p, miR-409-3p), ageing (miR-376a-3p), adipogenesis (miR-410-3p), post-prandial lipemia (miR-369-3p, miR-543, miR-409-3p) and mitochondrial dynamics (miR-382-5p, miR-409-3p). In contrast, no differences were found between the miRNA profiles of DAO and obese or normal weight participants. **Conclusion:** This is the first study of miRNA expression in a well-characterised group of women with DAO. No differences were found between DAO and obese women. This may indicate that DAO is a heterogeneous phenotype, with no distinct miRNA signature. However, compared with normal weight women, 38 miRs were differentially expressed in dynapenic women. These findings now require further validation in an external cohort.

OC21- SARCOPENIC OBESITY: DEVELOPMENT AND INITIAL VALIDATION OF A NEW DIAGNOSTIC APPROACH BASED ON BODY COMPOSITION PHENOTYPES. Vittoria Zambon Azevedo[1,2], Maharajah Ponnaiah[3], Pierre Bel Lassen[4,5], Vlad Ratziu[1,2,3,5,6], Jean-Michel Oppert[3,5,6] *(1. Doctoral School Physiology, Physiopathology and Therapeutics (DS 394), Sorbonne Université, Paris, France; 2. Centre de Recherche de Cordeliers, INSERM UMRS 1138, Paris, France; 3. Institute of Cardiometabolism and Nutrition, Paris, France; 4. Sorbonne Université, INSERM, Nutrition and Obesity: Systemic Approaches Research Unit, NutriOmics, Paris, France ; 5. Assistance Publique Hôpitaux de Paris, Hôpital Pitié-Salpêtrière, Paris, France ; 6. Sorbonne Université, Paris, France)*

Background: Sarcopenic obesity (SO) is defined by a decrease in lean body mass (LBM) associated with an excessive increase in fat mass (FM). Currently, SO has several diagnostic methods, definition criteria and thresholds without any established consensus resulting in largely discordant prevalence estimates in obese patients. **Objectives:** We evaluated previously described SO diagnostic criteria to analyze the limitations and propose a new diagnostic approach specifically for overweight/obese subjects. **Methods:** Cross-sectional study of overweight/obese patients who underwent clinical, laboratory, and body composition assessments by DXA. Unsupervised clustering analysis, multivariate logistic regressions and machine learning algorithms were performed to discriminate lean and fat compartments, which provided prognostic variables applied on sex-specific models for SO diagnosis evaluation based on 80% of sample (training dataset, n=1165). SO screening identified three categories: SO, indeterminate-SO, and non-SO, in which optimal cut-points were validated by AUROC curve in a cross-validation on the residual dataset (n=262). **Results:** 1427 subjects were assessed with a mean±s.d. age of 45.0±12.9 years, of which 42.7% with grade III obesity, 79.8% were women, all linked to many cardiometabolic complications such as diabetes (20.7%), dyslipidemia (86.3%), and hypertension (30.3%). Published definitions applied to this cohort resulted in a prevalence from 0.6% to 96.6%. Patients with grade III obesity had higher amounts of LBM, FM, and bone mass than overweight ones (p-values<0.001). We build a model who identified 62 (4.3%) individuals as SO and 240 (16.8%) as indeterminate-SO, both more prevalent in females than males. SO subjects showed higher body weight, FM, bone mass, leptin levels, and hepatic steatosis index, in contrast to lower LBM and all muscle indexes than those non-SO (p-values≤0.001). Patients with SO associated with indeterminate-SO presented increased cardiometabolic complications such as higher cardiovascular risk (for males), metabolic syndrome, hypertension, and respiratory disorders (for females), p-values<0.05. **Conclusion:** We developed and validated internally diagnostic criteria for sarcopenia in obese/overweight subjects. These criteria were based on body composition and identified patients at risk of metabolic and cardiovascular complications. If externally validated these criteria should improve the diagnosis of sarcopenia in obese subjects..

OC22- ASSOCIATION BETWEEN TRYPTOPHAN METABOLITES, PHYSICAL PERFORMANCE, AND FRAILTY IN OLDER PERSONS. Ahmed Al Saedi[1,2], Sharron Chow[3], Sara Vogrin[1,2], Gilles J Guillemin[3], Gustavo Duque[1,2] *(1. Australian Institute for Musculoskeletal Science (AIMSS), Geroscience & Osteosarcopenia Research Program, The University of Melbourne and Western Health, St. Albans, VIC, Australia; 2. Department of Medicine-Western Health, Melbourne Medical School, The University of Melbourne, St. Albans, VIC, Australia; 3. Neuroinflammation Group, Faculty of Medicine and Health Sciences, Macquarie University, Sydney, NSW, Australia)*

Frailty is defined as a syndrome of physiological decline in late life, characterized by marked vulnerability to adverse health outcomes. A robust biomarker for frailty is still lacking. Tryptophan (TRP) metabolism through the kynurenine pathway (KP) plays essential roles in aging, the musculoskeletal system and physical performance. In this study, we quantified eight KP metabolites, including kynurenine (KYN), kynurenine acid (KYNA), quinolinic acid (QUIN), picolinic acid (PIC), 3-hydroxykynurenine (3-HK), 3-hydroxyanthranilic acid (3-HAA) and anthranilic acid (AA) using ultra-high-performance liquid chromatography and gas chromatography-mass spectrometry in the serum of 85 participants (median age 75; 65% female; 28 non-frail, 29 pre-frail, and 28 frail) at the Nepean Osteoporosis and Frailty (NOF) Study. We looked at the association between TRP metabolites and physical performance, disability, and frailty. After adjusting for age and sex, we found that frailty was associated with lower KYNA (OR 0.93 (0.88, 0.98), p=0.009) and higher QUIN (OR 1.11 (1.01, 1.21) for 500nM increase in QUIN, p=0.029). Similarly, when using the Rockwood index, there was a weak association with KYNA (r=-0.241, p=0.028) and TRP (r=-0.220, p=0.045). Lower KYNA was also associated with sarcopenia (OR 0.88 (0.78, 1.00), p=0.049). In addition, serum interleukin (IL)-6 was positively associated with KYN (r=0.324, p=0.003),

3-HK (r=0.293, p=0.008) and QUIN (r=-0.293, p=0.008). No association was found between TRP metabolites and grip strength or gait speed. In conclusion, different TRP metabolites have various associations with physical performance and frailty. Lower serum KYNA had the stronger association with frailty and sarcopenia. Defining the underlying mechanisms may permit the development and validation of new biomarkers and therapeutics for frailty and musculoskeletal conditions targeting specific metabolites of the TRP catabolic pathway.

OC23- SEX-DEPENDENT GENOME-WIDE TRANSCRIPTOME DIFFERENCES IN AN URBAN, COMMUNITY-DWELLING MIDDLE-AGED FRAILTY COHORT. Natasha L. Pacheco[1], Nicole Noren Hooten[1], Yongqing Zhang[2], Calais S. Prince[1], Nicolle A. Mode[1], Ngozi Ezike[1], Kevin G. Becker[2], Alan B. Zonderman[1], Michele K. Evans[1] *(1. Laboratory of Epidemiology and Population Sciences,USA; 2. Laboratory of Genetics and Genomics, National Institute on Aging, National Institutes of Health, Baltimore, MD, USA)*

Background: Frailty is a clinical syndrome described as reduced physiological reserve and increased vulnerability. While predominantly investigated in older adults ≥ 65 years old, recent studies have shown middle-aged individuals can develop frailty and is associated with increased mortality. Discovering molecular mechanisms contributing to frailty pathophysiology in midlife is critical for early frailty detection, prevention, and reducing premature mortality. We previously investigated global transcriptome changes in a middle-aged cohort from the Healthy Aging in Neighborhoods of Diversity across the Life Span (HANDLS) study, and found genes associated with inflammatory processes were aberrantly expressed by frailty status and race. However, transcriptome differences in frailty by sex remain unclear. **Objectives:** We aimed to discover novel genes and pathways correlated with sex and frailty in a diverse middle-aged cohort using RNA-Sequencing. **Methods:** Differential gene expression and pathway analyses were executed for the following comparison groups: 1) frail women (FRAF, n = 4) vs non-frail women (NORF, n = 4); 2) frail men (FRAM, n = 4) vs non-frail men (NORM, n = 4); 3) FRAM vs FRAF. **Results:** We examined overlapping and exclusive significant genes and pathways between the comparison groups. Over 80% of the significant genes exclusive to FRAF vs NORF, FRAM vs NORM, and FRAM vs FRAF, respectively, were novel and associated with inflammatory and metabolic pathways. Frailty-related genes from previous studies such as OTUD1 (FRAF vs NORF), LRG1 (FRAM vs NORM), and TNF (FRAM vs FRAF) were also replicated in our study. Pathways exclusive to FRAF vs NORF were associated with reduced inflammation, while FRAM vs NORM exclusive pathways were related to decreased proteostasis and musculoskeletal integrity. Pathways exclusive to FRAM vs FRAF were associated with altered cell cycle processes and increased catabolism. Interestingly, genes related to inflammasome and apoptotic roles in the Coronavirus Pathogenesis Pathway were increased in FRAM vs FRAF. **Conclusions:** Our results suggest sex-specific gene expression changes occur in middle-aged frailty, enhancing knowledge on frailty progression and potential therapeutic targets for frailty prevention.

OC24- KEY VALUE OF INSPIRATORY MUSCLE PERFORMANCE AND TRAINING IN A HOME-BASED PROGRAM TO IMPROVE FUNCTIONAL CAPACITY AND BODY COMPOSITION IN OLDER HEART FAILURE PATIENTS. R.V. Shah[1], L.P. Cahalin[2], J.M. Haus[3], K. Allsup[4], A.Delligatti[1,4], J. Kostra[1,4], D. Gottlieb[5], C. Wolf[1,4], T.D. Byard[1,4], D.E. Forman[1,4] *(1. University of Pittsburgh, Pittsburgh, PA, USA; 2. University of Miami, Miami, FL, USA; 3. University of Michigan Ann Arbor, MI, USA; 4. VA Pittsburgh Healthcare System, Pittsburgh, PA, USA; 5. VA Boston Healthcare System, Boston, MA, USA)*

Background: Exercise intolerance is common among older adults with heart failure (HF). Exercise training has putative value but is often limited by the debilitating effects of frailty. Inspiratory muscle training (IMT) may have important clinical benefits which may improve functional capacity by reducing sympathetic peripheral vasoconstriction induced by respiratory fatigue. We hypothesize that poor inspiratory muscle performance (IMP) is an important predictor of exercise tolerance in older adults with HF and that home-based IMT can be performed safely and effectively. **Methods:** 34 male patients with HF (Age 69±7 years, left ventricular ejection fraction 37±11%, mean peak oxygen uptake [VO2]14.8±4.8 ml/kg/min, and mean gait speed 1.0±0.15 m/s) were randomized between IMT (n=11) and aerobic and/or strength training (AST; n=23) for a 12-week home-based program. IMT was performed progressively from 50-85% of maximal inspiratory pressure (MIP) with the PrO2 device (Smithfield, RI) which tracked data and adherence for comparison to AST regimens of cycle ergometry/walking and strength training individually advanced to achieve moderate to high intensities. Study endpoints included MIP, peak VO2, 6-minute walk distance (6MWD), 30-second sit-to-stand (STS), grip strength, lower extremity strength, CHAMPS and Duke Activity Standard Index questionnaires, and body composition. **Results:** Baseline MIP greater than the median of 66 cmH2O across all exercise forms (n=18) was associated with greater baseline and post-intervention peak VO2, Total Duke Score, and CHAMPS Duration and Frequency of all activity bouts (all $p<0.05$). IMT led to greater MIP (25.3±25.0% vs 3.6±11.0%, $p<0.05$) and greater baseline MIP correlated positively with change in 6MWD, STS, grip strength, lower extremity strength, and appendicular lean mass index (r=0.352-0.558, $p<0.05$). **Conclusion:** Home-based IMT significantly improved IMP and greater baseline IMP was associated with greater cardiorespiratory fitness, functional capacity, and body composition in older HF patients leading to greater exercise tolerance. Further research is needed to assess IMP and IMT performed alone or combined with AST regimens to address frailty within the growing HF population.

OC25- BIO101 IN SARCOPENIA: RESULTS OF THE SARA PROGRAM. Cendrine Tourette[1], Waly Dioh[1], Carole Margalef[1], Anait Azbekyan[2], Sandrine Rabut[1], Philippe Dupont[1], René Lafont[1,3], Pierre Dilda[1], Jean Mariani[1,4], Sam Agus[2], Rob Van Maanen[1], Stanislas Veillet[1] *(1. Biophytis - Sorbonne Université, BC9, Paris, France; 2. Biophytis, Inc., Cambridge, MA 02139, USA; 3. Sorbonne Université, CNRS - Institute de Biologie Paris Seine (BIOSIPE), Paris, France; 4. Sorbonne Université, CNRS - Institute de Biologie Paris Seine (UMR B2A), Paris, France)*

Background: Sarcopenia is a progressive muscle disorder in which the prevalence increases with age and may lead to mobility disability. **Objectives:** SARA-INT study strives to develop a viable pharmaceutical strategy to treat community dwelling older subjects suffering from age-related sarcopenia. **Methods:** SARA-INT is a randomized three-arm interventional study (BIO101 175 mg bid / BIO101 350 mg bid / placebo) with planned treatment duration of 6 Months (up to 9 months in 50 subjects). Eligibility criteria for sarcopenia were meeting FNIH criteria and Short Physical Performance Battery (SPPB) score ≤ 8/12 in men and women aged >= 65 years. Primary endpoint was the 400-meter walking test (400MWT), secondary endpoints being other physical activity assessments. **Results:** 233 participants were randomized, 232 and 156 participants were included in the Full Analysis Set (FAS) and Per-Protocol (PP) populations, respectively. Due to COVID-19 pandemic, most end-of-treatment efficacy assessments are missing for approximately half of the participants, reducing the studies' power. Although primary analysis (mix of 6/9-month in the FAS population) did not show a statistically significant improvement in 400MWT compared to placebo, BIO101 350 mg bid treatment after 6 months led to an improvement in the 400MWT of 0.07 m/s in the FAS population (not significant) and of 0.09 m/s in the PP population (nominally statistically significant, p=0.008); this is close to the Minimal Clinically Important Difference (MCID) in sarcopenia (0.1 m/s). BIO101 350 mg bid treatment effect on the 400MWT was also observed in pre-defined sub-populations at higher risk of mobility disability (slow walkers, obese or chair stand sub-score ≤2 from SPPB); trends were observed with other independent endpoints and other subgroups of interest. BIO101 showed a very good safety profile at both doses. **Conclusion:** After 6 to 9 months of treatment, 350 mg bid BIO101 showed promising results with a clinically relevant improvement in the primary endpoint 400MWT gait speed, confirmed in sub-populations at higher risk of mobility disability. BIO101 showed a very good safety profile at the doses of 175 and 350 mg bid. Biophytis is preparing to start a phase 3 program with BIO101, targeting a similar patient population.

OC26- MULTISYSTEM COMORBIDITIES CONTRIBUTE TO PHYSICAL FRAILTY. Yurun Cai[1], Xin Jiang[2,3,4], Yi Guo[3,4,5], Junhong Zhou[6,7,8] *(1. Department of Health and Community Systems, University of Pittsburgh School of Nursing, Pittsburgh, PA, USA; 2. Department of Geriatrics, Shenzhen People's Hospital, Shenzhen, Guangdong, China; 3. The Second Clinical Medical College, Jinan University, Shenzhen, Guangdong, China; 4. The First Affiliated Hospital, Southern University of Science and Technology, Shenzhen, Guangdong, China; 5. Department of Neurology, Shenzhen People's Hospital, Shenzhen, Guangdong, China; 6. Hinda and Arthur Marcus Institute for Aging Research, Hebrew SeniorLife, Roslindale, MA, USA; 7. Division of Gerontology, Beth Israel Deaconess Medical Center, Boston, MA, USA; 8. Harvard Medical School, Boston, MA, USA)*

Background: Older adults generally suffer from comorbidities, and these adverse conditions arising from alterations in multiple physiological systems (e.g., cardiovascular, musculoskeletal, metabolic system) interfere with daily function and may contribute to physical frailty in older adults. To date, few studies have quantified contributions of multiple conditions to physical frailty using a comprehensive approach. **Objectives:** We aim to examine the interrelationships between multisystem comorbidities and frailty phenotype in community-dwelling older adults using structural equation modeling (SEM). **Methods:** In 2020-2021, 477 (mean age=71.4±8.1 years, 252 women) participants were recruited via the search of clinical data repository in Shenzhen People's Hospital (China). Frailty phenotype was based on unintentional weight loss, exhaustion, slowness, low activity, and weakness, with having ≥3 conditions considered frail, 1 or 2 conditions considered pre-frail, and no conditions considered robust. Comorbidities include diabetes, sleep disorders (Pittsburgh Sleep Quality Index>5), sarcopenia, cognitive impairment (Mini-Mental State Examination≤24), and chronic pain. Latent factor vascular function was constructed based on pulse wave velocity (PWV) and blood pressure (BP) complexity as quantified using multiscale entropy. SEM with Bayesian estimation was used to characterize interrelationships between these conditions and their associations with frailty phenotype and its components. **Results:** Among 442 participants who completed frailty assessment, 50 (11.3%) were frail, 212 (48.0%) were pre-frail, and 180 (40.7%) were robust. We found better vascular function was directly associated with lower risk of slowness (standardized coefficient [SC]=-0.401, p<0.001), weakness (SC=-0.344, p<0.001, and exhaustion (SC=-0.324, p<0.001). Sarcopenia was associated with both slowness (SC=0.131, p=0.011) and weakness (SC=0.163, p=0.002). Cognitive impairment was associated with slowness (SC=0.175, p=0.014) and exhaustion (SC=0.201, p=0.001). Chronic pain was associated with exhaustion (SC=0.270, p<0.001). We did not find direct association of diabetes and sleep disorders to any frailty components, but they were significantly associated with other health conditions. **Conclusion:** The study findings provide novel insights into how deteriorations in multiple systems correlated with each other and further lead to physical

frailty in older adults. Future longitudinal studies are warranted to explore whether changes in these health conditions can alter frailty status.

