SYMPOSIA

S1- THE ENABLING REDUCTION OF LOW-GRADE INFLAMMATION IN SENIORS (ENRGISE) PILOT TRIAL TO AVERT INFLAMMATION, MOBILITY LOSS, AND FRAILTY: EARLY RESULTS

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Communication 1: *The Design and Rationale of the ENRGISE Study,* Marco Pahor[1], Walter Ambrosius[2], Anne Newman[3] ((1) Department of Aging and Geriatric Research, University of Florida, Gainesville, FL, USA; (2) Department of Biostatistical Sciences, Wake Forest School of Medicine, Winston-Salem, NC, USA; (3) Department of Epidemiology, University of Pittsburgh, Pittsburgh, PA, USA)

Low-grade chronic inflammation, characterized by elevations in Interleukin-6 (IL-6), is an independent risk factor of disability, frailty, and lower walking speed. It is unknown whether interventions that reduce the levels of inflammatory markers per se improve mobility, or avert decline in mobility in older persons. ENRGISE, a placebo-controlled randomized clinical trial, will test the ability of anti-inflammatory interventions for preventing major mobility disability by preserving walking ability. The ENRGISE Pilot study is testing whether 12 months of assignment to either losartan or omega-3 polyunsaturated fatty acids, or their combination reduces IL-6 levels in persons with elevated levels compared to a placebo, and whether the treatments can affect walking speed over 400 m. Both active treatments are safe, tolerable, acceptable, and affordable for vulnerable older persons. ENRGISE targeted the recruitment of 300 men and women > 69 years of age, with slow walking speed over 4 m (>.44 m/s, <1 m/s) but who are able to complete a 400 m test within 15 minutes. Entry IL-6 levels are >2.5 pg/ml and <30 pg/ml as determined by the average of two measures obtained prior to baseline. ENRGISE is supported by U01 AG054099 from the National Institute on Aging.

Communication 2: *The ENRGISE Pilot Study: Screening, Recruitment and Retention Preliminary Results,* Jane Cauley[1], Todd Manini[2], Mary McDermott[3], Michael Miller[4] ((1) Department of Epidemiology, University of Pittsburgh, Pittsburgh, PA, USA; (2) Department of Aging and Geriatric Research, University of Florida, Gainesville, FL, USA; (3) Division of Geriatrics, Feinberg School of Medicine, Northwestern University, Chicago, IL, USA; (4) Department of Biostatistical Sciences, Wake Forest School of Medicine, Winston-Salem, NC, USA)

ENRGISE's recruitment goal was to randomize 75 participants to omega-3 (only) or placebo, 75 participants to losartan (only) or placebo, and 150 participants to Losartan and omega-3 or placebo. Study participants were recruited to 5 academic medical centers. Participants were recruited over 15 months starting in April 2016 using multiple approaches to identify and screen potential participants. ENRGISE phone screened 5424 persons and randomized 289. Finding persons eligible for the losartan arms was challenging; 46% of those screened reported recent use of an angiotensin receptor blocker or an ace-inhibitor, 9% reported use of potassium-sparing diuretics and 16% had low blood pressure. The study over-recruited persons for the omega-3 arm to compensate for under-recruitment in the losartan arms. The study randomized 180 participants in the omega-3 arm, 43 in the losartan only arm, and 66 in the losartan+omega-3 arm. The mean age of ENRGISE participants was 78.3 ± 5.4 years (47% women; 22% minorities). Retention has been excellent with 93% of participants continuing in the study at 6 months.

Communication 3: *The Relationship between IL-6 levels and physical function in older adults with chronic low-grade inflammation,* Carlo Custodero[1], Roger Fielding[2], Dan Beavers[3], Stephen Anton[4] ((1) Department of Aging and Geriatric Research, University of Florida, Gainesville, FL, USA; (2) Jean Mayer USDA Human Nutrition Research Center on Aging, Tufts University, Boston, MA, USA; (3) Department of Biostatistical Sciences, Wake Forest School of Medicine, Winston-Salem, NC, USA; (4) Department of Aging and Geriatric Research, University of Florida, Gainesville, FL, USA)