OC27- DIRECTLY INDUCED MYOBLASTS - MODELLING THE INTERNAL AND EXTERNAL DRIVERS OF SARCOPENIA. Robert Radford, Ben Doyle, Jean Manguy, Sanja Trajkovic, Brian Keogh, Nora Khaldi *(Joshua Dawson House, Dublin, Ireland)*

Background: Loss of muscle function through advancing age, known as sarcopenia, is a key driver of morbidity and mortality in the ageing population. Treatments tackling sarcopenia have proven elusive, at least in part because of an incomplete understanding of the mechanistic basis driving age-related muscle loss. Current in vitro models fail to replicate the cumulative intracellular and extracellular insults accrued over the lifespan of an individual. Therefore, the key cellular drivers of sarcopenia are difficult to identify and subsequently target. As such, a novel approach is needed to model sarcopenia to reflect the ageing process in muscle holistically. **Objective:** This study aims to develop a more human-aligned aged in vitro muscle model to elucidate key pathways associated with sarcopenia. **Methods:** Fibroblasts from young and old donors were directly reprogrammed to myoblast-like cells through overexpression the myogenic master-regulator, MyoD. These Directly Induced Myoblasts (DIMs) were further differentiated into young and old myotubes, depending on donor age. Senescent fibroblasts were used to pre-condition DIMs differentiation media to replicate the chronic, pro-inflammatory signalling believed to promote atrophy in vivo. Key markers of muscle differentiation were examined by RT-PCR, Western Blot and immunofluorescence. Proteomic analysis using Tandem Mass-Tagging (TMT) was used to benchmark DIMs against their fibroblast progenitors and the current "gold-standard" HSkMC's. TMT proteomic analysis was used to compare young and old DIMs, as well as old DIMs exposed to SASP conditioned media. **Results:** After differentiation, DIMs expressed markers of skeletal muscle differentiation including striation, multi-nucleation, myotube formation and spontaneous contraction. Proteomic analysis of the DIMs revealed key sarcomere proteins were highly enriched in DIMs relative to their fibroblast progenitors while the proteome of both DIMs and HSkMCs showed a high degree of overlap. SASP conditioned media was shown to induce dedifferentiation and loss of DIMs muscle morphology. **Conclusions:** Our fibroblast derived DIMs have been shown to differentiate into functional myotubes, that perform as well or better than the current gold standard HSkMCs in several measures of skeletal muscle function. Preliminary data showing dedifferentiation of old DIMs following SASP conditioned media highlights the potential for this model to provide a more holistic in vitro model of sarcopenia.

OC28- A MECHANISTIC LINK BETWEEN IMPAIRMENTS IN MOTOR UNIT FIRING AND CLINICALLY MEANINGFUL WEAKNESS IN OLDER ADULTS? Nathan P. Wages[1,2], Leatha A. Clark[1,2,3], Mohamed H. Mousa[4,5], Sherif M. Elbasiouny[4,5], Dallin Tavoian[1,6], W. David Arnold[1,7], Brian C. Clark[1,2,8] *(1. Ohio Musculoskeletal and Neurological Institute, Ohio University, Athens, OH, USA; 2. Department of Biomedical Sciences, Ohio University, Athens, OH, USA; 3. epartment of Family Medicine, Ohio University, Athens, OH, USA; 4. Department of Neuroscience, Cell Biology & Physiology, Wright State University, Dayton, OH, USA; 5. Department of Biomedical, Industrial & Human Factors Engineering, Wright State University, Dayton, OH, USA; 6. Department of Physiology, University of Arizona, Tucson, AZ, USA; 7. Department of Neurology, The Ohio State University Wexner Medical Center, Columbus, OH, USA; 8. Division of Geriatric Medicine, Ohio University, Athens, OH, USA)*

Background: The mechanisms of age-related weakness are known to be multifactorial and determined by a combination of neurologic and skeletal muscle factors. Reductions in firing rates of the alpha-motor neurons, the final common pathway for transmitting neural information from a variety of sources to the skeletal muscles, has long been suggested to be one of the mechanistic causes of age-related weakness. However, reductions in motor neuron firing rates have yet to be mapped to phenotypic age-related weakness. **Objective:** To determine whether OAs with and without clinically meaningful leg extensor and handgrip weakness exhibited differences in their normalized MU firing rates (i.e., y-intercept of the firing rate vs. recruitment threshold plot). Methods: In 43 OAs (75.4±7.4 years) and 24 young adults (YAs; 22.0±1.8 years), we quantified leg extensor and handgrip strength, regional lean mass, and MU firing rates. MU firing rates were quantified via electromyographic recordings from the vastus lateralis muscle at force matching contraction intensities of 20%, 50%, and 80% of maximal strength. OAs were classified into weakness groups based on previous established leg extension and handgrip strength thresholds. **Results:** At 80% of maximal strength, OAs exhibiting leg extensor or handgrip weakness had respectively 3.1 and 1.6 pulses per second (pps) lower (i.e., 14% and 12% slower) firing rates than non-weak OAs. For OAs who had both leg extensor and handgrip weakness (referred to as 'generalized weakness'), a 3.3 pps lower (i.e., 15% slower) firing rate was noted in comparison to OAs without any weakness. **Conclusion:** These findings provide evidence suggesting a mechanistic link between impairments of MU firing and clinically meaningful, age-related weakness; thereby providing rationale for the development of neurotherapeutics to increase MU firing to mitigate age-related weakness. Acknowledgements: This work was funded in part by grants from the National Institutes of Health (R01AG044424 and F32AG069358).

OC29- IMPAIRED LOWER LIMB MUSCLE MASS, QUALITY AND FUNCTION IN PATIENTS WITH END STAGE LIVER DISEASE: A PROSPECTIVE CASE-CONTROL STUDY. J.I. Quinlan[1,2], A. Dhaliwal[1,3], F. Williams[1,3,4], S.L. Allen[1,2], S. Choudhary[5], L. Breen[1,2,6], G.G. Lavery[1,6,7], M.J. Armstrong[1,8], A.M. Elsharkawy[1,8], J.M. Lord[1,3,6], C.A. Greig[1,2,6] *(1. NIHR Birmingham Biomedical Research Centre, University Hospitals Birmingham NHS Foundation Trust and University of Birmingham, United Kingdom; 2. School of Sport, Exercise and Rehabilitation Sciences, University of Birmingham, United Kingdom; 3. Institute of Inflammation and Ageing, University of Birmingham, United Kingdom; 4. Therapies Department, University Hospitals Birmingham, United Kingdom; 5. Department of Imaging, University Hospitals Birmingham, United Kingdom; 6. MRC-Versus Arthritis Centre for Musculoskeletal Ageing Research, University of Birmingham, United Kingdom; 7. Department of Biosciences, Nottingham Trent University, United Kingdom; 8. Liver Unit, Queen Elizabeth Hospital Birmingham, Birmingham, United Kingdom)*

Background: End stage liver disease (ESLD) can result in the loss of muscle mass and function (secondary sarcopenia). The presence of sarcopenia in patients with ESLD is estimated to be 25-70%. Currently, the identification of sarcopenia in patients with ESLD occurs by muscle mass only, using computed tomography measurement of muscle cross sectional area (CSA) at L3/L4. Hence, myosteatosis and the functional component of sarcopenia in these patients has often been neglected. Furthermore, little is known about the condition (i.e., mass and quality) of functionally relevant lower limb muscle groups such as the quadriceps in patients with ESLD. **Objectives:** The aim of this study was to evaluate muscle mass, quality (myosteatosis), and function in patients with ESLD and in particular focusing on lower limb pathology. **Methods:** 57 individuals were recruited, 39 were patients with ESLD (24m/15f, 55.0 ±10.5 yrs) and 18 were age/sex-matched healthy control participants (11m/7f, 49.7±14 yrs) (HCL). Quadriceps anatomical CSA (ACSA), quadriceps volume index and quadriceps intermuscular adipose tissue (IMAT) were obtained using MRI. Handgrip strength, maximal isokinetic leg extension torque and chair rise time were also measured. In addition, 7-14 days of habitual physical activity was recorded via wrist worn accelerometers and average daily intensity (mg) was calculated. **Results:** Quadriceps ACSA (50.5±11.5cm^2 vs 61.6±16.4cm^2, P<0.01) and quadriceps volume index (346±72 cm3/m^2 vs 410±110 cm3/m^2, P<0.05) were significantly reduced in ESLD vs HCL. Quadriceps IMAT percentage was increased in ESLD (10.5±3.5% vs 5.2±1.7%, P<0.01). Handgrip strength (31.1±7.7kg vs 36.9±10.5kg, P<0.05), maximal isokinetic torque (100.7±36Nm vs 142.5±51.1Nm, P<0.001) and chair rise time (12.2±4.8s vs 7.8±2.0s, P<0.0001) were impaired in ESLD. Physical activity was also reduced in ESLD (18.3±7.4mg vs 29.1±8.9mg, P<0.0001). **Conclusion:** Patients with ESLD have significant myosteatosis in the lower limbs, as well as reduced muscle mass. In keeping with reduced muscle strength in the upper limbs, our study highlights that patients with ESLD have impaired lower limb strength, function and physical activity compared to age/sex matched healthy controls. It is key in ESLD that future therapies focus on on muscle quality and whole-body function, rather than solitary measures of muscle mass.

OC30- ASSESSING MUSCLE QUANTITY AND QUALITY FOR SARCOPENIA EVALUATION IN HEART FAILURE USING OPPORTUNISTIC THORACIC COMPUTED TOMOGRAPHY. Saeid Mirzai[1], Ian Persits[1], Pieter Martens[2], Jerry D. Estep[2], Po-Hao Chen[3], W. H. Wilson Tang[2] *(1. Department of Internal Medicine, Cleveland Clinic, Cleveland, OH; 2. Department of Cardiovascular Medicine, Heart, Vascular and Thoracic Institute, Cleveland Clinic, Cleveland, OH; 3. Section of Musculoskeletal Imaging, Imaging Institute, Cleveland Clinic, Cleveland, OH)*

Background: Sarcopenia, a reduction in skeletal muscle mass and strength, is a known predictor of poor outcomes in various clinical settings. Despite being extensively studied in cancer and cirrhosis, commonly accepted abdominal landmarks, such as total muscle area at the L3 vertebral level, are seldom used in cardiology due to infrequent abdominal imaging. **Objectives:** To investigate the correlation between specific thoracic landmarks and L3 muscle measurements to determine the best vertebral level and muscle group to assess sarcopenia in heart failure (HF) patients with thoracic computed tomography (CT). **Methods:** Patients hospitalized for acute decompensated HF (n=100) from January 1 of 2017 to 2018 with CT of the chest and abdomen/pelvis within 30 days before discharge were studied. Blinded, semi-automatic measurements of skeletal muscle and intramuscular adipose tissue (IMAT) cross-sectional areas were made using SliceOmatic (Version 5.0, Tomovision, Quebec, Canada) and ABACS+ module (Voronoi Health Analytics, Vancouver, British Columbia). Unilateral measurements were right-sided, but the left side was used when imaging artifacts, such as those arising from a pacemaker, obscured the right side. Pearson's correlation (r) was calculated between the L3 and CT chest measurements. **Results:** Positive correlation with L3 total muscles was seen at above the aortic arch (AbvAoAr) unilateral total (r=0.789, p<0.001), AbvAoAr unilateral pectoralis (r=0.693, p<0.001), T8 total (r=0.817, p<0.001), and T12 total (r=0.844, p<0.001). The ratio of IMAT-to-muscle also showed positive correlation with L3 at AbvAoAr unilateral total (r=0.738, p<0.001), AbvAoAr unilateral pectoralis (r=0.362, p<0.001), T8 total (r=0.711, p<0.001), and T12 total (r=0.762, p<0.001). **Conclusion:** Among the measured levels, T12 showed the strongest correlation with the L3 measurements of skeletal muscle mass and IMAT-to-muscle ratio. Further work is underway to better characterize the correlation between CT chest measurements and outcomes.

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OC31- SARCOPENIA AND COGNITIVE PERFORMANCE IN A COHORT OF MIDDLE-AGED AND OLDER EUROPEAN MEN: DATA FROM THE EUROPEAN MALE AGEING STUDY (EMAS). Nadjia Amini[1], Jolan Dupont[1,2], Laura Vercauteren[1], Laurence Lapauw[1], Leen Antonio[3], Dirk Vanderschueren[3], Jos Tournoy[1,2], Evelien Gielen[1,2] *(1. Department of Public Health and Primary Care, KU Leuven, Leuven, Belgium; 2. Department of Geriatric medicine, UZ Leuven, Belgium; 3. Clinical and Experimental Endocrinology, Department of Chronic Diseases and Metabolism, KU Leuven, Belgium)*

Background: Previous research suggests that sarcopenia is associated with cognitive functioning. However, data on the longitudinal relationship between cognition and sarcopenia, according to the revised criteria of the European Working Group on Sarcopenia in Older People (EWGSOP2), are scarce. **Objective:** This study aims to investigate cross-sectional and longitudinal associations between sarcopenia, its defining parameters (muscle strength, mass and physical performance) and cognition in middle-aged and older men from the European Male Ageing Study (EMAS). **Methods:** EMAS is a multicenter cohort study of men aged 40-79 years (y) recruited from population registers in eight European centers. Fluid cognition (Rey-Osterrieth Complex Figure (Copy and Recall: visual cognition), Camden Topographical Recognition Memory (CTRM: topographical memory), Digit Symbol Substitution Test (DSST: processing speed)) and sarcopenia outcomes (gait speed (GS), chair stand test (CST), appendicular lean mass (aLM) and handgrip strength (HGS)) were assessed at baseline and after a median follow-up of 4.3y. Cross-sectional associations between cognitive function, sarcopenia-defining parameters, prevalent and incident sarcopenia (EWGSOP2) were analyzed. Longitudinally, the predictive value of baseline cognition on decline in sarcopenia-defining parameters and vice-versa was examined. Linear and logistic regression were used and adjusted for age, education, center, physical activity, insulin resistance, depression, alcohol, smoking, comorbidities and psychotropic medications. **Results:** In 3233 participants, data were available on GS and CST, demonstrating that at baseline, GS was associated ($P<0.05$) with ROCF-copy ($\beta=0.017$), ROCF-recall ($\beta=0.010$), CTRM ($\beta=0.015$), DSST score ($\beta=0.032$) and overall fluid cognition ($\beta=0.037$). In the Leuven+ Manchester cohort (n=456), additional data were available on aLM and HGS. HGS was associated ($P<0.05$) with ROCF-copy ($\beta=0.990$), ROCF-recall ($\beta=0.906$) and fluid cognition ($\beta=1.417$). aLM was associated ($P<0.05$) with ROCF-copy ($\beta=0.554$), DSST ($\beta=0.523$) and fluid cognition ($\beta=0.744$). No associations were found between cognition and prevalent nor incident sarcopenia. Longitudinally, low ROCF-copy score was associated with an increase in CST in men ≥70y ($\beta=-0.599$,$P=0.024$) and low GS was associated with a decline on ROCF-recall score ($OR=0.41$,$P=0.027$). **Conclusion:** Sarcopenia was not associated with cognition in this population, whereas individual components of sarcopenia (muscle mass, strength and physical performance) were associated with cognition. A bidirectional association was found between muscle function and visual cognition, an association that warrants further investigation.

OC33- THE IN VITRO AND IN VIVO EFFECTS OF A PLANT-BASED FUNCTIONAL INGREDIENT FOR MUSCLE ATROPHY. Brian Keogh, Alish Kerr, Nora Khaldi *(Nuritas, Joshua Dawson House, Dawson Street, Dublin, Ireland)*

Background: Dysregulation of muscle metabolism is multifactorial and can have devastating effects such as muscle atrophy, commonly associated with immobilisation, sarcopenia, cachexia and other wasting disorders. There is a lack of validated nutritional interventions to prevent or reduce muscle atrophy. Hence, finding a validated nutritional intervention is an urgent need in a rapidly ageing global population. Presently, animal-based solutions for muscle health have mainly been favoured, however, a plant-based solution might be even more relevant from a sustainability perspective. A plant-based nutritional intervention to maintain the balance between protein synthesis and degradation, whilst also addressing inflammatory factors would therefore be of enormous benefit. **Objectives:** Using an integrative AI approach, we identified a plant-derived natural peptide network, NPN_1, and determined in vitro and in vivo effects on protein synthesis and muscle atrophy. **Methods:** NPN_1 was tested in cell culture assays to evaluate safety, muscle metabolism and inflammatory effects. Oral bioavailability and stability were assessed using simulated in vitro gastrointestinal digestion and plasma studies. A hindlimb suspension murine model was used to determine the effects of NPN_1 on muscle atrophy. The potential of NPN_1 compared to an animal-derived ingredient, MC-80, to prevent muscle loss and accelerate recovery was carried out in an induced muscle atrophy model. **Results:** NPN_1 treatment exhibited no adverse effects on cell viability, demonstrated an increase of phosphorylated S6 and reduced TNF-α circulation in cells. Two bioactive peptides within NPN_1 survived simulated digestion with the potential to cross the GI tract and exhibited substantial stability in human plasma studies. 18 days of NPN_1 treatment, resulted in significant attenuation of muscle loss in the soleus, increased expression of a myogenesis biomarkers, and enhanced integrated density of Type I and Type II soleus muscle fibres in mice. In the human intervention trial, NPN-1 performed similarly to MPC-80 for recovery of muscle mass, however, NPN-1 significantly outperformed MPC-80 in muscle protein synthesis, indicating a benefit on anabolic resistance. NPN-1 also significantly decreased circulating creatine kinase, indicating potentially reduced muscle damage. **Conclusion:** Ultimately, we show that NPN-1 is safe and clinically proven to fully recover muscle strength lost during one week of immobilization within two weeks of recovery.

Online Oral Communications

OCD1- PREVALENCE OF SARCOPENIA AND ITS ASSOCIATION WITH ANTIRHEUMATIC DRUGS IN MIDDLE-AGED AND OLDER ADULTS WITH RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS. Thang Dao[1,2], Ben Kirk[1,2], Steven Phu[2,3], Sara Vogrin[1,2], Gustavo Duque[4,5] *(1. Department of Medicine-Western Health, Melbourne Medical School, University of Melbourne, St Albans, Melbourne, VIC, Australia; 2. Australian Institute for Musculoskeletal Science (AIMSS), University of Melbourne and Western Health, Albans, VIC, Australia; 3. Falls, Balance and Injury Research Centre, Neuroscience Research Australia, University of New South Wales, Sydney, NSW, Australia; 4. Department of Medicine-Western Health, Melbourne Medical School, University of Melbourne, St Albans, Melbourne, VIC, Australia; 5 Australian Institute for Musculoskeletal Science (AIMSS), University of Melbourne and Western Health, Albans, VIC, Australia)*

Background: Adults with RA have several factors that can be associated with the development of sarcopenia, including chronic systemic inflammation, physical inactivity, and anti-rheumatic drug use. However, at the time of this review, the prevalence of sarcopenia and the relationship between anti-rheumatic drugs and sarcopenia were lacking. **Objectives:** To examine the prevalence of sarcopenia and its association with anti-rheumatic drugs in adults with rheumatoid arthritis (RA). **Methods:** This review was registered on PROSPERO and followed PRISMA guidelines. Electronic databases were searched for studies reporting on the prevalence of sarcopenia in adults with RA using any muscle index (muscle mass, strength and/or physical performance) and cutpoints as recommended by established criteria (EWGSOP1/2, AWGS, FNIH, SDOC). The secondary objective was to investigate the relationship between anti-rheumatic drugs and sarcopenia. **Results:** Among 2240 middle-aged and older adults with RA (mean age: 47.7 ± 5.5 to 75.0 ± 6.2 years, 83.8% women), the pooled prevalence of low muscle mass/sarcopenia was 30.2% [95% confidence interval (CI) 24.2-36.2%; 16 studies; I2: 89.2%]. Sub-group analysis showed a non-significant higher prevalence of low muscle mass alone (32.6%, 95% CI 25.0-40.3%; I2: 87.9%) versus consensus definitions of sarcopenia (25.4%, 95% CI 15.4-35.3%; I2: 91.2%, p = 0.255). In adults with RA, corticosteroid use was positively associated with sarcopenia [odds ratio (OR) 1.46, 95% CI 0.94-2.29, 7 studies; I2: 47.5%] while conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) was inversely associated (OR 0.70, 95% CI 0.52-0.94; 6 studies: I2: 0.00%) with this muscle disease. No association was found for biological/targeted synthetic disease-modifying antirheumatic drugs (b/tsDMARDs) (OR 0.83, 95% CI 0.54-1.30; 6 studies: I2: 47.6%). **Conclusion:** Sarcopenia is a common comorbidity of RA, and as such, clinicians should screen for this muscle disease in adults with RA. Further longitudinal studies are needed to understand the role of anti-rheumatic drugs (particularly type, dosing, and duration) in the development of sarcopenia.

OCD2- EFFECTS OF AN INDIVIDUALISED EXERCISE PROGRAMME PLUS BEHAVIOURAL CHANGE ENHANCEMENT (BCE) STRATEGIES FOR MANAGING FATIGUE IN FRAIL OLDER ADULTS: A CLUSTER RANDOMISED CONTROLLED TRIAL. Justina YW Liu[1,2], Yue-Heng Yin[1], Patrick PK Kor[1], Wai Tong Chien[3], Parco M Siu[4], Keith D Hill[5] *(1. Centre for Gerontological Nursing, School of Nursing, The Hong Kong Polytechnic University, Hong Kong, China; 2. Research Institute of Smart Ageing, The Hong Kong Polytechnic University, Hong Kong, China; 3 . The Nethersole School of Nursing, The Chinese University of Hong Kong, Hong Kong, China; 4. Division of Kinesiology, School of Public Health, The University of Hong Kong, Hong Kong, China; 5. Rehabilitation Ageing and Independent Living (RAIL) Research Centre, School of Primary and Allied Health Care, Monash University, Melbourne, Australia)*

Background: There is currently no evidence-based intervention for ageing-induced fatigue, although it could cause adverse outcomes such as frailty. **Aim:** This study evaluated the effects of an individualised exercise programme with/without BCE strategies on reducing fatigue in older adults. **Method:** A three-armed cluster-RCT was conducted with 184 participants (mean age: 79.1±6.4; mean frailty score: 2.8+0.8) from 21 community centres (ClinicalTrials.gov: NCT03394495). They were randomised into either: the COMB group (n=64) receiving 16 weeks of exercise training plus the BCE programme, the EXER group (n=65) receiving exercise training and health talks, or the control group (n=55) receiving only health talks. Fatigue levels were assessed using the Multi-dimensional Fatigue Inventory at baseline, immediately, and 6 and 12 months post-intervention. **Results:** The GEE analyses showed significant interaction (time x group) between the COMB and control groups immediately ($p<0.001$), 6 months ($p<0.001$), and 12 months ($p<0.001$) post-intervention. Comparing the COMB and EXER groups, there was a significant interaction immediately ($p=0.013$) and 12 months post-intervention ($p=0.007$). However, no significant difference was seen between the EXER group and control group at any time point. **Conclusion:** The combined intervention of the BCE programme and exercise used in this trial showed more significant immediate and sustainable benefits than exercise alone or health education on improving general fatigue in frail older adults. This intervention has the potential to be sustainably implemented in the community to prevent frailty in the early stage and to help ease the healthcare burden on society.

OCD3- INFLUENCE OF IGF-I SERUM CONCENTRATION ON MUSCULAR REGENERATION CAPACITY IN PATIENTS WITH SARCOPENIA. Michael Drey[1], Stefanie Jarmusch[1], Lisa Baber[1], Martin Bidlingmaier[4], Fabian Hofmeister[1], Stefan Hintze[2], Stefan Mehaffey[3], Peter Meinke[2], Carl Neuerburg[3], Benedikt Schoser[2] *(1. Department of Medicine IV, Geriatrics, University Hospital of LMU Munich, Germany; 2. Friedrich-Baur-Institute, Department of Neurology, University Hospital of LMU Munich, Germany; 3. Department of General, Trauma- and Reconstructive Surgery, University Hospital of LMU Munich, Germany; 4. Department of Medicine IV, Endocrinological Laboratory, University Hospital of LMU Munich, Germany)*

Background: Previous research has described a neuroprotective effect of IGF-I, supporting neuronal survival, axon growth and proliferation of muscle cells. **Objectives:** The association between IGF-I concentration, muscle histology and electrophysiological markers in a cohort of patients with sarcopenia dares investigation. **Methods:** Measurement of serum concentrations of IGF-I and binding partners, electromyographic measurements with the MUNIX (Motor Unit Number Index) method and muscle biopsies were performed in 31 patients with acute hip fracture older age 60 years. Molecular markers for denervation (neural cell adhesion molecule NCAM) and proliferation markers (Ki67) were assessed by immunofluorescence staining of muscle biopsy tissue. Skeletal muscle mass by bioelectrical impedance analysis and hand-grip strength were measured to assess sarcopenia status according to EWGSOP2 criteria. **Results:** 31 patients (20 women) with a mean age of 80.6±7.4 years were included. Concentrations of IGF-I and its binding partners were significantly associated with sarcopenia (β= -0.360; p = 0.047) and MUNIX (β = 0.512; p = 0.005). Further, expression of NCAM (β = 0.380; p = 0.039) and Ki67 (β = 0.424; p = 0.022) showed significant associations to IGF-I concentrations. **Conclusion:** The findings suggest a pathogenetic role of IGF-I in sarcopenia based on muscle denervation.

OCD4- ASSOCIATION BETWEEN FRAIL STATUS AND OUTCOMES FOLLOWING COVID-19 INFECTION AMONG US VETERANS. Catherine Park[1,2,3,4], Aanand D Naik[1,2,3,4,7], Ariela Orkaby[5,6], Nicola A Hanania[5,6], Drew Helmer[1,2], Kristine E. Lynch[8], Christopher I Amos[2], Amir Sharafkhaneh[1,2], Javad Razjouyan[1,2,3,4] *(1. VA HSR&D, Center for Innovations in Quality, Effectiveness and Safety, Michael E. DeBakey VA Medical Center, Houston, TX 77030, USA; 2. Baylor College of Medicine, Houston, Texas, USA; 3. Michael E. DeBakey VA Medical Center, Houston, Texas, USA; 4. Big Data Scientist Training Enhancement Program, VA Office of Research and Development, Washington, DC, USA; 5. New England Geriatrics Research, Education, and Clinical Center, Boston VA Health Care System, Boston Massachusetts, USA; 6. Brigham & Women's Hospital, Harvard Medical School, Boston Massachusetts, USA; 7. University of Texas School of Public Health, Houston, Texas, USA; 8. VA Salt Lake City Health Care System and Division of Epidemiology, University of Utah, Salt Lake City, Utah, USA)*

Backgrounds: Frailty is associated with an increased risk of adverse outcomes in the presence of stressors such as COVID-19 infection. **Objectives:** This study sought to examine the association between different levels of frailty and outcomes following COVID-19 infection. **Methods:** This is a retrospective cohort study of US Veterans who received care at the national Veterans Health Administration (VHA) between February 15, 2020, and September 30, 2021. We included all Veterans age 50 and older who were active users of VHA care and tested positive for COVID-19. We measured frailty using a 31-item frailty index based on VHA electronic medical record data (VA-FI) from one year prior to the COVID-19 testing date. We used VA-FI to define three groups: robust (≤0.1), prefrail (0.1-0.2), and frail (>0.2). The primary outcome was hospitalization, defined as any hospital admission within 7 days after the COVID-19 test date. We defined secondary outcomes for hospitalized patients as ICU admission, ventilation use, in-hospital mortality due to COVID-19. We compared the odds of each outcome between the three VA-FI groups using logistic regression adjusted by age, sex, body-mass-index, and race. **Results:** Of 1,720,095 Veterans tested for COVID-19, 204,426 Veterans (age: 68.5±10.4 years, BMI: 30.5±6.5 kg/m^2) were positive of which 32,965 (16.1%) were hospitalized (age: 71.4±10.4 years, BMI: 29.5±7.1 kg/m^2). Compared to the robust group, prefrail (adjusted odds ratio (aOR), 2.57, 95%CI: 2.47-2.67) and frail (aOR, 8.64, 95%CI: 8.32, 8.97) group had a higher risk of hospitalization. Among hospitalized Veterans, we observed higher ICU admission (frail, aOR, 1.58, 95%CI: 1.46, 1.70; prefrail, aOR, 1.32, 95%CI: 1.22,1.44), ventilation use (frail, aOR, 1.97, 95%CI: 1.74, 2.23; prefrail, aOR, 1.57, 95%CI: 1.37, 1.79), and in-hospital mortality (frail aOR, 2.15, 95%CI: 1.90, 2.43; prefrail, aOR, 1.55, 95%CI: 1.35, 1.77) in frail and prefrail groups compared to robust. **Conclusion:** Veterans with COVID-19 who were frail and prefrail had a higher risk of hospitalization, and subsequent ICU admission, ventilation use, in-hospital mortality, and COVID-19 severity of illness compared to the robust group. A VA-FI to identify

frailty status may be a useful tool to triage patients at risk of adverse outcomes following COVID-19 infection.

OCD5- SEX DIFFERENCES IN VASTUS LATERALIS MUSCLE DURING AGEING ARE PREDOMINANTLY QUANTITATIVE RATHER THAN QUALITATIVE.

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Backgrounds: Sex differences in muscle-ageing are incompletely understood and could be crucial for the optimalisation of sarcopenia-related interventions. **Objective:** To gain insight in potential sex differences in the etiology of muscle-ageing by analysis of underlying processes. **Methods:** Young (13 males and 13 females; 23 ± 2 yrs) and old subjects (26 males and 28 females; 80 ± 3.5 yrs) were recruited. Males and females were highly matched and did not differ in age, BMI or Fried frailty index score. Muscle biopsies were taken from vastus lateralis muscle. RNA-seq analysis was performed and old versus young subjects were compared for each sex separately. Further, analyses were performed to confirm RNA-seq data and we examined whether the observed sex differences were quantitative or qualitative. **Results:** Overall gene expression separated the sexes, with parallel age-related changes. Analysis of differentially expressed genes (DEGs) revealed 1367 DEGs specific for males, 3146 DEGs specific for females and 2354 shared DEGs. Nearly all (99.8%) shared DEGs were regulated in the same direction in males and females, revealing that some features of muscle-ageing are highly similar between the sexes. Pathway analysis of male-specific DEGs revealed pathways involved in oxidative phosphorylation (OXPHOS) and (mitochondrial) metabolism, but similar changes were found in the transcriptome of females and both sexes lost comparable amounts of protein levels of OXPHOS subunit COX4. Pathway analysis of female-specific DEGs revealed pathways involved in cell growth mediated by Akt signalling. Males displayed less DEGs involved in Akt signalling, but notably the direction of regulation (up or down) was highly similar for the majority (89%) of these genes. No sex specific effects were found on p-Aktthr308 levels. **Conclusion:** Pathway analysis of sex specific DEGs suggested that loss of OXPHOS subunits was specific for males and decreased Akt signalling was specific for females. However, more detailed analyses revealed that males and females displayed similar loss of OXPHOS subunits, and that Akt signalling also tended to be downregulated in males. Therefore, we conclude that sex differences in the ageing of vastus lateralis muscle are predominantly of quantitative rather than of qualitative nature.

OCD6- COMBINED VITAMIN D, OMEGA-3 FATTY ACIDS AND A SIMPLE HOME STRENGTH EXERCISE PROGRAM MAY REDUCE CANCER RISK AMONG ACTIVE ADULTS AGE 70 AND OLDER: A RANDOMIZED CLINICAL TRIAL.

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Background: The role of vitamin D, omega-3 fatty acids and home exercise as prevention strategies for the risk of any invasive cancer is unclear. **Objective:** To test the individual and combined benefit of vitamin D, omega-3 and a simple home strength exercise program on the risk of any invasive cancer. **Methods:** The DO-HEALTH trial is a three-year, multi-centre,

2x2x2 factorial design double-blind randomized-controlled trial to test the individual and combined benefit of three public health interventions. The trial was conducted between December 2012 and December 2017 in five European countries. Participants were generally healthy community-dwelling adults ≥ 70 years. The interventions were supplemental 2000 IU/day of vitamin D3, and/or 1 g/day of marine omega-3s, and / or a simple home strength exercise (SHEP) programme compared to placebo and control exercise. In this pre-defined exploratory analysis, time-to-development of any verified invasive cancer was the primary outcome in an intent-to-treat analysis. Adjustments included age, sex, prior fall, body mass index, study site, and cancer history. **Results:** 2157 participants (mean age 74.9 years; 61.7% women; 40.7% with 25-OH vitamin D below 20 ng/mL, 83% at least moderately physically active) were randomized. Over a median follow-up of 2.99 years, 81 invasive cancer cases were diagnosed and verified. For the three individual treatments, adjusted hazard ratios (HR, 95% CI, cases intervention versus control) were 0.76 (0.49-1.18; 36 vs 45) for vitamin D3, 0.70 (0.44-1.09, 32 vs 49) for omega-3s, and 0.74 (0.48-1.15, 35 vs 46) for SHEP compared to control. For combinations of two treatments, adjusted HR were 0.53 (0.28-1.00; 15 vs 28 cases) for omega-3s plus vitamin D3, 0.56 (0.30-1.04; 11 vs 21) for vitamin D3 plus SHEP, and 0.52 (0.28-0.97; 12 vs 26 cases) for omega-3s plus SHEP. For all three treatments combined compared to placebo, the adjusted HR was 0.39 (0.18-0.85; 4 vs 12 cases). **Conclusion:** Supplementation with daily high-dose vitamin D3 plus omega-3s, combined with a simple home exercise program showed a cumulative reduction in cancer risk in generally healthy and active, and largely vitamin D replete adults ≥70 years. Trial Registration: ClinicalTrials.gov Identifier: NCT01745263

OCD7- EFFECTS OF TRANSDERMAL TESTOSTERONE AND/OR MONTHLY VITAMIN D ON FALL RISK IN PRE-FRAIL HYPOGONADAL MEN AGE 65 AND OLDER: A DOUBLE BLIND 2X2 FACTORIAL DESIGN RANDOMIZED PLACEBO-CONTROLLED TRIAL. Heike A Bischoff-Ferrari[1,2,3], Stephanie Gaengler[1,2], Thomas Muenzer[4], Bess Dawson-Hughes[5], Wei Lang[1,2], Robert Theiler[1,2], Andreas Egli[1,2], Gregor Freystätter[1,2,3] *(1. Center on Aging and Mobility, University Hospital Zurich, City Hospital Waid&Triemli and University of Zurich, Zurich, Switzerland; 2. Department of Aging Medicine and Aging Research, University Hospital Zurich and University of Zurich, Zurich, Switzerland; 3. University Clinic for Aging Medicine, City Hospital Zurich, Switzerland; 4. Geriatrische Klinik, St. Gallen, Switzerland; 5. Jean Mayer USDA Human Nutrition Research Center on Aging, Tufts University, Boston, Massachusetts, USA)*

Backgrounds: Low testosterone blood levels have been associated with an increased risk of falling in older men, however evidence from randomized controlled trials is lacking. Also, combined benefits with vitamin D supplementation are unknown. **Objectives:** To test whether transdermal testosterone at a dose of 75 mg per day and/or 24'000 IU Vitamin D once per month reduce the fall risk in community dwelling men age 65 and older with low total testosterone levels (<11.30 nmol/l) and fulfilling at least 1 criteria of Fried-based frailty criteria. **Methods:** The primary outcomes were number of persons who fell and the rate of falls, assessed prospectively at two follow-up clinical visits (6 and 12 months) and four follow-up phone calls (2, 4, 8, and 10 months). Analyses adjusted for age, fall history, person-time and the baseline measures of BMI, 25-(OH)D, total testosterone level, and short physical performance test battery score (SPPB). As there were no significant interactions between treatments, main effects are presented. **Results:** 553 of 1126 men met the pre-screening inclusion criteria, and of those only 91 men met the blood level targets to be enrolled in the trial (mean age: 72.2± 5.9 years, baseline mean total testosterone blood levels: 10.8 ±3.0 mmol/L, mean 25(OH) D concentration: 26.8±7.6 ng/ml (20.9% below 20 ng/ml)). Over 12 months, 38 participants had 74 falls. The odds of falling was not significantly influenced by testosterone versus no testosterone (OR = 0.62 (0.23, 1.68)), but participants who received monthly vitamin D versus no monthly vitamin D had a 2.6-fold increased odds of falling (OR = 2.63 (1.03, 6.70)). The rate of falls was neither influenced by testosterone (IRR = 0.69 (0.37, 1.30), nor by vitamin D (IRR = 1.8 (0.94, 3.42)), significantly. Only men treated with testosterone and achieving the highest quartile of total testosterone levels at follow-up had a reduced rate of falls (IRR = 0.15 (0.02, 0.94)). **Conclusion:** Transdermal testosterone did not reduce the odds or the rate of falling significantly, although a benefit among those achieving the highest testosterone blood levels cannot be excluded. Conversely, monthly vitamin D increased the odds of falling independent of testosterone supplementation.