Background: Circulating levels of IL-6 greater than 2.5 pg/mL are associated with an almost two times the risk of functional decline compared to those with levels below this cut-point. Less is known about the relationship between IL-6 and physical function among persons with elevated IL-6 levels. **Purpose:** To assess the cross-sectional relationship between circulating IL-6 levels and physical function at ENRGISE study baseline. **Methods:** IL-6 levels were based on the average to two baseline fasting measures. Physical performance tests included the short physical performance battery, knee extensor strength measured by isokinetic dynamometry at 60 deg/sec and usual gait speed over 4 and 400 meters. Mean performance by IL-6 tertiles and the partial correlations between log IL-6 and performance measures were adjusted for age, gender, race, BMI, smoking status and comorbidities. **Results:** The IL-6 tertile cutpoints were: tertile 1: > 2.5 < 3.48 pg/ml; tertile 2: 3.48 - 4.61 pg/ml; tertile 3: > 4.61 - < 30 pg/ml. Only mean (95% CI) adjusted muscle strength differed significantly ($p < 0.05$) across IL-6 tertiles -- Tertile 1: 88.7 (81.4, 96.0) Newton-meters (Nm); Tertile 2: 84.1 (77.0, 91.3) Nm; Tertile 3: 73.6 (66.3, 73.6) Nm. The partial correlation between log IL-6 and knee strength was -0.21 ($p=0.002$). **Conclusion:** In older persons with elevated IL-6, muscle strength was inversely associated with IL-6 levels across the high normal range.

S2- FRAILTY RESEARCH AT THE VA GRECCS (GERIATRIC RESEARCH EDUCATION AND CLINICAL CENTER).

Jorge G. Ruiz *(Miami VAHS GRECC and University of Miami Miller School of Medicine, Miami, Florida, USA)*

Communication 1: *An automated cumulative deficit index to identify frailty in the VA.,* Jane Driver (New England GRECC, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts, USA)

The «cumulative deficit index» (CDI), a simple count of age-related impairments, is a powerful measure of global health and mortality risk. The objective of this study was to develop an algorithm to assign an automated CDI to a national cohort of veterans and determine its value in predicting mortality. We assembled a cohort of veterans' 65 who were regular users of VA between 2002 and 2008 using VA databases linked to Medicare/Medicaid data and followed the cohort through 2014. The CDI includes a minimum of 30 age-related deficits from multiple health domains. The number of deficits is divided by the number of possible variables to give a score between 0 and 1. We created a VA-CDI that contains 32 deficits identified from diagnostic and procedure codes. Death was confirmed using the National Death Index. Frailty was defined using cutoffs established in large non-VA populations (robust < 0.1, pre-frail 0.1-0.2, frail > 0.21). We used Cox proportional hazards models to assess the association between CDI and 2-year mortality. In 2002, the cohort included 1,606,751

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veterans; 36.9% were classified as robust and 29.6% as frail. By 2012, the prevalence of frailty had doubled (26.5% robust and 43.9% frail). In a subset of 1,542,786 veterans followed from 2012 to 2014, the risk of death increased logarithmically with the CDI to a maximum of 0.81; higher scores were not compatible with life. The index predicted survival more robustly than age alone, even when adjusted for age, sex and race. The VA-CDI promises to be a valuable and easily accessible tool that could be used to help individualize the care of older veterans.

Communication 2: *Metformin: A Potential Intervention for Preventing Frailty in Older Adults with Pre-Diabetes,* Sara E. Espinoza (San Antonio GRECC and Barshop Institute for Longevity and Aging Studies, University of Texas Health Science Center at San Antonio, Texas, USA)

Older adults with pre-diabetes are at increased risk for frailty. Metformin is a widely-used, well-tolerated drug that improves insulin sensitivity and has anti-inflammatory properties, two major contributors to frailty. Metformin is known to prevent diabetes incidence. We hypothesize that metformin will prevent frailty in older adults with pre-diabetes. We are conducting a randomized, double-blinded, placebo-controlled trial of metformin for frailty prevention over two years in adults aged 65+ years with pre-diabetes as assessed by 2-hour oral glucose tolerance test. Exclusion criteria are baseline frailty, diabetes, dementia, untreated depression, active malignancy, or severe cardiovascular, pulmonary, and neurologic diseases. Primary outcome is frailty as assessed by Fried criteria; secondary outcomes are physical function, systemic and tissue (muscle) inflammation, tissue insulin signaling, insulin sensitivity, glucose tolerance, and body composition. Baseline characteristics for 15 subjects currently enrolled in the study are reported. Mean age is 74.7 ±5.7 years, body mass index is 29.1 ±4.6 kg/m2, and Hemoglobin A1c is 5.8 ±0.3%. Eleven (73%) participants are non-frail and four (27%) are pre-frail. Metformin is being examined as a potential therapeutic agent to prevent frailty in this randomized-controlled trial. The study aims to study 120 participants over the next five years. Findings from this trial may have implications for the future screening and prevention of frailty.

Communication 3: *Physical Resilience and Frailty,* Heather E. Whitson (Durham VA GRECC, and Duke University Aging Center, Duke University School of Medicine, Durham, North Carolina, USA)

This session will focus on the emerging construct of physical resilience, defined as one's ability to withstand or recover from functional decline following acute and/or chronic health stressors. The session will introduce a conceptual framework for physical resilience that addresses measurement of resilience and characterization of clinically relevant resilient phenotypes. One goal will be to highlight areas of overlap with and distinction from the related construct of frailty. Whereas age-related declines associated with frailty often evolve near the end of life and represent an extreme stage in the healthspan, we conceptualize resilience as a continuous spectrum that applies across the lifespan such that young people exhibit different degrees of resilience. We propose that one's likelihood to suffer physical decline associated with frailty and one's likelihood to counteract or recover from functional loss during and after stressors (physical resilience) may depend on different mechanisms. We will consider the hypothesis that favorable biology in molecular and cellular processes involved in adaptive stress response may be particularly important determinants of resilience. Likewise, we will discuss how resilience to biomedical stressors may be enhanced by social, psychological, and external factors. In our model, the spectrum from robustness to frailty reflects the amount of physiological reserve one has to react to stressors, while physical resilience refers to the actualization of that potential. For this reason, to quantify an individual's resilience, measurements of health and function must be collected after the stressor. Finally, we will discuss clinical test paradigms (e.g., stimulus-response tests, dual-tasking, and complex dynamical output monitoring) and biomarkers that may be useful in predicting resilience to common health stressors.

S3- WHO-ESCEO SYMPOSIUM: "ASSESSMENT OF PHYSICAL PERFORMANCE IN DAILY CLINICAL PRACTICE: OUTCOMES OF AN EXPERTS' CONSENSUS MEETING ORGANIZED BY THE EUROPEAN SOCIETY FOR CLINICAL AND ECONOMIC ASPECTS OF OSTEOPOROSIS, OSTEOARTHRITIS AND MUSCULOSKELETAL DISEASES (ESCEO) UNDER THE AUSPICES OF THE WORLD HEALTH ORGANIZATION" Islene Araujo de Carvalho - René Rizzoli *(Geneva, Switzerland)*

S4- THE CRITICAL ROLE OF PERIODIC INACTIVITY AND MUSCLE DISUSE IN WORSENING SARCOPENIA AND HASTENING DISABILITY AND FRAILTY. Stuart Philips *(Department of kinesiology McMaster University Hamilton Canada)*

Communication 1: *Mechanisms of muscle loss in older persons during disuse and their consequences,* Luc J.C. Van Loon (Department of Human Biology NUTRIM School of Nutrition and Translational Research in Metabolism Maastricht, the Netherlands)

A period of muscle disuse due to sickness or injury can lead to substantial loss of skeletal muscle mass and strength in otherwise healthy individuals. The resulting health consequences, such as impaired functional capacity, decreased muscle strength, onset of peripheral insulin resistance, and a decline in basal metabolic rate, are of particular concern to older individuals, who are already functionally and/or metabolically compromised. Even a few days of disuse can already results in substantial loss of muscle mass and strength. These findings are of particular clinical relevance because hospitalization of (older) individuals with acute illness generally results in a mean hospital stay of 5–7 days. Such short successive periods of muscle disuse occurring throughout the lifespan may be instrumental in the progressive loss of muscle mass with aging. Loss of skeletal muscle mass due to disuse must be attributed to an imbalance between muscle protein synthesis and breakdown rates. A decline in basal (post-absorptive) muscle protein synthesis rates has been reported following both bed rest as well as limb immobilization. Furthermore, more recent work has shown that the muscle protein synthetic response to protein or amino acid administration becomes blunted following a period of disuse. Though declines in both post-absorptive and postprandial muscle protein synthesis rates seem to play the biggest causal role in the loss of muscle mass during a period of disuse, there is also some indirect evidence that increases in muscle protein breakdown rates occur during the first few days of muscle disuse.