OCD8- RISK AND TYPE OF FRACTURES ASSOCIATED WITH OSTEOSARCOPENIA IN COMMUNITY-DWELLING OLDER ADULTS. Simon Zhang[1,2], Ben Kirk[1,2], Christel Harijanto[1,2], Sara Vogrin[1,2], Myrla Sales[1,2], Gustavo Duque[1,2] *(1. Department of Medicine, Western Health, Melbourne Medical School, University of Melbourne, St Albans, Melbourne, VIC, Australia; 2. Australian Institute for Musculoskeletal Science (AIMSS), University of Melbourne and Western Health, St Albans, Melbourne, VIC, Australia)*

Background: It is currently unclear if the combined presence of osteopenia/osteoporosis and sarcopenia, termed osteosarcopenia, predisposes older adults to a greater likelihood or type of fracture. **Objectives:** To determine whether osteosarcopenia is associated with a greater risk and type of fracture than osteopenia/osteoporosis or sarcopenia alone. **Methods:** Body composition (bone density and appendicular lean mass via dual-energy x-ray absorptiometry), grip strength (hydraulic dynamometer) and gait speed (4 metres) were used to identify musculoskeletal phenotypes: osteopenia/osteoporosis, sarcopenia (SDOC and EGWSOP2 definitions) and osteosarcopenia (osteopenia/osteoporosis plus sarcopenia). The number and location of fractures were self-reported and cross-validated via medical records, radiology reports and

discharge summaries. Univariate- and multivariate-logistic regressions were used to examine the relationship between the exposure and outcome, while adjusting for potential confounders. **Results:** Among 310 community-dwelling older adults (median age: 79, interquartile range: 73, 83; 80.0% women), a total of 501 minimal trauma fractures were reported. In multivariate analysis adjusting for age, sex and comorbidities, the likelihood of recurrent fractures (≥2) was significantly higher in those with osteosarcopenia versus osteopenia/osteoporosis alone using the SDOC (odds ratio [OR]: 2.49, 95% confidence interval (CI): 1.22, 5.09] but not the EWGSOP2 (OR: 1.72, 95% CI: 0.84, 3.55) definition. Compared to osteopenia/osteoporosis alone, osteosarcopenia was associated with a greater likelihood of arm (OR: 2.13, 95% CI: 1.07, 4.28) and sacral spine (OR: 12.36, 95% CI: 1.39, 109.95) fractures when incorporating the EWGSOP2 and SDOC definitions, respectively. No other differences in fracture sites were observed between osteosarcopenia and osteopenia/osteoporosis ($p>0.05$). Comparisons with sarcopenia alone were not possible due to the extremely low (n=3) numbers of participants presenting with this phenotype. **Conclusion:** Osteosarcopenia, using the SDOC definition, increases the likelihood of recurrent fractures when compared to osteopenia/osteoporosis alone. Osteosarcopenia also increases the likelihood of fractures at falls-related sites such as the arm, as well as non-falls related sites such as the sacral spine, when compared to osteopenia/osteoporosis alone. Further research is needed to determine the fracture profile associated with these musculoskeletal phenotypes and how the definition employed may influence these epidemiological patterns. **Key words:** Aging, Osteosarcopenia, Musculoskeletal, Fractures, Bone, Skeletal Muscle.

OCD9- LONGITUDINAL ANALYSIS OF FRAILTY FREQUENCY AND ASSOCIATION WITH DISABILITY IN A LARGE COHORT OF OLDER ADULTS: THE ITALIAN LONGITUDINAL STUDY ON AGING. Lucia Galluzzo[1], Marianna Noale[2], Stefania Maggi[2], Graziano Onder[1], and the ILSA Working Group *(1. Department of Cardiovascular, Endocrine-Metabolic Diseases, and Aging, Istituto Superiore di Sanità (ISS), Rome, Italy; 2. Neuroscience Institute, Aging Branch, National Research Council (CNR), Padua, Italy)*

Background: Frailty is widely recognized as one of the major challenges of world population aging, offering ample potential for effective interventions because of its dynamic nature. Nevertheless, data on its epidemiology at population level, especially regarding longitudinal aspects, are sporadic and heterogeneous. **Objectives:** We aimed to conduct a comprehensive longitudinal analysis of the frequency of frailty status and its impact on incident disability in a large cohort of older adults, in order to tackle the current fragmentation of data. **Methods:** Using data derived from the Italian Longitudinal Study on Aging (ILSA) population-based cohort (n=5632, 65-84), frailty status was operationalized according to Fried criteria (n=2457). Weighted prevalence and incidence rates were calculated at each ILSA waves (T0 1992-1993, T1 1995-1996, T2 2000-2001). The association with incident disability in ADL or IADL was investigated through Cox proportional hazard models, controlling for possible confounders. **Results:** Prevalence of frailty and pre-frailty at baseline (mean age 71.6 years) were 4.0% (95% confidence interval [CI] 3.4-4.6), and 44.6% (95% CI 43.1-46.1) respectively. Incidence rates per 1000 person-years for the T0-T1 interval were 7.3 (95% CI 5.2-9.3) for frailty, and 83.7 (95% CI 73.6-93.8) for pre-frailty. Prevalence and incidence of frailty, and to a lesser degree of pre-frailty, were overall higher for women and increased with age, yet no increasing trend with advancing age was detected for pre-frailty incidence. Frailty incidence rates were significantly higher among pre-frail than non-frail individuals at follow-up entry. After full adjustment, being frail markedly increased the risk of incident disability in ADL (Hazard Ratio [HR] 3.58, 95% CI 1.97-6.52) and IADL (HR 2.56, 95% CI 1.58-4.16) over a 4-year period. **Conclusion:** To our knowledge, this is the first comprehensive longitudinal analysis of the frequency of frailty status and its association with disability conducted on a nationally representative population-based sample of older adults. Our results show that frailty is a common condition among older individuals, strongly and independently related to incident disability. These findings can be useful to provide reliable information to calibrate adequate public health measures and to set the basis for more in depth studies on frailty progression over time.

OCD10- THE ROLE VEGF-A IN REGENERATIVE FAILURE OF AGED SKELETAL MUSCLE. Yori Endo[1], Charles D. Hwang[1], Yuteng Zhang[1], Shayan Olumi[1], Shailesh Agarwal[1], Ronald L. Neppl[2], Indranil Sinha[1] *(1. Division of Plastic and Reconstructive Surgery, Department of Surgery, Brigham and Women's Hospital, Harvard University, Boston, MA, USA; 2. Department of Orthopedic Surgery, Brigham and Women's Hospital, Harvard University, Boston, MA, USA)*

Background: The regenerative potential of muscles declines with aging and, with it, its ability to maintain its mass and functions. Intrinsic molecular changes and an altered niche, as occurs with aging, can influence proliferation and differentiation of muscle stem cells (MuSC) in response to regenerative stimuli. In particular, the hypoxia signaling pathway has emerged as a key regulator of muscle regeneration and growing evidence suggests that the hypoxia signaling is necessary for MuSC proliferation and differentiation. We hypothesized that differential regulation of vascular endothelial growth factor (VEGF)-A with aging partially underlies this loss of regenerative capacity. This study was conducted to assess the role of VEGF-A in muscle regeneration and regenerative failure in aged muscle. Young C57BL/6 mice (10-12 weeks old) and old C57BL/6 mice (24-25 months old) were subjected to cryoinjury to induce regenerative response in tibialis anterior (TA) muscle, and regenerative response and the whole muscle VEGF-A levels were evaluated. Cross-sectional area (CSA) of regenerating myofibers was 33% smaller in old as compared to

young ($p < 0.01$) mice, which correlated with a 2-fold reduction in the VEGF-A protein levels as assessed by immunoblotting ($p = 0.02$). Capillary density in TA of was similar between the two groups. Knockdown of VEGF in a primary muscle cell line impaired differentiation in vitro. Young VEGFlo mice with a 75% decrease in VEGF-A systemic activities, exhibited a 56% reduction in the average regenerating fiber CSA following cryoinjury ($p < 0.01$), in comparison to their littermate controls. ML228, a pharmacological hypoxia signaling activator, augmented the whole muscle VEGF-A levels by 2 folds and increased the average CSA of regenerating fibers in both old mice (25% increase, $p < 0.01$) and VEGFlo (20% increase, $p<0.01$) mice, but not in young or littermate WT controls, respectively, independent of changes in capillary density. A marked fat deposition in the regenerating area observed in VEGFlo group was significantly improved with ML228 supplementation. These results suggest that exogenous activation of VEGF-A may be a therapeutic target in aging patients with skeletal muscle loss.

OCD11- DECLINED INTRINSIC CAPACITY PREDICTS LONG-TERM ADVERSE OUTCOMES IN A LONGITUDINAL STUDY WITH 8-YEAR FOLLOW-UP: RESULTS FROM BLSA. Lina Ma, Li Zhang, Fei Sun, Yaru Zhou, Pan Liu, Zhe Tang *(Department of Geriatrics, Xuanwu Hospital Capital Medical University, National Clinical Research Center for Geriatric Disorders, China)*

Backgrounds: Intrinsic capacity was proposed by WHO as a new model to capture an individual's functions and capacities across lifetime. We have previously showed the prevalence of declined intrinsic capacity was high in a nationwide survey and validated the WHO ICOPE screening tool in a Chinese population. **Objectives:** To explore the effect of intrinsic capacity on the long-term adverse outcomes in Chinese older adults. **Methods:** Data were derived from Beijing Longitudinal Study of Aging (BLSA) which is a prospective epidemiological cohort study with 1699 community-dwelling adults aged ≥60 years. All the participants were followed up for 8 years. Intrinsic capacity was assessed with the WHO definition including five domains: cognition, mobility, sensory, and psychological capacity. The predictive ability for outcome was assessed by age and sex adjusted Cox proportional hazards model. **Results:** The average intrinsic capacity score was 4.28 (1.01). There were 729 (42.9%) participants who showed one or more declines in intrinsic capacity (one declined domain: 23.4%; two declined domains: 12.7%; three or more declined domains: 6.8%). The percentages of declines in mobility, cognition, vitality, sensory, and psychological capacity were 21.8%, 15.1%, 11.4%, 9.10%, and 14.2%, respectively. Intrinsic capacity decreased with increasing age. Low intrinsic capacity was associated with worse physical function, frailty index, social frailty, falls, and 8-year mortality. Declined intrinsic capacity were associated with a higher mortality rate: one declined domain—hazards ratio (HR), 2.11, 95% confidence interval (CI), 1.71–2.61, P<0.001; two declined domains—HR, 3.54; 95% CI, 2.81–4.45, P <0.001; three or more declined domains—HR, 5.30; 95% CI, 4.09–6.87, P <0.001; adjusted models did not affect the estimates of the association. All the five domains can predict mortality, with cognition the strongest predictor (HR, 3.17; 95% CI, 2.63–3.81, P <0.001). The combination of the five components provided the best risk prediction. **Conclusions:** The concept of intrinsic capacity is useful to detect older adults with higher risk of adverse health outcomes, which has important implications for health-care policies in China.

OCD12- ASSOCIATION OF BASELINE FRAILTY STATUS AND AGE WITH POSTOPERATIVE OUTCOMES IN METASTATIC BRAIN TUMOR PATIENTS: A NSQIP ANALYSIS OF 5,943 PATIENTS. Christine J. Colasacco[1], Joanna Abouezzi[1], Sophia Arbuiso[1], Syed Faraz Kazim[2], Alis J. Dicpinigaitis[1], Jose Dominguez[3], Rohini G. McKee[4], Meic H. Schmidt[2], William T. Couldwell[5], Christian A. Bowers[2] *(1. School of Medicine, New York Medical College, Valhalla, New York, USA; 2. Department of Neurosurgery, University of New Mexico Hospital, Albuquerque, New Mexico, USA; 3. Department of Neurosurgery, Westchester Medical Center & New York Medical College, Valhalla, New York, USA; 4. Department of Surgery, University of New Mexico, Albuquerque, New Mexico, USA; 5. Department of Neurosurgery, Clinical Neuroscience Center, University of Utah, Salt Lake City, Utah, USA)*

Background: Cranial metastases, most often originating from lung cancer, breast cancer, or melanoma, account for most brain tumors. The impact of baseline frailty status versus that of chronological age on surgical outcomes of metastatic brain tumor patients remains largely unknown. **Objective:** The present study aimed to evaluate this relationship for preoperative risk stratification using a large national database. **Methods:** The National Surgical Quality Improvement Program database was queried to extract data of metastatic brain tumor patients who underwent surgery between 2015 and 2019 (n=5,943). Univariate and multivariate analyses were performed to assess the effect of age and modified frailty index-5 (mFI-5) on mortality, major complications, unplanned readmission and reoperation, extended length of stay (eLOS), and non-home discharge. Receiver operating characteristic (ROC) curve analysis was also conducted. **Results:** Both univariate and multivariate analyses demonstrated that frailty status was significantly predictive of 30-day mortality, major complications, eLOS, and non-home discharge. Although increasing age was also a significant predictor of eLOS and discharge to non-home destination, effect sizes were smaller compared with frailty. On multivariate analysis, patients scored as "severely frail" had the highest odds of major complications (OR 1.75 [95% CI 1.06-2.87], p=0.028), eLOS (OR 2.57 [95% CI 1.79-3.69], p<0.001), and non-home discharge (OR 2.78 [95% CI 1.94-3.97], p<0.001). The ROC curve analysis showed superior discriminative performance of mFI-5 score versus age for mortality (AUC 0.590, 95% CI 0.533-0.647 vs. AUC 0.576, 95% CI 0.518-0.633, respectively), major complications (AUC 0.564, 95% CI 0.540-0.589 vs. AUC 0.526, 95% CI 0.501-

0.550, respectively), and hospital eLOS (AUC 0.574, 95% CI 0.557-0.591 vs. AUC 0.556, 95% CI 0.539-0.572, respectively). **Conclusion:** The present study, based on analysis of data from a large national registry, shows that frailty, when compared with age, is a superior predictor of postoperative outcomes in metastatic brain tumor patients.

OCD13- LYSOPHOSPHOLIPIDS AND BRANCHED CHAIN AMINO ACIDS ARE ASSOCIATED WITH AGING: A METABOLOMICS-BASED STUDY IN CHINESE OLDER ADULTS. Yiming Pan, Pan Liu, Yun Li, Lina Ma *(Department of Geriatrics, Xuanwu Hospital Capital Medical University, National Research Center for Geriatric Medicine, Beijing, China)*

Background: Aging is a time-dependent loss of physiological capacity in multiple organ systems, accompanied by increased risk of comorbidity and disability and reduced health-span, which cannot be completely quantified by chronological age. Metabolomics platform can reflect the metabolic characteristics of aging at the molecular level, and may contribute to the identification of anti-aging targets. **Objective:** To identify candidate biomarkers and pathways related to aging with untargeted metabolomics analysis. **Methods:** Liquid chromatography-mass spectrometry (LC-MS) was performed on serum samples from 32 older adults and 32 sex-matched young controls. Multivariate statistical analysis and pathway analysis were conducted on the metabolomics data. **Results:** The two groups had significant differences in metabolite profiling. Among the 80 candidate biomarkers of aging identified in our research, the levels of 16 lysophospholipid were significantly down-regulated in the older group, including LysoPC (18:2, 20:4, 22:4), sn2 LysoPC (18:2, 20:4, 22:4), LysoPE (20:1, 20:4, 20:5, 18:1, 18:2, 22:6), and sn2 LysoPE (18:1, 18:2, 20:4, 22:6). The levels of L-isoleucine and L-leucine were reduced in older adults, and the valine, leucine and isoleucine degradation and biosynthesis were important pathways associated with aging. **Conclusions:** Down-regulation of lysophospholipid, L-isoleucine and L-leucine levels are relevant to aging, and dysfunction of branched chain amino acids metabolism may have twosided effects on aging. **Key words:** Aging; metabolomics; lysophospholipid; branched-chain amino acid; biomarker.

OCD14- INDIVIDUALISED THERAPY FOR ELDERLY PATIENTS USING EXERCISE AND NUTRITION TO REDUCE DEPENDENCE POST DISCHARGE (INDEPENDENCE): A RANDOMISED CONTROLLED PILOT TRIAL. Chad Yixian Han[1], Yogesh Sharma[2,3], Alison Yaxley[1], Claire Baldwin[1], Michelle Miller[1] *(1. Caring Futures Institute, College of Nursing and Health Sciences, Flinders University, Australia; 2. College of Medicine and Public Health, Flinders University, Australia; 3. Department of General Medicine, Flinders Medical Centre, Australia)*

Background: The burden of frailty on public health care systems is expected to rise with a global ageing population. Frailty in older adults is associated with poor health outcomes, and increased health-care costs and service use. During acute illness requiring hospitalization, older adult patients who are prefrail or frail are especially vulnerable. This is because catabolic stress and physical deconditioning, due to immobility, can further aggravate this syndrome. **Objective:** We aimed to examine the effect of an intervention targeted at prefrail or frail hospitalised older adults – an individualized, combined exercise and nutrition intervention that started during inpatient admission and followed up with a three-month community support program, based on the Flinders Chronic Condition Self-Management Model. **Methods:** This was a single center, randomised controlled pilot trial with concealed allocation. Thirty-two pre-frail/frail older adults were recruited during hospitalization and randomised into two groups: a control group that received usual care or the aforementioned intervention group. Frailty status was assessed by Edmonton Frail Scale (EFS), a frailty assessment tool ranging 0–17, where the higher the score, the frailer the individual. Three- and six-month follow-up outcomes were assessed by an independent assessor, blinded to group allocation. Independent sample t-tests comparing EFS scores at three- and six- months compared to baseline, between-groups, were conducted with participants that completed the study. **Results:** Participants in the intervention group had significantly greater reduction in EFS scores compared with those in the control group at three months (mean -3.4, SD 2.3 vs mean -0.2, SD 1.9; P<0.001). The effect was also observed at six-months follow up, as the intervention group maintained significantly greater reduction in EFS scores compared to the control (mean -4.0, SD 2.7 vs mean -1, SD 1.0; P<0.05). **Conclusion:** This study provides preliminary evidence that a patient self-managed, hospital to home, exercise and nutrition intervention can improve frailty status in pre-frail or frail hospitalised older adults.