Communication 2: *Therapeutic Intervention and strategies to alleviate loss and promote recovery,* Douglas Paddon-Jones (Department of Nutrition and Metabolism, The University of Texas Medical Branch Galveston USA)

The negative health consequences of muscular disuse (bed rest, inactivity, immobilization, sedentary behavior) are unequivocal. As little as 5 days of inactivity can significantly compromise muscle

health - particularly in middle-aged and older adults. Protecting skeletal muscle health during disuse and promoting recovery during rehabilitation is clinically and intuitively desirable. However, key knowledge gaps limit our ability to implement targeted, evidence-based, preventative and/or rehabilitative strategies. Limiters include: i) a poor understanding of the early molecular and metabolic changes during inactivity that precede overt, clinically observable outcomes; ii) a limited ability to identify at-risk individuals; iii) insufficient information to prescribe sex and age-specific therapeutic interventions and iv) the assumption that disused and healthy skeletal muscle have similar, positive responses to rehabilitative exercise. Recent clinical trials have demonstrated that i) nutrition (protein/amino acid/leucine), ii) lower volume/intensity exercise, and iii) anabolic drug interventions can partially protect muscle health during periods of disuse and may hasten recovery. Future trials should seek to refine current intervention strategies by identifying and targeting key time-sensitive elements of the disuse/recovery pathway.

Communication 3: *Reduced Activity Accelerates Sarcopenia and leads to metabolic Dysfunction in Aging,* Chris McGlory (Department of kynesiologie, Mc Master University Hamilton Canada)

Sarcopenia, defined as the age-related loss of muscle mass and strength, begins in earnest in the 5th decade of life, and is associated with the reduced ability to perform activities of daily living as well as a host of metabolic disease states. In recent years, there has been a worldwide increase in life expectancy and thus, a greater proportion of older adults who suffer from sarcopenia. Older adults are also known to be at greater risk for periods of acute physical inactivity (API) due to, for example, hospitalization and/or convalescence from illness or surgery that independently act to hasten the loss of muscle mass and functional capacity. In a series of studies aimed at recapitulating the episodes of API experienced by older persons, our laboratory has demonstrated that reduced daily stepping for 2-weeks induces declines in muscle mass, integrated rates of muscle protein synthesis, the onset of insulin resistance, and increases in circulating inflammatory markers. Importantly, we discovered that nearly all of these factors failed to fully recover within 2-weeks of returning to habitual stepping. The reduction in rates of muscle protein synthesis and emergence of a hyperglycemic inflamed state may represent an alarming, pernicious confluence of factors that may serve to precipitate declines in metabolic health over time. Given that return to ambulation is currently the standard clinical practice for older adults convalescing from API, these recent findings suggest that proactive interventions such as exercise and or pharmacology are now needed to facilitate full recovery of metabolic function in this population.

S5- MACROVASCULAR AND MICROVASCULAR CONTRIBUTORS TO SARCOPENIA IN AGING AND DISEASE. Steven J. Prior *(University of Maryland, USA)*

Communication 1: *Skeletal muscle capillarization as a determinant of muscle fiber size and muscle mass in the development of sarcopenia,* Odessa Addison (University of Maryland School of Medicine, USA)

Primary aging may account for some proportion of sarcopenia; however, aging is associated with poor nutrition, low levels of physical activity and the presence of co-morbid conditions including diabetes and cardiovascular diseases that may also contribute. The development of sarcopenia across these conditions may at least be partially attributable to vascular dysfunction and microvascular rarefaction, resulting in limited substrate delivery and anabolic resistance. In conditions where muscle capillarization is reduced, such a peripheral arterial disease and type 2 diabetes, a higher incidence of sarcopenia is found when compared with age-matched populations. Furthermore, these individuals with sarcopenia have lower fitness levels and mobility function. Cross-sectional studies demonstrate the presence and degree of sarcopenia is associated decreased capillary-to-fiber ratio, and that lower capillarization is associated with reduced mobility function. Both cross-sectional and longitudinal studies in older adults show that skeletal muscle capillary-to-fiber ratio is tightly linked to muscle fiber cross-sectional area. Taken together, these studies support the hypothesis that reduced capillarization may be one important contributing mechanism to the development of sarcopenia and mobility disability in older adults. Understanding the contributions of skeletal muscle capillarization to reduced muscle mass and function is important for designing and implementing future interventions aimed at increasing muscle mass and function. **Objectives:** This communication will discuss recent findings that sarcopenia, as well as low physical fitness and function are related to low skeletal muscle capillarization, and will also present evidence that low skeletal muscle capillarization may contribute to the development of sarcopenia and reduced mobility function in older adults.