OCD15- ARE INTAKE AND NUTRITIONAL STATUS OF SPECIFIC POLYUNSATURATED FATTY ACIDS CORRELATED WITH SARCOPENIA OUTCOMES IN COMMUNITY-DWELLING OLDER ADULTS WITH SARCOPENIA? Jolan Dupont[1,2], Eva Wauters[1], Lenore Dedeyne[1], Laura Vercauteren[1], Nadjia Amini[1], Laurence Lapauw[1], Christophe Matthys[4,5], Sabine Verschueren[3], Jos Tournoy[1,2], Katrien Koppo[6], Evelien Gielen[1,2] *(1. Geriatrics & Gerontology, Department of Public Health and Primary Care, KU Leuven, Belgium; 2. Department of Geriatric Medicine, University Hospitals Leuven, Belgium; 3. Research Group for Musculoskeletal Rehabilitation, Department of Rehabillitation Sciences, KU Leuven, Leuven, Belgium; 4. Clinical and Experimental Endocrinology, Department of Chronic Diseases and Metabolism, KU Leuven, Leuven, Belgium; 5. Department of Endocrinology, University Hospitals Leuven, Leuven, Belgium; 6. Exercise Physiology Research Group, Department of Movement Sciences, KU Leuven, Belgium)*

Background: Diet plays an important role in the development and treatment of sarcopenia, the age-related loss of muscle mass and function. Besides protein intake, the intake of polyunsaturated fatty acids (PUFAs) is also suggested to influence muscle physiology and sarcopenia

progression. Therefore, omega-3 PUFAs supplementation is currently being studied as potential sarcopenia treatment. However, little is known about the habitual dietary intake and nutritional status of specific PUFAs in older adults with sarcopenia, nor how this correlates with sarcopenia outcomes. **Objectives:** To assess dietary intake and status of PUFAs in sarcopenic older adults. Moreover, this study aimed to explore the relationship between dietary PUFAs' intake, nutritional PUFAs' status and sarcopenia outcomes in sarcopenic older adults. **Methods:** The Exercise and Nutrition for Healthy AgeiNg(ENHANce) is an ongoing 5-armed triple blinded randomized controlled trial(NCT03649698) in sarcopenic older adults (>65y) aiming to assess the effect of combined anabolic interventions (protein, omega-3 supplement and exercise) on physical performance in these adults, compared to single/placebo interventions. Baseline data of participants included until May 2021, were used for a secondary, exploratory, cross-sectional analysis. Dietary PUFAs intake was assessed with four-day food records and PUFAs' status with RBC membrane fatty acids profiles. Spearman's rho(ϱ) correlation coefficients were calculated to explore associations of PUFAs intake and status with sarcopenia-defining parameters (muscle strength, mass and physical performance), physical activity (step count) and quality of life (SF-36, SarQoL). **Results:** In total, 29 subjects (9♂/20♀, mean age 76.3±5.4y) were included. Total omega-3 intake of participants (1.99±0.99g/d) was below the recommended intake (♂:2.8-5.6g/d; ♀:2.2-4.4g/d). Intake and status of PUFAs were not correlated. Regarding correlations with outcomes, α-linolenic acid status was inversely associated with appendicular lean mass (aLM) (ϱ:-0.439;p=0.017), whereas docosahexaenoic acid status was positively associated with aLM (ϱ:0.388;p=0.038). Some omega-3 PUFAs intake and status markers were positively associated with step count, SF-36 and SarQoL scores, whereas gamma-linolenic acid status was inversely associated with SF-36 physical component summary score (ϱ=-0.426; p=0.024). **Conclusions:** Although intake of omega-3 and omega-6 was low, present exploratory study generated new hypotheses for potential correlations of PUFAs intake and status with several sarcopenia outcomes in older adults with sarcopenia.

OCD16- MODULATING THE EXPRESSION OF THE MITOCHONDRIAL FISSION PROTEIN DRP1 IS NOT A VIABLE THERAPEUTIC TARGET TO COUNTERACT SARCOPENIA. Maude Dulac[1,2], Jean-Philippe Leduc-Gaudet[2,3,4], Marie-Belle Ayoub[2], Olivier Reynaud[1,2], Anwar Shams[4,5], Alaa Moamer[4], Sabah NA Hussain[3,4], Gilles Gouspillou[2,4] *(1. Département des sciences biologiques; 2. Département des sciences de l'activité physique, UQAM, Canada; 3. Meakins-Christie Laboratories and Translational Research in Respiratory Diseases Program, RIMUHC; 4. Division of Experimental Medicine, Department of Medicine, McGill University, Canada; 5. Department of Pharmacology, College of Medicine, Taif University, Taif, Saudi Arabia)*

Backgrounds: The aging-related loss of skeletal muscle mass and function, or sarcopenia, is a debilitating process dramatically impairing the quality of life of afflicted individuals. Although the mechanisms underlying sarcopenia are still only partly understood, impairments in mitochondrial dynamics, and notably in mitochondrial fission, have been proposed as an underlying mechanism. Importantly, conflicting data exist in the field and both excessive and insufficient mitochondrial fission were proposed to contribute to sarcopenia. Interestingly, promoting mitochondrial fission in midlife through Drp1 overexpression was recently shown to extend lifespan and attenuate several key hallmarks of muscle aging in flies. However, to date, whether modulating mitochondrial fission can impact the muscle aging process in mammals has never been investigated. **Objectives:** To define whether altering Drp1 expression in skeletal muscles of late middle-aged mice can impact the muscle aging process. **Methods:** Drp1 expression was knocked down or overexpressed for 4 months in the gastrocnemius and tibialis anterior muscles of 18 months-old C57BL/6J mice using intramuscular injections of adeno-associated viruses. **Results:** Drp1 knockdown in middle-aged mice resulted in severe muscle atrophy (-35 to 52%). Drp1 overexpression also resulted in muscle atrophy, although to a milder extend (-9%). Drp1 knockdown resulted in reduced mitochondrial respiration coupled with an increase in mitochondrial content. Drp1 overexpression did not impact maximal mitochondrial respiration but increased the content of proteins involved in the oxidative phosphorylation, indicating altered mitochondrial quality. Neither Drp1 overexpression nor Drp1 knockdown altered mitochondrial H2O2 emission. Drp1 knockdown, but not Drp1 overexpression, resulted in an increase in markers of oxidative stress, muscle degeneration and impaired autophagy. Drp1 overexpression, but not Drp1 knockdown, increased the proportion of fibers harboring abnormal staining for succinate dehydrogenase activity, indicating that Drp1 overexpression triggered abnormal mitochondrial positioning. **Conclusions:** Taken altogether, our results indicate that both overexpressing and knocking down Drp1 late in life negatively impact skeletal muscles and their mitochondria. These results highlight that Drp1 content must be remain within a fairly narrow physiological range to preserve muscle and mitochondrial integrity during aging. Our results finally indicate that altering Drp1 expression is unlikely to be a viable target to counter sarcopenia.

OCD17- UNDERSTANDING THE ROLE OF NUTRITIONAL STATUS, BODY COMPOSITION AND INSULIN RESISTANCE ON HEALTHCARE COSTS AMONG COMMUNITY-DWELLING OLDER ADULTS.

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Aim: To assess the association of body composition, nutritional status and habits, and insulin resistance with hospitalization-related outcomes (probability of hospitalization, number of hospitalizations and average length of stay per admission and hospitalization costs) in older subjects living in the community. **Methods and data:** Data from 985 community-dwelling adults (≥65 years) from the Toledo Study on Healthy Ageing baseline, waves 2 (year 2011-2013), and 3 (year 2015) follow-up, were analysed. The parameters of interest were: muscle and fat mass; sarcopenia (Foundation for the National Institutes of Health criteria); nutritional status; adherence to the Mediterranean diet andinsulin resistance. Two-part regression models, with generalized-linear models as second part, were employed for the association between the variables of interest and hospitalization use and costs. **Results:** At the cross-sectional level, sarcopenia was associated with longer average length of stay (0.99-3.46 days more compared to non-sarcopenic). Being at nutritional risk or malnourished was associated with a higher length of hospital admission at the cross-sectional level (1-72-4.70 additional days vs well-nourished), as well as at the longitudinal level (0.98-2.46 days more). Insulin resistance was associated with longer length of hospital stay (1.42-2.45 additional days) and hospital costs (560€ for every 1% increase in insulin resistance) at follow-up. **Conclusions:** Among Spanish older adults, insulin resistance seems to be a significant determinant of higher hospital use both at the cross-sectional level and at follow-up. Being malnourished or at risk of malnutrition was also associated with higher hospital admissions. Body composition, sarcopenia status or diet did not significantly influence health care resource use in this population.

OCD18- FRAILTY AND NEW ONSET ATRIAL FIBRILLATION IN OLDER PATIENTS HOSPITALIZED WITH COVID-19 INFECTION.

Gustavo A. Vargas[1], Fei Tang[1], Nimrah Bader[1,2,3], Iriana R. Hammel[1,2,3], Jorge G. Ruiz[1,2,3] *(1. Miami VAHS Geriatric Research, Education and Clinical Center (GRECC), Miami, FL, USA; 2. University of Miami/Jackson Health System, Miami, FL, USA; 3. University of Miami Miller School of Medicine, Miami, FL, USA)*

Background: Frailty -a state of vulnerability to stressors due to multisystemic dysfunction- and atrial fibrillation are common conditions that often coexist in older adults. Older patients with frailty are at higher risk of hospitalization with COVID 19 infection. COVID-19 infection may cause atrial fibrillation through inflammation, increased adrenergic discharge, oxidative stress, myocardial injury, and cardiac remodeling. Acute SARS-CoV-2 infection in patients with frailty may lower the threshold for arrythmias including the onset of atrial fibrillation. **Objectives:** To determine the association between frailty and new-onset atrial fibrillation among hospitalized older patients with COVID-19 infection. **Methods:** This is a retrospective cohort study of Veterans ≥65 years, hospitalized with COVID-infection between January 1, 2021, to September 30, 2021. Socio-demographic and clinical information including documentation of atrial fibrillation ICD 10 codes was obtained from the VA Informatics and Computing Infrastructure (VINCI) database. A 31-item VA Frailty Index (VA-FI) was generated from as a proportion based on the number of items in several domains (morbidity, function, sensory loss, cognition/mood, and other variables) present. Hazard ratios (HRs) and 95% Confidence Intervals (CIs) were calculated using the Fine-Gray competing risk model, adjusting for age, gender, ethnicity, race, sex, BMI, alcohol, substance abuse, smoking status and COVID-19 symptoms severity. **Results:** We identified 13,173 Veterans, mean age 74.86(SD=7.17), 97.1% male, 2.9% female, 70.2% Caucasian, 89.6% Non-Hispanic. There were 1,088 cases of new onset atrial fibrillation (Robust: 326, 30.0%, prefrail 286, 26.3%, and frail 476, 43.8%). Frailty was associated with a lower risk of atrial fibrillation, adjusted HR=0.52 (95%CI:0.45-0.60) compared to robust. Pre-frailty was also associated with lower risk of atrial fibrillation, adjusted HR=0.66 (95%CI:0.56-0.78). **Conclusion:** Older Veterans with frailty hospitalized with COVID-19 infection had a lower risk of new onset atrial fibrillation compared to robust hospitalized patients. These unexpected results suggest that factors other than frailty may contribute to new onset atrial fibrillation in patients with COVID 19 infection. Longitudinal studies in frail hospitalized COVID-19 positive individuals with atrial fibrillation are needed to clarify these findings.

OCD19- MYOSTEATOSIS AND POST-KIDNEY TRANSPLANT OUTCOMES. Yi Liu[1], Omid Shafaat[1], Xiaomeng Chen[1], Cliff Weiss[1], Dorry L. Segev[2], Mara McAdams-DeMarco[2] *(1. Department of Surgery, Johns Hopkins University, Baltimore, MD, USA; 2. Department of Surgery, New York University, New York City, NY, USA)*

Backgrounds: Pre-kidney transplant (KT) body composition, measured by BMI, is predictive of adverse long-term outcomes. However, BMI is impacted by intradialytic weight gain in this population. Computed tomography (CT)-based measurements of body composition may be an objective measure of body composition. functional measures is needed. **Objectives:** We aimed to estimate the association between pre-KT CT measurements of body composition and post-KT outcomes and test whether these risks differ by functional status. **Methods:** We leveraged a perspective cohort of frailty among KT recipients (n=291; 2008-2020) who underwent pre-KT abdominal CT scans in Johns Hopkins hospital within 1-year pre-KT. Body composition measurements were obtained, including skeletal muscle index (SMI) and skeletal muscle radiation attenuation (SM-RA). Sarcopenia was defined as an SMI< 50 cm^2 /m^2 for males and an SMI<39 cm^2 /m^2 for females. Myosteatosis was defined as an SM-RA<41 mean HU for recipient with a BMI< 25 kg/m^2 and an SM-RA<33 mean HU for recipient with a BMI≥ 25 kg/m^2. Sarcopenic obesity was defined as a BMI≥ 30 kg/m^2 for sarcopenic recipients. Functional status was also assessed using the physical frailty phenotype, lower extremity impairment (SPPB) and Instrumental Activities of Daily Living (IADL) dependence. Cox proportional hazard models were used to quantify associations of each measure with post-KT mortality and all-cause graft loss and corresponding interactions with functional status. **Results:** Among 291 recipients, 117 (40.2%) had sarcopenia, 202 (69.4%) had myosteatosis and 23 (7.9%) had sarcopenic obesity before KT. SMIs were not different by any measure of functional status. Patients without IADLs had higher median SM-RAs (p=0.03 for BMI≤24.9 kg/m^2 and p<0.01 for BMI>24.9 kg/m^2). Patients without lower extremity impairment had higher median SM-RAs (p<0.01 for BMI>24.9 kg/m^2). Neither sarcopenia nor sarcopenic obesity was associated with post-KT outcomes. Myosteatosis was associated with elevated hazard of both mortality (aHR: 2.16; 95% CI: 1.08, 4.32) and all-cause graft loss (aHR: 2.02; 95% CI: 1.11, 3.70) after adjusting for confounders. No differed by functional status. **Conclusions:** Myosteatosis was the only CT-based measures of body composition associated with post-KT outcomes. Existing CT scans could be a valuable tool for identifying high-risk recipients regardless of functional status.

OCD20- PREVALENCE OF FRAILTY IN OLDER ADULTS DURING THE COVID-19 PANDEMIC IN SOUTHERN SWITZERLAND: THE CORONA IMMUNITAS TICINO COHORT STUDY. Jiang Miao[1], Amati Rebecca[1], Corna Laurie[2], Franscella Giovanni[1], Crivelli Luca[2], Albanese Emiliano[1,3], for the Corona Immunitas Ticino study team *(1. Institute of Public Health, Universit della Svizzera italiana, Lugano, Switzerland; 2. Department of Business Economics, Health and Social Care, University of Applied Sciences and Arts of Southern Switzerland, Manno, Switzerland; 3. Department of Psychiatry, University of Geneva, Geneva, Switzerland)*

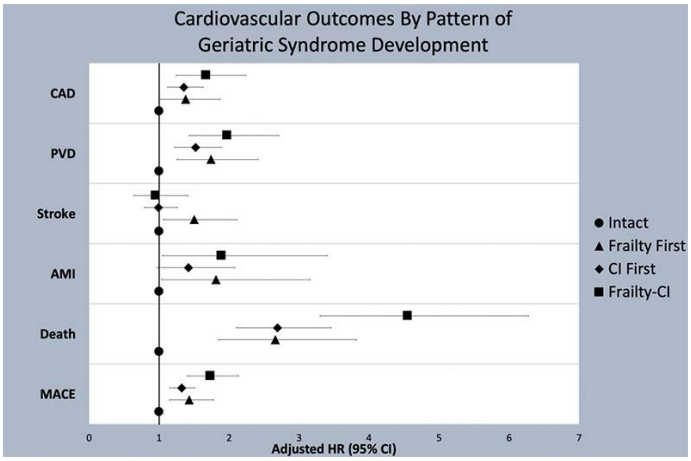
Background: Lack of epidemiological data on frailty hinders accurate estimates of the spread of the COVID-19 infections in frail older adults. Epidemiological evidence on frailty is extremely limited from southern Switzerland, one of the oldest regions in the world, which was severely hit by the pandemic. **Objectives:** To derive a robust frailty index (FI) and to describe its distribution in a representative sample of community-dwelling older adults in southern Switzerland (Ticino), and association with COVID-19 infections. **Methods:** In September 2020, we invited an age and sex-stratified probabilistic sample of older people (65+) to participate in Corona Immunitas Ticino (CIT), a prospective seroprevalence study (i.e., repeated serological tests of anti-SARS-CoV-2 antibodies). We used data from the CIT cohort study to construct a Rockwood FI based on the method described by Searle et al. (2008). We included 30 variables that covered domains including chronic diseases, activities of daily living, lifestyle, physical measurements, self-reported health status, and psychological symptoms. We applied a previously validated cutoff (i.e., 0.21) for frailty caseness. We described the sample and the distribution of frailty and explored the associations between frailty and sociodemographic characteristics, and seropositivity. **Results:** Out of 874 respondents (age ≥ 65 years), complete data to construct the FI was available for 660 participants. The mean age was 72.7 years old, 56.8% were female, and 18.2% had a university degree. The FI score ranged between zero (no frailty) and 0.59 (Median = 0.11; IQR: 0.07, 0.16). 10.3% of the study participants were frail, and 48.2% were pre-frail. On average, the log-transformed FI increased 2.8% (SE = 0.004, p < 0.001) per one year increase in age. Out of 481 participants with a valid serological test, 11.2 % were seropositive to either anti-SARS-CoV-2 IgA or IgG. The median FI score in the seropositive group did not significantly differ from the seronegative group. (p = 0.375). **Conclusion:** Frailty was common in older adults from Southern Switzerland and it was associated with age but not with seropositivity. Our results highlight the pervasiveness of frailty in the region and suggest a non-differential risk of infection in frail older adults.

OCD21- FACTORS ASSOCIATED WITH PHYSICAL PERFORMANCE IN OLDER ADULTS WITH LONG COVID. Matteo Tosato[1], Riccardo Calvani[1], Anna Picca[1], Elisabetta Rota[1], Emanuele Marzetti[1,2], Roberto Bernabei[1,2], Francesco Landi[1,2] *(1. Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy; 2. Universit Cattolica del Sacro Cuore, Rome, Italy)*

Backgrounds: A significant number of COVID-19 survivors experience symptom persistence for weeks or months following viral clearance, a condition known as long COVID. Commonly reported symptoms include, but are not limited to shortness of breath, fatigue, and limitations in daily activities. The impact of long COVID on objectively measured physical performance in older adults is presently unknown. **Objectives:** The purpose of the study was to objectively evaluate the physical performance of older adults with long COVID and identify factors associated with worse functional status. **Methods:** All people aged 65+ attending the Post-COVID outpatient service of the Policlinico Universitario A. Gemelli in Rome were enrolled in this study. All patients received a comprehensive assessment to explore all possible sequelae caused by SARS-CoV-2 infection. Physical performance was evaluated by the 6-min walk test (6MWT) and handgrip strength testing. Predicted 6MWT distance was calculated using a validated formula. Participants were categorized into low-function (LF) and no-low-function (NLF) groups using the 25TH percentile of percentage of predicted distance at the 6MWT as the cutoff. Dynapenia was established according to EWGSOP2 cutoffs for the handgrip strength. Factors associated with poor performance on the 6MWT were explored using logistic regression. **Results:** The study sample included 254 participants (mean age 72 ± 6 yrs; 39% women). The most commonly reported symptom was exertional dyspnea (57%). The handgrip strength was 31.3 ± 7.7 kg in men and 19.6 ± 5.0 kg in women. The mean distance covered during 6 min was 444 ± 110 m. LF participants covered a mean distance of 312.9 ± 107.3 m, while NLF participants walked 489.0 ± 65.6 m. LF and NLF participants had a mean percentage of expected distance of 66.9 ± 19.6% and 104.3 ± 11.6%, respectively. Multimorbidity (odds ratio 2.10, 95% CI 1.09-4.05) and dynapenia (odds ratio 3.36, 95% CI 1.67-6.74) were associated with low functional status. The severity of the COVID-19 severity was not found to be associated with poor performance on the 6MWT. **Conclusion:** In a sample of well-characterized older adults, multimorbidity and dynapenia are associated with low functional status following recovery from a COVID-19 episode. Future studies are warranted to explore whether behavioral or pharmacological interventions may be proposed to improve physical performance in older COVID-19 survivors.