Communication 2: *Endothelial function and nutritive flow as potential determinants of anabolic resistance and sarcopenia,* Elena Volpi (University of Texas Medical Branch at Galveston, USA)

Nutritive blood flow normally increases in response to anabolic stimulation by feeding, insulin and exercise, and is an important component in the regulation of skeletal muscle protein anabolism and muscle homeostasis in humans. Aging is associated with endothelial dysfunction which reduces nutritive flow in response to feeding and insulin. Moreover, with advancing age skeletal muscle becomes resistant to anabolic stimulation, which contributes to sarcopenia. Recent studies have identified endothelial dysfunction as a major mechanism that underlies the muscle anabolic resistance of aging via reductions in nutritive flow. Vasodilators and aerobic exercise are important tools that enhance endothelial function and also improve nutritive flow and muscle protein anabolism in older adults. If confirmed in larger clinical trials, vasodilators and aerobic exercise may become clinical interventions for prevention and treatment of sarcopenia. **Objectives:** This communication will present evidence that endothelial dysfunction and reduced nutritive flow contribute to anabolic resistance, and that strategies to enhance endothelial function and nutritive flow may improve the anabolic potential of muscle in older adults.

Communication 3: *Skeletal muscle capillarization and satellite cell function; Implications for interventions targeting sarcopenia,* Tim Snijders (Maastricht University Department of Human Biology and Movement Sciences, the Netherlands)

The age-related loss of skeletal muscle mass and strength is associated with the development of functional impairments increased risk of morbidity and mortality, and the need for institutionalization. Key to the development of sarcopenia is the reduced capacity of aged muscle to regenerate, repair and remodel. Over the years, research has focused on elucidating underlying mechanisms of sarcopenia and the impaired ability of muscle to respond to stimuli with aging. Muscle specific stem cells, termed satellite cell, play an important role in maintaining muscle health throughout the lifespan. It is well established that satellite cells are essential in skeletal muscle regeneration, and it has been hypothesized that a reduction or dysregulation of this stem cell pool, may contribute to accelerated

loss of skeletal muscle mass that is observed with advancing age. The preservation of skeletal muscle tissue and its ability to respond to stimuli may be impacted with the reduced satellite cell content and impaired function observed with aging. Aging is also associated with a reduction in capillarization of skeletal muscle. We have recently demonstrated that the spatial distance between type II fiber associated satellite cells and capillaries is greater in older compared to younger adults. The greater distance between satellite cells and capillaries in older adults may contribute to the dysregulation in satellite cell activation ultimately impairing muscle's ability to remodel and in extreme circumstances, regenerate. Maximizing skeletal muscle capillarization in older adults may prove to be critical in restoring muscle satellite cell function and improve the blunted response of aged muscle to resistance exercise training, ultimately delaying and reducing the impact of sarcopenia. **Objectives:** This communication will provide an update on recent research investigating the connection between muscle satellite cell function and fiber capillarization in both young and older adults in response to exercise.

S6- OSTEOPOROSIS AND SARCOPENIA : TWO DISEASES OR ONE ? Olivier Bruyère[1], Cyrus Cooper[2], René Rizzoli[3], Jean-Yves Reginster[1] *((1) Department of Public Health, Epidemiology and Health Economics, University of Liège, Liège, Belgium; (2) MRC Lifecourse Epidemiology Unit, University of Southampton, Southampton, UK; (3) Division of Bone Diseases, Faculty of Medicine, Geneva University Hospitals, Geneva, Switzerland)*