OCD22- CARDIOVASCULAR OUTCOMES BASED ON PATTERNS OF FRAILTY AND COGNITIVE IMPAIRMENT DEVELOPMENT. Naila Ijaz[1], Shang-En Chung[2], Qian-Li Xue[2], David Roth[2], Mauro Moscucci[2], Daniel E. Forman[3], Karen Badeen-Roche[2], Wayne B. Batchelor[1], Jeremy Walston[2], Jon R. Resar[2], Gary Gerstenblith[2], Abdulla A. Damluji[1,2] *(1. Inova Heart and Vascular Institute, Falls Church, VA, USA; 2. Johns Hopkins University, Baltimore, MD, USA; 3. University of Pittsburgh, Pittsburgh, PA, USA)*

Background: Geriatric syndromes including frailty and cognitive impairment (CI) have been associated with poor cardiovascular outcomes(1,2), however the association between pattern of syndrome development and cardiovascular outcomes is unknown. **Objectives:** In this study, we use data from the National Health and Aging Trends Study (NHATS) database to study cardiovascular outcomes based on the temporal development of frailty and CI in an older adult population without a history of coronary artery disease (CAD). **Methods:** Adults age 65 years and older without a history of CAD from the NHATS baseline visit (2011) who also had linked Medicare data available for analysis were included in the study. They were assessed for frailty using Fried criteria and CI using the AD8 report at each subsequent visit (2012-2017). Continuous time to event analysis was used to correlate temporal onset of frailty and CI with major adverse cardiac events (MACE) at 5 years. **Results:** Of a total 2,188 participants, 39.5% were male, 86.1% were non-Hispanic white, and average age was 75.1 years. A total of 154 (7%) participants developed frailty first, 830 (38%) developed CI first, and 196 (9%) developed both simultaneously (Frailty-CI group). The remaining 1,008 (46%) developed neither frailty nor CI, i.e. remained intact. Those who developed frailty and CI simultaneously had the highest incidence of MACE (HR 1.73; 95% CI 1.40-2.13) and all-cause mortality (HR 4.55; 95% CI 3.30-6.28). Participants in this group were older, more likely to be female and have multiple chronic diseases. **Conclusion:** Simultaneous development of frailty and CI is associated with significantly higher risk of MACE and all-cause mortality as compared to development of frailty first or CI first. Screening for these geriatric syndromes in routine care can identify patients at risk of poor cardiovascular outcomes. References: 1. Damluji



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OCD23- USING THE CLINICAL FRAILTY SCALE TO CHARACTERIZE PHYSICAL FUNCTION RECOVERY TRAJECTORIES OF HOSPITALIZED ADULTS REFERRED TO A PHYSIOTHERAPY REHABILITATION SERVICE: PRELIMINARY ANALYSIS OF 738 PATIENTS. Jennifer Jones[1,2,3], Tessa O'Dea[2], Chris Michael[4], Rebekah McGaw[2], Lucy Gao[1], Mark Hindson[2], Joleen Rose[2], Sue Berney[1,2], David J Berlowitz[1,2,3] *(1. Physiotherapy Department, The University of Melbourne, Parkville, Australia; 2. Physiotherapy Department, Division of Allied Health, Austin Health, Heidelberg, Australia; 3. Institute of Breathing and Sleep, Heidelberg, Australia; 4. Business Intelligence Unit, Austin Health, Heidelberg, Australia)*

Background: At Austin Health in Melbourne Australia, physiotherapists provide an Early Rehabilitation (ER) service and use the Clinical Frailty Scale (CFS; a nine-point scale ranging from very fit to terminally ill) to inform assessment of the rehabilitation potential of patients. **Objectives:** To describe physical function recovery trajectories and responsiveness to physical rehabilitation according to frailty severity using categories of the CFS for hospitalized adults referred to the physiotherapy ER service. Methods: Retrospective cohort from January 1 2019 to December 31 2020 of patients with a CFS score recorded in the electronic medical record. Data abstracted included CFS, age, sex, Deyo-Charlson Comorbidity Index (DCCI), age-adjusted DCCI, socioeconomic status, emergency department and hospital admissions 12 months prior. Physical function was assessed using the modified Iowa Level of Assessment Scale (mILOA), a 37-point scale with higher values representing greater physical disability. The mILOA was completed at the beginning (pre-mILOA) and end (post-mILOA) of the ER program. **Results:** There were 738 patients with a CFS score ranging from one to seven (CFS score = patients: 1=31, 2=100, 3=136, 4=141, 5=157, 6=119, 7=54). Age, proportion of females and age-adjusted DCCI score increased with CFS score. Pre-mILOA scores were completed for 96% (n=710) of patients and physical disability increased with CFS score (CFS score = median (IQR) mILOA score: 1=18 (9, 27), 2=19 (11, 28), 3=20 (13, 27), 4=21 (16, 27), 5=23 (18, 29), 6=26 (21, 30), 7=31 (29, 32)). Post-mILOA scores were completed for 66% (n=486) of patients. The change in mILOA scores exceeded the minimal detectable change of 5.8 points across the CFS except for patients with severe frailty. The greatest improvement in mILOA scores from pre- to post- were observed in patients who were less frail (CFS score = change in mILOA score mean (SD): 1=-9.5 (6.7), 2=-8.6 (7.6), 3=-8.0 (6.9), 4=-8.9 (6.8), 5=-6.6 (7.2), 6=-6.6 (5.6), 7=-2.8(4.6)). **Conclusion:** From preliminary analysis of over 700 hospitalized adults, patients with less frailty had a better physical function recovery trajectory following a physiotherapy ER program. These findings provide opportunity to predict recovery trajectories, explore rehabilitation dose-response and targeting health care resources in future research.

OCD24- DIAGNOSIS OF SARCOPENIC DYSPHAGIA IN THE ELDERLY: CRITICAL REVIEW. Sara Abu-Ghanem[1], Alexander Graf[1], Jigar Govind[2] *(1. Department of Otolaryngology, SUNY Downstate Medical Center, Brooklyn, New York, USA; 2. SUNY Downstate- School of Medicine, Brooklyn, New York, USA)*

Background: Sarcopenic dysphagia (SD) is swallowing difficulty associated with loss of generalized skeletal muscles and swallowing-related muscles. Diagnostic criteria for SD were suggested, yet there is a variability in instruments and cut-offs used. **Objectives:** The aim of current review is to critically evaluate tools used in diagnosis of sarcopenic dysphagia in the elderly. **Methods:** Comprehensive review of the literature was performed. Studies were qualitatively evaluated for the diagnostic tools used to make a diagnosis of "sarcopenic dysphagia" and compared to the known diagnostic criteria for SD and other accepted measures. **Results:** Fourteen studies (N=10,282) were selected from a search yield of 331 de-duplicated studies. Ninety-three percent of studies (13/14) were conducted in Japan. All subjects included were over the age of 65 years old (mean, 76.5 years). Various tools were used to assess sarcopenia including handgrip strength (14/14 of studies), followed by skeletal muscle mass/index (7/14), tongue pressure, gait speed and calf circumference in 5/14 studies. The most commonly tool used for dysphagia and/or swallowing dysfunction was the food level intake scale (5/14 of studies) followed by the functional oral intake scale (3/14). The 100-mL water swallow test was used in 2 of the 14 included SD studies. Fiberoptic endoscopic evaluation of swallowing, videofluoroscopic swallowing study, EAT-10 questionnaire, and standardized swallow assessment were each used in only one SD study. **Conclusions:** Further research is required to validate SD diagnostic tools, establish cut-offs in different populations, and investigate their role in screening of dysphagia and swallowing dysfunction in the elderly.

OCD25- LOWER PROTEIN, FIBER INTAKE AND PHYSICAL ACTIVITY ARE ASSOCIATED WITH MORE IMPAIRED COGNITIVE STATUS AMONG ENROLLEES IN THE TRIAL OF THE INTERACTIVE PHYSICAL AND COGNITIVE EXERCISE SYSTEM (IPACES) FOR MILD COGNITIVE IMPAIRMENT (MCI). Paul Arciero[1,2], IreLee Ferguson[2], Steven Sadek[2], Darlingtina Esiaka[3], John P. Arciero[2], Tobi Saulnier[2], David Merrill[4], Stella Panos[4], Cay Anderson-Hanley[2,5] *(1. Health and Human Physiological Sciences, Skidmore College, Saratoga Springs, NY, USA; 2. iPACES LLC, Clifton Park, NY, USA; 3. Center for Molecular and Behavioral Neuroscience, Rutgers University, Newark, NJ, USA; 4. Pacific Brain Health Center, Providence Neurosciences Institute, Santa Monica, CA, USA; 5. Neuroscience Program, Union College, Schenectady, NY, USA)*

Backgrounds: The increasing prevalence of Alzheimer's Disease and related dementias (ADRDs) is a worldwide concern, with lifestyle interventions remaining the most efficacious in mitigating cognitive decline. A growing body of scientific evidence supports high quality protein intake and sufficient exercise to mitigate cognitive decline in those most at risk. Unfortunately, most elders do not meet these guidelines. **Objectives:** The current randomized control trial (RCT) aims to ameliorate mild cognitive impairment (MCI) via an affordable in-home neuro-exergame: iPACES (the interactive Physical and Cognitive Exercise System). The iPACES utilizes a tablet-based game interconnected with an under-table pedaler designed to target executive function, while tracking energy intake and expenditure (kcals/day). **Methods:** Participants are enrolled in iPACES remotely, due to the on-going COVID-19 pandemic and also to increase national accessibility. Enrollees were assessed for: nutrition intake (kcals; protein, carbohydrate, fat, sugar, fiber, sodium, cholesterol), physical activity (PAQ), physical ability (Sit-n-Stand) and baseline cognitive status (MoCA). Initial participants (n = 7) completed baseline neuropsychological evaluation via videoconference, including a 4-day food log and physical activity questionnaires. **Results:** At baseline, enrollees were 71±2 years old, 79±7.5 kg (mean ± SE), and consumed adequate energy (1446±47 kcals/d), carbohydrate (158±19 g/d), fat (68±6 g/d), sodium (1761±516 mg/d), sugar (45±15 g/d), and cholesterol (250±77 mg/d). However, protein (56±3 g/d) and fiber (18±4 g/d) were far below the recommendations of 130±27 g/d and 31±3 g/d, respectively. In addition, enrollees expended only 129±27 kcals/d with physical activity. A survey of food accessibility confirms good access to quality nutrition, and thus mostly sufficient intakes of fruits and vegetables across the sample. Among MCI patients there was a strong association (r = .90) between physical ability (Sit-n-Stand) and overall cognitive status (MoCA), lending further support to the literature linking physical and cognitive frailty, and partially replicating our pilot data (Michielli et al., 2020). **Conclusion:** These findings provide additional support for recommending increased protein and fiber intake, as well as increased physical activity among MCI and caregivers, with potential implications for cognitive health among those enrolled in the iPACES neuro-exergaming clinical trial. Trial Registration: The trial was registered August 17 2021 at www.clinicaltrials.gov as NCT05009524.

OCD26- PROTEIN INTAKE AND THE RISK OF PRE-FRAILTY/FRAILTY IN NORWEGIAN OLDER ADULTS. THE TROMSØ STUDY 1994 - 2016. Dina Moxness Konglevoll[1], Anette Hjartåker[1], Laila Arnesdatter Hopstock[2], Bjørn Heine Strand[3,4,5], Magne Thoresen[6], Lene Frost Andersen[1], Monica Hauger Carlsen[1] *(1. 1Department of Nutrition, Institute of Basic Medical Sciences, University of Oslo, Oslo, Norway; 2. Department of Community Medicine, UiT The Arctic University of Norway, Tromsø, Norway 3. Norwegian National Advisory Unit on Ageing and Health, Vestfold Hospital Trust, Tønsberg, Norway 4. Department of Geriatric Medicine, Oslo University Hospital, Oslo, Norway; 5. Department of Chronic Disease and Ageing, Norwegian Institute of Public Health, Oslo, Norway; 6. Department of Biostatistics, Institute of Basic Medical Sciences, University of Oslo, Oslo, Norway)*

Background: Protein intake is suggested as an important dietary factor in the prevention of frailty, however, the influence of lifelong intake remains unclear. **Objectives:** The present study investigated the relationship between daily protein intake and patterns of protein intake over 21 years and the risk of pre-frailty/frailty. **Methods:** Design: Prospective cohort study. Setting: The population-based Tromsø Study in Tromsø municipality, Norway. Participants: In total, 1,906 women and 1,820 men aged >45 years in 1994 who participated in both Tromsø4 (1994–95) and Tromsø7 (2015–16). Measurements: Frailty status in Tromsø7 was measured according to Fried's phenotype, classifying participants as "robust" (frailty components present: 0), "pre-frail" (1–2) or "frail" (>3). Daily intake of protein was estimated from self-reported habitual dietary intake using food frequency questionnaires and assessed as grams per kilogram bodyweight (g/kg BW) and per megajoule energy intake (g/MJ). The protein–frailty association was assessed via longitudinal and cross-sectional multivariable logistic regression analyses. **Results:** The prevalence of pre-frailty and frailty in this study was 27% and 1.0%, respectively. Longitudinal analysis showed that the odds of pre-frailty/frailty decreased by 57% (odds ratio (OR) = 0.43, 95% confidence interval (CI) = 0.31;0.58, p<0.001) with the increase in intake of one additional gram of dietary protein per kg BW. The results obtained from cross-sectional analysis were similar. Tracking analysis showed that, compared to a stable high intake of protein in g/kg BW over time, other patterns of protein intake increased the risk of pre-frailty/frailty. No associations were found between intake of protein in g/MJ and pre-frailty/frailty. **Conclusion:** Intake of protein in g/kg BW both in mid-life and later in life was inversely associated with pre-frailty/frailty in older adults. This emphasizes the importance of an adequate protein intake to facilitate healthy ageing in Norwegian older adults.

OCD28- FRAILTY INDEX, PHENOTYPIC AGE, AND RISK OF ALL-CAUSE MORTALITY AMONG THE US ADULTS. Zilun Shao[1], Haiming Yang[2], Yuxuan Zhao[2], Meng Xiao[2], Mingyu Song[2], Yueqing Wang[2], Dianjianyi Sun[2,3] *(1. West China School of Public Health, Sichuan University, Chengdu, Sichuan, China; 2. Department of Epidemiology and Biostatistics, School of Public Health, Peking University Health Science Center, Beijing, China; 3. Peking University Center for Public Health and Epidemic Preparedness & Response, Beijing, China)*

Background: Both Frailty Index (FI) and Phenotypic Age (PA), two mildly correlated markers reflecting biological aging, have been independently confirmed as effective predictors of all-cause mortality, however, their joint association haven't been tested yet. **Objective:** To prospectively examine the joint association of the FI and PA with all-cause mortality. **Methods:** Prospective analyses were performed using data from 20,089 adults aged 20 and over recruited in NHANES from 2003 to 2010 (4 cycles) and linked with death records till Dec 31, 2015. FI and its categories (robust, prefrail, and frail) were derived from 34-item questions of disease histories, physical functions, and symptoms. PA and its categories (decreased, normal, and accelerated) were calculated based on chronological age and nine routine clinical markers. Adjusted hazard ratios (aHRs) were estimated using Cox proportional hazards models, and prediction performances were evaluated by C-statistic, net reclassification index (NRI), and integrated discrimination improvement (IDI). **Results**: During a median follow-up of 8.2 years, 2,578 deaths were recorded. FI and PA were independently associated with increased death risk [aHRs (95%CIs): 1.49 (1.44-1.54) for per 0.1 increment in FI; 1.05 (1.04-1.05) for per 1 increment in PA], but no interaction was found (Pinteraction=0.054). Joint association analyses showed that participants in the frail-accelerated aging group had the highest risk of all-cause mortality [HR (95%CI): 6.94 (5.63-8.56), P<0.001] compared with the reference group (robust FI + decreased PA). Compared with conventional risk model, inclusion of FI and PA significantly improved the prediction performance (C-index 0.866 vs 0.848; NRI 29.71%; IDI 4.50%, all P<0.001). **Conclusion:** Increased FI and PA can jointly predict long-term mortality in adults, suggesting that pharmacological and non-pharmacological treatments are needed targeting FI and/or PA lowering for a prolonged healthy lifespan.

OCD29- IMPACT OF MUSCLE MASS ON SURVIVAL OF PATIENTS WITH HEPATOCELLULAR CARCINOMA AFTER LIVER TRANSPLANTATION BEYOND THE MILAN CRITERIA. BR Beumer[1], JLA Van Vugt[1], G Sapisochi[2], P Yoon[2,3], M Bongini[5], D Lu[6], X Xu[6], P De Simone[7], L Pintore[7], N Golse[9], M Nowosad[10], W Bennet[12], E Tsochatzis[13], E Koutli[13], F Abbassi[14], MPAW Claasen[1,2], M Merli[15], J O'Rourke[16], M Gambato[17], A Benito[18], A Majumdar[19], Ek Tan[20], M Ebadi[21], AJ Montano-Loza[21], M Berenguer[22], HJ Metselaar[23], WG Polak[1], V Mazzaferro[5], JNM IJzermans[1], MA Haider[4], E Salinas-Miranda[4], S Bhoori[5], P Rossi[8], P Remiszewski[11], K Korzeniowski[10], F Arico[13], C Toso[14], T Shah[16], L Puchades[22], J Herreras[22], RA De Man[23], D Van Klaveren[24] *(1. Erasmus MC Transplant Institute, Department of Surgery, Division of HPB & Transplant Surgery, University Medical Centre Rotterdam, Rotterdam, The Netherlands; 2. Multi Organ Transplant Program, University Health Network, University of Toronto, Toronto, Canada; 3. Department of Surgery, Westmead Hospital, Sydney, Australia; 4. Joint Department of Medical Imaging, University Health Network, Sinai Health System and University of Toronto, Toronto, ON, Canada; 5. Gastrointestinal Surgery and Liver Transplantation, National Cancer Institute of Milan, Department of Oncology, University of Milan, Italy; 6. Division of Hepatobiliary and Pancreatic Surgery, Department of Surgery, First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, China; 7. Hepatobiliary Surgery and Liver Transplantation, Azienda Ospedaliero-Universitaria Pisana, Pisa, Italy; 8. Radiology, Azienda Ospedaliero-Universitaria Pisana, Pisa, Italy; 9. Centre Hépato-Biliaire, Hôpital Paul Brousse, Université Paris-Sud, Villejuif, France; 10. Department of General Transplant and Liver Surgery, Medical university of Warsaw, Warsaw, Poland; 11. Department of General, Endocrine and Transplant Surgery Medical University of Gdansk; 12. Transplant Institute, Sahlgrenska University Hospital, Sahlgrenska Academy, Gothenburg, Sweden; 13. Royal Free Sheila Sherlock Liver Centre, Royal Free Hospital and UCL Institute of Liver and Digestive Health, London, UK; 14. Division of Digestive Surgery, University Hospitals of Geneva, Genève 1211, Switzerland; 15. Gastroenterology, Department of Translational and Precision Medicine, Sapienza University of Rome, Rome, Italy; 16. The Liver Unit, Queen Elizabeth Hospital Birmingham, Edgbaston, Birmingham, UK; 17. Section of Gastroenterology, Department of Surgery, Oncology and Gastroenterology, University of Padova, Padova, Italy; 18. Radiología, Clinica Universidad de Navarra, España 19. AW Morrow Gastroenterology and Liver Centre, Royal Prince Alfred Hospital, Sydney, NSW, Australia; 20. Department of Hepatopancreatobiliary and Transplant Surgery, Singapore General Hospital, Singapore; 21. Division of Gastroenterology and Liver Unit, Zeidler Ledcor Centre, University of Alberta, 8540 112 Street NW, Edmonton, AB, T6G 2X8, Canada; 22. Hepatology & Liver Transplantation Unit and Ciberehd and ISS La Fe, Hospital Universitario y Politécnico La Fe, Valencia Spain; University of Valencia, Valencia, Spain; 23. Erasmus MC Transplant Institute, Department of Gastroenterology and Hepatology, University Medical Centre Rotterdam, Rotterdam, The Netherlands; 24. Department of Public Health, Erasmus MC - University Medical Centre, Rotterdam, The Netherlands)*

Background: Access to the liver transplant waitlist for patients with hepatocellular carcinoma (HCC) depends on tumour presentation, biology, and response to treatments. The Milan Criteria (MC) represent the benchmark for expanded criteria that incorporate additional prognostic factors. **Objective:** The purpose of this study was to determine the added value of skeletal muscle index (SMI) in HCC patients

beyond the MC. **Method:** HCC patients that were transplanted beyond the MC were included in this retrospective multi-centre study. SMI was quantified using Computed Tomography (CT) within 3 months prior to transplantation. Cox regression models were used to identify predictors of overall survival (OS). The discriminative performance of SMI was also assessed. **Results:** Out of 889 patients transplanted outside the MC, 528 had a CT within 3 months prior to LT, of whom 205 (39%) were classified as sarcopenic. The median time between assessment of the SMI and LT was 1·8 months (IQR: 0·77-2·67). In a linear regression model with SMI as the dependent variable, only male (8·55 95%CI [6·51 – 10·59], p <0·001) and BMI (0·74 95%CI [0·59 – 0·89], p <0·001) were significant. Univariable survival analysis of patients with sarcopenia versus patients without sarcopenia showed no significant difference in OS (HR 1·31 95%CI [0·97 - 1·76], p = 0·076). However, SMI was significant (HR 0·98 95%CI [0·96 - 0·99], p = 0·014). The survival difference between the lowest SMI quartile versus the highest SMI quartile was significant (log-rank: p=0·005) with five-year OS of 57% and 71%, respectively. Data from 423 patients was used for multivariate analysis. Both sarcopenia (HR 1·47 95%CI [1·04 - 2·06], p = 0·027) and SMI were (HR 0·98 95%CI [0·95 - 0·99], p = 0·035) significant. On the survival scale this translates to a 5-year OS difference of 10% between sarcopenia and no sarcopenia. Whereas for SMI this translates to a survival difference of 8% between first and third quartiles for both genders. **Conclusion:** Overall, we can conclude that higher muscle mass contributes to a better long-term survival. However, for individual patients, low muscle mass should not be considered an absolute contra-indication for LT as its discriminatory performance was limited.

OCD30- GENOME WIDE-ASSOCIATION META-ANALYSIS OF PHYSICAL PERFORMANCE IN OLDER ADULTS. Adam J. Santanasto[1], Douglas P. Kiel[2,3], David Karasik[3], Ryan K. Cvejkus[1], Mary Lou Biggs[5], Kathryn L. Lunetta[6], Joanne M. Murabito[7], Joseph M. Zmuda[1] *(1. Department of Epidemiology, University of Pittsburgh, Pittsburgh, PA, USA; 2. Department of Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA; 3. Marcus Institute for Aging Research, Hebrew SeniorLife, Boston, MA, United States; 4. Department of Human Genetics, University of Pittsburgh, Pittsburgh, PA, USA; 5. Department of Biostatistics, University of Washington, Seattle, WA, USA; 6. Department of Biostatistics, Boston University, Boston, MA, USA; 7. School of Medicine, Boston University, Boston, MA, USA)*

Although measures of physical function such as walking speed and time to complete chair-rises are highly heritable, the genetic architecture underlying these phenotypes remains poorly defined. To identify potentially novel genes and pathways underlying physical performance in older adults, we conducted a genome-wide association meta-analysis of the short physical performance battery (SPPB) (Score 0-12) and one of its components, chair-rise time (seconds) in 24,033 Caucasian adults aged 60+ from 13 cohorts (mean cohort age 66.2 ± 5.3 to 84.3 ± 4.1 years; 56.5% women). Cohorts had a genome wide scan imputed to either the Haplotype Reference Consortium or Trans-Omics for Precision Medicine imputation panels. Single nucleotide polymorphism (SNPs) with a minor allele frequency ≥0.1% and imputation quality score ≥0.7 were included (range 7.5-10.5 million per cohort). Analyses were adjusted for age, sex, height, and population substructure. Meta-analysis was performed using a fixed-effects model. Although no genome-wide significant loci were identified, 67 and 60 suggestive loci (p< 5*10-5) were detected for SPPB score and chair-rises time, respectively. Pathway-based analyses indicated significant enrichment of genes affecting negative regulation of calcium channel activity (Bonferroni corrected p-value < 0.05). Sex-stratified gene-based analyses identified clathrin vesicle-associated sec14 protein 1 (CLVS1), significantly associated with chair-rise time in women (p= -1.5*10-7). CLVS1 is highly expressed in the cerebellum, which is involved in postural and motor function control. A larger sample size is needed to confirm and extend our findings, but our results potentially implicate a novel pathway and locus for physical performance in older women.

OCD31- SLOW GAIT SPEED IS ASSOCIATED WITH WORSE POST-OPERATIVE OUTCOMES IN CARDIAC SURGERY: A SYSTEMATIC REVIEW AND META-ANALYSIS. Jaewon Chang[1], Janice Nathalie[2], Minhtuan Nguyenhuy[3], Ruiwen Xu[4], Sohaib A Virk[5], Akshat Saxena[6] *(1. The Royal Melbourne Hospital, Parkville, Melbourne, VIC, Australia; 2. St Vincent's Hospital Melbourne, Fitzroy, Melbourne, VIC, Australia; 3. Western Hospital, Footscray, Melbourne, VIC, Australia; 4. The University of Melbourne, Parkville, Melbourne, VIC, Australia; 5. Department of Cardiology, Concord Repatriation General Hospital, Concord West, NSW, Australia; 6. Department of Cardiothoracic Surgery and Transplantation, Fiona Stanley Hospital, Murdoch, WA, Australia)*

Background: Frailty is associated with poorer outcomes in cardiac surgery, but the heterogeneity in frailty assessment tools makes it difficult to ascertain its true impact in cardiac surgery. Slow gait speed is a simple, validated, and reliable marker of frailty. We performed a systematic review and meta-analysis to examine the effect of slow gait speed on postoperative cardiac surgical patients. **Methods:** PubMED, MEDLINE and EMBASE databases were searched from January 2000 to August 2021 for studies comparing slow gait speed and 'normal' gait speed. Primary outcome was in-hospital mortality. Secondary outcomes were composite mortality and major morbidity, AKI, stroke, deep sternal wound infection, prolonged ventilation, discharge to a healthcare facility and ICU length of stay. **Results:** There were seven eligible studies with 36,697 patients. Slow gait speed was associated with increased likelihood of in-hospital mortality (RR:2.32; 95%CI 1.87-2.87). Additionally, they were more likely to suffer from composite mortality and major morbidity (RR:1.52; 95%CI 1.38-1.66), AKI (RR:2.81; 95%CI 1.44-5.49), deep sternal wound infection (RR:1.77; 95%CI 1.59-1.98), prolonged

ventilation > 24 hours (RR:1.97; 95%CI 1.48-2.63), reoperation (RR:1.38; 95%CI 1.05-1.82), institutional discharge (RR:2.08; 95%CI 1.61-2.69) and longer ICU length of stay (MD:21.69; 95%CI 17.32-26.05). **Conclusion:** Slow gait speed is associated with poorer outcomes in cardiac surgery. Frail patients are two-fold more likely to die during hospital admission than non-frail counterparts and are at an increased risk of developing various perioperative complications. Key words: frailty; gait speed; cardiac surgery

OCD32- PREVALENCE AND RISK FACTORS OF COGNITIVE FRAILTY IN COMMUNITY-DWELLING OLDER ADULTS WITH DIABETES: A SYSTEMATIC REVIEW AND META-ANALYSIS. Ling-Na Kong[1], Qiong Lyu[2], Chi-Xun Guan[3], Jia-Lu Zhu[1] *(1. School of Nursing, Chongqing Medical University, Chongqing, PR China; 2. Department of General Practice, The first Affiliated Hospital of Chongqing Medical University, Chongqing, PR China; 3. School of Nursing, Dalian University, Dalian, PR China)*

Background: Diabetes has been demonstrated a common risk factor of frailty and cognitive impairment in older adults. Cognitive frailty is the coexistence of frailty and mild cognitive impairment and can increase the risk of adverse health outcomes in older adults. Given the accumulative effects of physical frailty and cognitive impairment on health, it is necessary to screen cognitive frailty in older adults with diabetes. **Objectives:** A systematic review and meta-analysis was conducted to assess the pooled prevalence of cognitive frailty and risk factors of cognitive frailty in community-dwelling older adults with diabetes. **Methods:** PubMed, Web of Science, Cochrane Library, Embase, CINAHL, Proquest, China National Knowledge Infrastructure and China Biology Medicine database were searched from inception to September 30th, 2021. The reviewers independently selected studies, extracted data and assessed the quality of studies. The pooled prevalence of cognitive frailty and the association between cognitive frailty and risk factors were estimated. Subgroup analysis, sensitivity analysis and publication bias were also conducted. This systematic review followed the updated PRISMA guidelines. **Results:** A total of 11 studies were included, involving 4656 participants. The pooled prevalence of cognitive frailty in community-dwelling older adults with diabetes was 12.6% (95% CI=8.3-16.9%). The prevalence of cognitive frailty in Asia and other regions was 14.5% and 8.0%, respectively. The prevalence of cognitive frailty was 16.3% in developing countries and 8.8% in developed countries. Age (75 years or above) and depression were the risk factors of cognitive frailty among this population. **Conclusion:** This review revealed that cognitive frailty was common in community-dwelling older adults with diabetes, especially higher in Asian region and developing countries. Older adults with increasing age and depression were more likely to develop cognitive frailty. Healthcare providers should pay attention to the screening of cognitive frailty, exploring its risk factors and developing cost-effective interventions in older adults with diabetes in community settings.

OCD33- THE RELEVANCE OF FRAILTY STATUS FOR PLASMA CONCENTRATIONS OF DIRECT ORAL ANTICOAGULANTS IN OLDER PATIENTS – RESULTS OF AN EXPLORATORY STUDY. Annette Eidam[1], Julian Marji[1], Stefan Grund[1], Kathrin I. Foerster[2], Jürgen Burhenne[2], David Czock[2], Felicitas Stoll[2], Antje Blank[2], Gerd Mikus[2], Walter E. Haefeli[2], Jürgen M. Bauer[1,3] *(1. Center for Geriatric Medicine, Heidelberg University, AGAPLESION Bethanien Hospital Heidelberg, Heidelberg, Germany; 2. Department of Clinical Pharmacology and Pharmacoepidemiology, Heidelberg University, Heidelberg, Germany; 3. Network Aging Research (NAR), Heidelberg University, Heidelberg, Germany)*

Background: The presence of frailty indicates higher vulnerability to adverse health outcomes in older adults and may modify the pharmacokinetics of drugs. **Objectives:** The aim of this study was to explore the potential of different frailty assessments to predict trough plasma concentrations of direct oral anticoagulants (DOACs) in older patients. **Methods:** After ethical consent, adults aged ≥ 70 years and regularly taking one of four DOACs (apixaban, rivaroxaban, edoxaban, or dabigatran) were categorized according to their frailty status by four different frailty assessments: the physical phenotype by Fried, a 38-item frailty index by Rockwood, the short physical performance battery (SPPB), and the FRAIL scale. The two Fried frailty criteria "gait speed" and "grip strength" were used to build a separate score according to the number (none, one, or two) of criteria met. A single steady-state DOAC trough plasma sample was collected for each participant. Dose-normalized trough concentrations were analyzed for correlations with the various frailty assessments and differences between frailty categories. **Results:** A total of 42 participants completed the study with the majority taking apixaban (n = 22). Dosenormalized apixaban trough concentrations were positively correlated with the participants' score on the physical phenotype (rs = 0.535, p = 0.010) and negatively correlated with SPPB (rs = - 0.434, p = 0.044). Apixaban trough concentrations were 2.48-fold higher in frail than in robust participants (p = 0.009) according to the physical phenotype of frailty. Compared to participants who met none of the frailty criteria "gait speed" and "grip strength", apixaban trough concentrations were approximately 1.9-fold higher in participants who met either one (p = 0.018) or two (p = 0.013) of these criteria. Rivaroxaban trough concentrations (n = 14) did not correlate with any of the frailty assessments. Owing to the small sample sizes, we did not perform analyses of the edoxaban (n = 4) and dabigatran subgroups (n = 2). **Conclusion:** In this exploratory study a higher degree of frailty based on performance-based frailty assessments was associated with higher apixaban trough concentrations in older adults, supporting the known association of sarcopenia and DOAC exposure (1). **Reference:** 1. Bendayan M, Mardigyan V, Williamson D, Chen-Tournoux A, Eintracht S, Rudski L et al. Muscle Mass and Direct Oral Anticoagulant Activity in Older Adults With Atrial Fibrillation. J Am Geriatr Soc. 2021;69(4):1012-8. doi:10.1111/jgs.16992.

OCD34- SLOWNESS IS BETTER THAN FRAILTY TO IDENTIFY FUNCTIONAL DECLINE IN OLDER ADULTS. Dayane Capra de Oliveira[1], Roberta de Oliveira Maximo[1], Paula Camila Ramirez[1,2], Aline Fernanda de Souza[1], Mariane Marques Luiz[1], Maicon Luis Bicigo Delinocente[3]; Marcos Hortes Nisihara Chagas[3,4]; Andrew Steptoe[5], Cesar de Oliveira[5], Tiago da Silva Alexandre[1,3,4,5] *(1. Postgraduate Program in Physical Therapy, Federal University of Sao Carlos, Sao Carlos, Brazil; 2. Escuela de Fisioterapia, Universidad Industrial de Santander, Bucaramanga, Columbia; 3. Postgraduate Program in Gerontology, Federal University of Sao Carlos, Sao Carlos, Brazil; 4. Gerontology Department, Federal University of Sao Carlos, Sao Carlos, Brazil; 5. Department of Epidemiology and Public Health, University College of London (UCL), London, England)*

Background: There are no longitudinal studies that analyze the trajectory of incidence of disability in BADL and IADL as a function of changes in frailty status and their components by sex in individuals without disability and frailty at baseline in models adjusted for a wide range of covariates. **Objective:** To analyze the trajectory of the incidence of disability on basic and instrumental activities of daily living (BADL and IADL) as a function of the frailty changes and their components by sex over time. **Method:** Longitudinal study with 1,522 and 1,548 participants of the English Longitudinal Study of Ageing (ELSA) without BADL and IADL disability respectively, and without frailty at baseline. BADL and IADL were evaluated by Katz and Lawton scales and frailty by phenotype in four, eight and twelve years of follow-up. Generalized linear mixed models were calculated for the incidence of BADL and IADL disability, presented in this study as an outcome, and the changes in the frailty status and their components as exposure. All models were stratified by sex and controlled for sociodemographic, behavioral, clinical and laboratory characteristics. **Results:** The incidence of pre-frailty for women and frailty for both sexes were risk factors for the worst trajectory of incidence BADL and IADL disability ($p<0.05$). Slowness was the only component capable to determine the incidence of disability in BADL and IADL in both sexes ($p<0.05$). In addition to slowness, the incidence of weakness and low level of physical activity for men and exhaustion for women also determined the incidence of disability ($p<0.05$). **Conclusion:** Slowness seems to be better than frailty in identifying the loss of functional capacity in the older adults. As its evaluation is easy, fast and accessible, the screening of this component should be prioritized among health professionals and in different clinical contexts in order to implement fast interventions before the onset of functional disability.

OCD35- CAN LONG-TERM PHYSICAL PERFORMANCE TRAJECTORIES IN OLDER ADULTS BE AFFECTED BY DYNAPENIC ABDOMINAL OBESITY? Roberta de Oliveira Maximo[1], Dayane Capra de Oliveira[1], Paula Camila Ramirez[1], Mariane Marques Luiz[1], Aline Fernanda de Souza[1], Maicon Luis Bicigo Delinocente[2], Andrew Steptoe[3], Cesar de Oliveira[3], Tiago da Silva Alexandre[1,2,3,4] *(1. Postgraduate Program in Physical Therapy, Federal University of Sao Carlos, Brazil; 2. Postgraduate Program in Gerontology, Federal University of Sao Carlos, Brazil; 3. Department of Epidemiology and Public Health, University College London, London, United Kingdom; 4. Gerontology Department, Federal University of Sao Carlos, Brazil)*

Background: The decline in physical performance is considered the sixth vital sign in the evaluation of older adults, as it indicates a pre-clinical transition phase to disability and predicts negative outcomes such as hospitalization, early institutionalization, and death. Although multifactorial in nature, it is affected by two common and sex-differentiated processes in aging, dynapenia and abdominal obesity. There is still little evidence of the combined effect of dynapenia and abdominal obesity on the decline in physical performance over time. **Objectives:** To investigate whether the decline in physical performance is worse in individuals with dynapenic abdominal obesity and whether there are sex differences in this association. **Methods:** Longitudinal study involving 3,875 participants aged 60 years or older of the English Longitudinal Study of Aging (ELSA). At baseline, four and eight years of follow-up, the outcome physical performance was measured by the Short Physical Performance Battery (SPPB). Participants were classified as non-dynapenic/non-abdominal obesity (ND/NAO), non-dynapenic/abdominal obesity (ND/AO), dynapenic/non-abdominal obesity (D/NAO), and dynapenic abdominal obesity (DAO) according to waist circumference (>88 cm for women and >102 cm for men) and grip strength (<16 kg for women and <26 kg for men). Generalized linear mixed models adjusted for sociodemographic, behavioral, and clinical characteristics were performed. **Results:** The prevalence of D/AO and ND/AO was slightly higher in women than men (3.7%, [95% CI: 3.0 – 4.6] versus 2.0% [95% CI: 1.4 – 2.7] and 50.3% [95% CI: 48.2 – 52.5] versus 42.3% [95% CI: 40.0 – 44.6], respectively). No difference in the prevalence of D/NAO was found between sexes (3.3% [95% CI: 2.6 – 4.3] versus 3.9% [95% CI: 3.2 – 4.8]). At baseline, men (-1.11 points; 95% CI: -1.58 – -0.65) and women (-1.39 points; 95% CI: -1.76 – -1,02) DAO had worse SPPB performance compared to their ND/NAO counterparts. At eight years of follow-up, only DAO men had a faster rate of decline in SPPB performance compared to ND/NAO men (-0.11 points per year; 95% CI: -0.21 – -0.01). **Conclusion:** DAO accelerates the decline in physical performance only in men. Thus, the identification and management of this modifiable condition seem essential to avoid the first signs of functional impairment in these individuals. Descriptors: waist circumference, handgrip strength, SPPB, physical performance, trajectories, older adults, ELSA.

OCD36- MORTALITY HAZARD OF HYPERTENSION AND DIABETES, AND INVERSIVE EFFECTS OF OBESITY AND CIRCULATING BRANCHED-CHAIN AMINO ACIDS IN OLD AGE. Erik Fung[1,2,3], Leong-Ting Lui[1,2,] Saranya Palaniswamy[3,4], Queenie Chan[3], Lee-Ling Lim[5], Juliana C. N. Chan[1,6,7,8], Timothy Kwok[1,9], Alice P. S. Kong[1,7,8], Marjo-Riitta Järvelin[3,4,10,11], Jean Woo[1,12] *(1. Department of Medicine & Therapeutics, Faculty of Medicine, The Chinese University of Hong Kong; 2. Gerald Choa Cardiac Research Centre, Laboratory for Heart Failure + Circulation Research at Li Ka Shing Institute of Health Sciences, Prince of Wales Hospital, and CARE Programme of Lui Che Woo Institute of Innovative Medicine, Faculty of Medicine, The Chinese University of Hong Kong; 3. Department of Epidemiology & Biostatistics, School of Public Health, Imperial College London, London, United Kingdom; 4. Center for Life Course Health Research, Faculty of Medicine, University of Oulu, Oulu, Finland; 5. Dept of Medicine, University of Malaya, Kuala Lumpur, Malaysia; 6. Asia Diabetes Foundation, Shatin, Hong Kong SAR; 7. Hong Kong Institute of Diabetes and Obesity, The Chinese University of Hong Kong, Shatin, Hong Kong SAR; 8. Li Ka Shing Institute of Health Sciences, Faculty of Medicine, The Chinese University of Hong Kong, Shatin, Hong Kong SAR; 9. CUHK Jockey Club Centre for Osteoporosis Care and Control, Faculty of Medicine, The Chinese University of Hong Kong, Shatin, Hong Kong SAR; 10. Unit of Primary Health Care, Oulu University Hospital, Oulu, Finland; 11. Department of Life Sciences, College of Health and Life Sciences, Brunel University London, Kingston Lane, Uxbridge, Middlesex, United Kingdom; 12. CUHK Jockey Club Institute of Ageing, Faculty of Medicine, The Chinese University of Hong Kong, Shatin, Hong Kong SAR)*

Background: Previous prospective studies suggested that elevated levels of circulating branched-chain amino acids (BCAAs) were indicative of cardiometabolic disorder. However, adequate nutrition may also potentiate BCAA levels and possibly confer survival advantage in old age as for increased body mass index (obesity paradox). **Objective:** This prospective study aimed to elucidate these interrelationships and long-term survival in older adults. **Methods:** Fasting serum levels of BCAAs in 2997 older adults of the Hong Kong cohort were quantified using mass spectrometry and analyzed by regression for association with cardiometabolic disorders and variables. Associations were validated in over 5000 Finnish adults (NFBC66) profiled by proton-NMR. In the former, nutritional and dietary information were collected at baseline, and deaths were ascertained at 14-year follow-up. Kaplan-Meier analysis was performed to determine survival probability. **Results:** In both cohorts, fasting serum BCAA levels were incrementally associated with hypertension (HT) and/or diabetes (DM). The BCAA concentrations for non-HT (510.4 80.5μL) vs. HT (533.6 84.5μL) (p=7.31e-13), and for non-DM (513.2 80.4μL) vs. DM (563.2 86.0μL) (p=2.15e-27), were significantly different. This relationship was also observed in the NFBC66 cohort. Obesity and increased body mass index were the most significant determinants of BCAA levels among cardiometabolic variables assessed, whereas dietary and nutritional variables had modest effects. In the HK cohort, with each unit increase in BMI the BCAA was increased by 1.61% (p=5.21e-84), whereas obesity increased BCAA by 8.55% (p=8.59e-45). In the NFBC66, each unit increase in BMI led to an increase in BCAA by 0.56% (p=1.22e-99) and obesity increased BCAA by 5.55% (p=7.26e-45). HT and/or DM were associated with reduced survival. Importantly, above-median levels of BCAA in obese but not non-obese older adults were significantly associated with improved survival at longterm follow-up (p=0.03). **Conclusion:** Increased circulating BCAA levels are associated with HT, DM and obesity to varying extents. Improved survival associated with increased BCAA levels in obese older adults may partially explain the obesity paradox in old age.

OCD38- VITAMIN D DEFICIENCY AND SARCOPENIA IN WOMEN. Nataliia Grygorieva, Maryna Bystrytska, Anna Musiienko, Nataliia Zaverukhar *(SI «D. F. Chebotarev Institute of Gerontology, NAMS of Ukraine», Kyiv, Ukraine)*

Background: Sarcopenia is a generalized disease of the skeletal muscles, which is manifested by a decrease in muscle strength, mass, and function. Vitamin D deficiency is one of the risk factors of sarcopenia that are the focus of scientific research today. Recent studies demonstrated the relationship between serum 25(OH)D concentration and muscle function, however, the results of some randomized trials about the influence of vitamin D supplementation in older patients for prevention or treatment of sarcopenia are controversial. The research aims to determine the body composition and sarcopenia frequency in patients with vitamin D deficiency. **Methods:** 300 women aged 20-89 were included being divided into three groups: 1st group of subjects with normal vitamin D level, 2nd group - subjects with vitamin D insufficiency, and 3rd one – females with vitamin D deficiency. The patients in these three groups did not differ by age and body weight. Women taking vitamin D supplementation anytime in the past have not been included in the study. Body composition was measured using DXA («Prodigy», CE Medical systems, model 8743, 2005). Vitamin D (25(OH)D) was analyzed using the electrochemiluminescence immunoassay method. The level of vitamin D was classified as normal (>30 ng/ml), insufficient (>20 and ≤30 ng/ml), or deficient (≤20 ng/ml). **Results:** There was detected no association between weight or body mass index and serum level of vitamin D. In a group with vitamin D deficiency, the number of women with normal body weight were significantly lower than among women with optimal vitamin D level – 53.8 vs. 71.1% ($\chi 2$=7.2, 95% Confidential interval (CI) 4.6-29.6, p=0.007), and amount of women with overweight was significantly higher – 25.8 vs. 14.1% ($\chi 2$=4.9, 95% CI 1.3-22.6, p=0.03), also among women with vitamin D deficiency were more persons with underweight (20.4 vs. 14.8%, p=0.3). The appendicular lean mass of women with vitamin D deficiency was significantly lower than normal vitamin D levels ones (16.18±2.17 vs 16.85±2.04 kg, p<0.05). In contrarily, the fat mass of the three groups did

not differ significantly. The frequency of sarcopenia due to appendicular lean mass (ALM<15 kg) was significantly higher among vitamin D deficiency women (24.1% vs 9.6%, $\chi 2$= 10.6, $p<0.05$). **Conclusions:** The study has shown significant differences in body composition in women with different levels of vitamin D. Vitamin D deficiency is associated with a decrease in appendicular lean mass that is associated with sarcopenia.

OCD39- LIPID SIGNALING MEDIATORS REGULATE BONE-MUSCLE CROSSTALK DURING AGEING. Ahmed Al Saedi[1,2], Zhiying Wang[3], Marco Brotto[3], Anup Shah[4], Gustavo Duque[1,2] *(1. Australian Institute for Musculoskeletal Science (AIMSS), The University of Melbourne and Western Health, St. Albans, VIC, Australia; 2. Department of Medicine-Western Health, Melbourne Medical School, The University of Melbourne, St. Albans, VIC, Australia; 3. Bone-Muscle Research Center, College of Nursing and Health Innovation, The University of Texas-Arlington, Arlington, TX, USA; 4. Monash Bioinformatics Platform and Monash Proteomics & Metabolomics Facility, Monash University, Clayton, VIC, Australia)*

Due to its association with adverse outcomes, the simultaneous concurrence of sarcopenia and osteoporosis, a condition termed osteosarcopenia, is of public health concern and interest. Osteosarcopenia is an age-related pathological condition characterized by fragile bone and exhibiting low muscle mass and function thus leading to high mortality and financial threat. Fat infiltration contributes to age-related bone and muscle decline. This effect could be explained by fat-secreted factors, which could be locally secreted in the muscle and bone milieu thus affecting cell-cell interactions, and cell function and survival. However, the specific fat-related secretory factors that simultaneously affect those tissues remain unknown. Using new targeted-lipidomics approach via a targeted liquid chromatography with tandem mass spectrometry (LC-MS/MS) approach, we comprehensively quantified fat composition (lipid mediators [LMs]) in gastrocnemius, serum and bone marrow flushes from tibia and femur obtained from 6, 24 and 42 weeks C57BL6 mice. Compared to young mice (6wks), all tissues in older mice showed significantly higher levels of arachidonic Acid (AA) ($p=0.042$) and AA-derived eicosanoids, PGA2 ($p<0.0001$), TXB2 ($p<0.001$), 11,12-EET, which are known to affect muscle and bone function. Moreover, Lipoxin B4, another AA product and an enhancer of bone turnover and negative regulator for muscle, showed significantly lower values in older mice compared to young mice in both genders ($p= 0.0092$). Furthermore, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) autoxidation products (20-HDoHE, 11-HDoHE, 7-HDoHE and 4-HDoHE), an omega-3 fatty acids that negatively regulate bone and muscle health were significantly higher in older mice ($p=0.003$, $p=0.020$, $p=0.025$, $p=0.045$ respectively). In conclusion, elucidation of those LMs that are present in ageing muscle, serum and bone marrow could provide valuable evidence on the role of fat infiltration in osteosarcopenia. These results suggest that LMs could play a role in modulating musculoskeletal function during aging, which might relate to sarcopenia and osteoporosis, and could become therapeutic targets in the future.

OCD40- MULTIMODAL PREHABILITATION PREVENTS POST-SURGICAL DETERIORATION OF PHYSICAL FUNCTION IN OLDER-AGED INDIVIDUALS WHO UNDERGO COLORECTAL SURGERY: A PROSPECTIVE COHORT STUDY. Foo Li Xin, Frederick Koh Hong Xiang, Harriet Shannon *(Miss, Singapore)*

Background: Frail older-aged patients undergoing colorectal surgery have an increased risk of poorer surgical outcomes. However, their physical performance is less studied despite its importance. This study aims to explore the potential benefit of a structured prehabilitation programme on the surgical and physical outcomes for this group of patients. **Methods:** A single-center prospective cohort study was conducted. A philanthropically-sponsored prehabilitation programme was conducted for participants who were 70-years or older and due for elective colectomies. They were group into "pre-frail/frail" or "fit" using an in-house frailty score. Participants underwent a 2-4 weeks-long prehabilitation involving dietician-guided nutritional supplementation and physiotherapy-guided resistance training. Hand grip strength (HGS), 6-minute walk test (6MWT), 4m gait speed (4m-GS), 30s chair rise (CST) and functional reach test (FRT) were measured at pre-determined time intervals before and after surgery. **Results:** Eighty patients who underwent elective colectomies from 2017 to 2021 were recruited. They had a median age of 80 (75.0-83.8) years. There were significant improvements between baseline and pre-operation for HGS($P=0.002$), 6MWT($P=0.012$), 4m-GS($P=0.002$) and 30s-CST($P<0.001$) but not FRT($P=0.064$). Between baseline and post-operation, there were no significant differences in FRT($P=0.428$), 6MWT($P=0.215$), 4m-GS($P=0.588$) and 30s-CST($P=0.816$), except HGS($P=0.024$). Post-hoc analysis shows no significant differences between "pre-frail/frail" and "fit" groups in the outcome measures across all time points comparison. **Conclusion:** Prehabilitation may improve the potentially poorer physical functional performance of pre-frail/frail elderly patients prior to surgery. With prehabilitation, there was no deterioration of functional performance from baseline to post-operation. Key words: Prehabilitation; Surgery; Aged; Quality-of-Life; Value; Frailty.

OCD41- A PROBIOTIC CAPABLE TO REDUCE SARCOPENIA IN UNDERNOURISHED ELDERLY, RESULTS FROM A PRE-CLINICAL STUDY. Muriel Giron[1,2], Muriel Thomas[3], Stéphanie Bornes[2], Marianne Jarzaguet[1], Camille Mayeur[3], Dominique Dardevet[1], Christophe Chassard[2], Isabelle Savary-Auzeloux[1] *(1. Université Clermont-Auvergne, INRAE, UMR 1019, Unité Nutrition Humaine, Clermont-Ferrand, France; 2. Université Clermont-Auvergne, INRAE UMR 0545, Unité Mixte de Recherche sur le Fromage, Aurillac, France; 3. Université Paris-Saclay, INRAE UMR 1319, Institut MICALIS, Jouy-en-Josas, France)*

Backgrounds: In 2050, older adults (65+) will reach 20% of world population with sarcopenic individuals representing a third of them. Specific nutritional strategies based on proteins coupled or not with exercise have shown some beneficial effects to limit sarcopenia but depending of the physio-pathological state, they may not be optimal or not applicable in case of poor appetite or disabilities to perform exercise. **Objectives:** Hence, complementary strategies independent of food intake need to be developed to limit sarcopenia. We recently observed on small intestine-resected patients a specific microbiota with a tremendous increased in Lactobacilli (1). Following the transfer of this specific microbiota in axenic rats (2), we showed an improved energy metabolism regulation which could be an adaptation of the gut physiology and metabolism to optimize the challenged utilization of nutrients in those patients. We hypothesized that this microbiota could be of interest to optimize energy utilization in malnourished frail elderly and then to limit sarcopenia. **Methods:** From feces of these patients, specific strains were selected on their capacity to preserve Caenorhabditis elegans survival and muscle integrity. Lacticaseibacillus casei CNCM I-5663 (LC-63) were then tested in old rats (18 months, n=25 per group) under moderate food restriction for 4 weeks (75% of ad libitum (AL group)) to experimentally mimic the development of sarcopenia with malnutrition. Body composition, muscle mass, and insulin sensitivity (OGTT, HOMA-IR, insulin signaling pathway in muscle) were assessed. **Results:** Moderate food restriction induced a decrease in muscle mass (-10%, $p < 0.05$, R vs AL) but concomitant daily intake of LC-63 (~109 CFU) minimized the loss of lean mass (-51%, $p<0.05$, R+63 vs R) and the muscle protein content (-12%, $p<0.05$, R+63 vs R). An improvement in overall insulin sensitivity was also observed in the R+63 group at whole body level and at the muscle level suggested by the 73% increased p-S6/S6 ratio ($p<0.05$, R+63 vs R). **Conclusion:** We observed the existence of a microbiota-gut-muscle crosstalk that could be modulated positively by LC-63 and then represents an interesting complementary approach to limit sarcopenia in the elderly. The inter-organ signals involved and the mechanisms involved in both insulin sensitivity and on muscle protein preservation remain to be determined. References: 1. Joly, F.; Mayeur, C.; Bruneau, A.; Noordine, M.-L.; Meylheuc, T.; Langella, P.; Messing, B.; Duée, P.-H.; Cherbuy, C.; Thomas, M. Drastic Changes in Fecal and Mucosa-Associated Microbiota in Adult Patients with Short Bowel Syndrome. Biochimie 2010, 92, 753–761, doi:10.1016/j.biochi.2010.02.015. 2. Gillard, L.; Mayeur, C.; Robert, V.; Pingenot, I.; Le Beyec, J.; Bado, A.; Lepage, P.; Thomas, M.; Joly, F. Microbiota Is Involved in Post-Resection Adaptation in Humans with Short Bowel Syndrome. Front. Physiol. 2017, 8, doi:10.3389/fphys.2017.00224.

OCD42- TOWARDS EXTENDED BODY COMPOSITION THROUGH AUTOMATED WHOLE-BODY SEGMENTATION OF SKELETAL MUSCLE, ADIPOSE TISSUE, BONE, AND MULTI-ORGAN AND VERTEBRAL LEVEL IDENTIFICATION FROM MULTI-SLICE CT IMAGES. Da Ma, Vincent Chow, Karteek Popuri, Mirza Faisal Beg *(Simon Fraser University, School of Engineering Science, Burnaby, British Columbia, Canada)*

Background: Body composition is an important driver and risk factor for a wide variety of diseases, and a predictor of individual patient-specific clinical outcomes. CT images are routinely acquired in the oncological workflows and deliver accurate rendering of internal anatomy and therefore can be used to assess the amount of skeletal muscle and adipose tissue compartments. **Objectives:** We aim to build and evaluate automated tools to enable harvesting of multi-slice and whole-body measurements from 3D CT images, by segmenting skeletal muscle, adipose tissue, bone, multiple organs, and vertebral level identification, to enable the discovery of various diseases based on individual tissue, organ volume, shape, and functional status. **Methods:** We developed a multi-slice CT segmentation method that can provide body composition analysis from the whole body, from head to toe. This method delivers accurate segmentation of the bony tissue, the skeletal muscle, subcutaneous (SAT) and visceral (VAT) fat, multiple organs such as liver, spleen, pancreas, kidney, gallbladder, lung, and aorta, as well as accurate predictions and annotations of vertebrate body levels. **Results:** Evaluation on the dataset achieved an average dice coefficient of 0.980 for bone, 0.974 for skeletal muscle, 0.986 for SAT, and 0.960 for VAT, over 0.9 for most of the organs. Most of the error distance in predicting the mid-vertebrate slices is close to 0. The comprehensive evaluation results demonstrate the accurate performance of the proposed multi-slice whole-body 3D tissue segmentation algorithm. **Conclusion:** This study confirms the feasibility of going beyond single-slice-based tissue area measurements to multi-slice measurements of volumes and texture for these tissues from multiple slices, as well as other internal organ volumes, shape, location, texture, and radiomic texture features in the body. This is a necessary step to unleash the full power of AI into supporting new and personalized treatment approaches in the domain of precision medicine.