Loss of bone and muscle with advancing age represents a huge threat to loss of independence in later life. Osteoporosis is defined as a systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue with a consequent increase in bone fragility and susceptibility to fracture. Osteoporotic fractures, a major cause of morbidity in the population, are associated with increased mortality and generate direct costs in excess of 35 billion euros, in 2010, in the 27 EU countries. Sarcopenia corresponds to a progressive and generalized loss of muscle mass with either a loss of muscle strength or a loss of physical performance. However, a single consensual operational definition of sarcopenia is lacking and none of the definitions, proposed so far, unequivocally emerge as providing benefits over previous ones, leading to inconsistent reports across cohorts on its prevalence. Nevertheless, there is a wide consensus to consider that consequences of sarcopenia, including physical disability, nursing home admissions, depression, hospitalizations and mortality are linked to direct healthcare costs estimated in 2000, in the USA, to raise up to 18.5 billion USD. During the last decade, bone and muscle were increasingly recognized as interacting tissues, not only because of their adjacent surfaces or as a result of the mechanical effects of muscle loading on bone function. In this perspective, the «bone» «muscle» unit would be the site of privileged exchanges in which the two tissues communicate via paracrine and endocrine signals to coordinate their development and adapt their response to loading and injury from embryologic stages to involution. Growing evidence shows that sarcopenia and osteoporosis share many common pathways including the sensitivity to reduced anabolic hormone secretion, increased inflammatory cytokine activity, anabolic or catabolic molecules released by the skeletal muscle or by the bone cells (i.e. myokines and osteokines) and eventually, reduced physical activity. With adipose tissue and cartilage being also involved in their complex interactions came the suggestion that obesity, sarcopenia and osteoporosis could be concomitantly found in a subset of the population, presenting with an entity called osteosarcopenic obesity (OSO) with health outcomes likely to be worse compared with individuals with only one of these disorders. This Symposium will review recent publications which help to better understand the complex relationship between osteoporosis and sarcopenia, hopefully paving the way for the development of chemical entities that are able to target both diseases.

Communication 1: *Lifetime course of muscle and bone wasting,* M. Peterson, Cyrus Cooper (Lifecourse Epidemiology Unit, University of Southampton, Southampton, UK)

Communication 2: *Role of nutrition and physical exercise in the prevention of bone and muscle wasting,* René Rizzoli (Division of Bone Diseases, Faculty of Medicine, Geneva University Hospitals, Geneva, Switzerland)

Communication 3: *What can we learn from osteoporosis to get a treatment against sarcopenia approved?* Jean-Yves Reginster, (Department of Public Health, Epidemiology and Health Economics, University of Liège, Liège, Belgium)

S7- THE MID-FRAIL STUDY. EFFECTS OF THE FIRST STUDY A MULTIMODAL INTERVENTION IN ODER FRAIL/PREFRAIL PEOPLE WITH DIABETES MELLITUS FROM A FUNCTIONAL PERSPECTIVE. CHANGING THE PARADIGM OF APPROACHING DIABETES IN OLDER PEOPLE. Leocadio Rodriguez-Mañas[1], Alan J Sinclair[2] *((1) Geriatric Department, Getafe University, Hospital, Getafe, Madrid, Spain; (2) Foundation for Diabetes Research in Older People, Diabetes Frail, Medici Medical, Practice, 3 Windsor Street, Luton, LU1 3UA, UK)*

Communication 1: *Why we undertook the European Mid-Frail Study and how the Intervention was defined?* Alan J Sinclair[1], Mikel Izquierdo[2] ((1) Foundation for Diabetes Research in Older People, Diabetes Frail, Medici Medical Practice, 3 Windsor Street, Luton, LU1 3UA, UK; (2) Department of Health Sciences, Public University of Navarra, Spain)

Background: Diabetes is the commonest metabolic and disabling disorder in ageing communities and represents an important independent risk factor for the development of Frailty which is becoming an important public health priority for action. Examination of functional loss in Diabetes suggests a multimodal causology due to peripheral neuropathy, accelerated muscle loss, sarcopenic change, and frailty. Analysis of the cycle of functional decline in older adults identifies Frailty as a pre-disability condition which raises the posssibility of intervention being involved to decrease disability in Diabetes since disability leads to significant health and social care expenditure and decreased quality of life. Resistance training with or without combination with endurance training has been shown to increase physical function in aging subjects with and without Frailty but studies in older diabetic subjects have been limited and small scale. The Mid-Frail study represents the first large-scale intervention study which has sought to determine if Frailty and reduced functional performance in Diabetes in older adults (>70 years) can be reversed/improved by an intervention composed of resistance exercise training, nutritional education, and optimisation of medical care. This randomised trial funded by the European Commission and will be regarded as a landmark study in this area. **Objectives:** To assess the effectiveness of a multimodal intervention in older frail and pre-frail patients with Type 2 Diabetes Mellitus

Communication 2: *Design and implementation of the MID-FRAIL study,* Olga Laosa (Foundation of Biomedical Research, Getafe University Hospital, Getafe, Madrid, Spain)

Methods: MID-Frail is an open, randomised, multicentre and international clinical trial, with random allocation by clusters to usual care group (UCG) or intervention group (IG). Main objective was to evaluate, in comparison with usual clinical practice, the effectiveness of a multi-modal intervention (educational program to avoid and detect mainly hypoglycemia, specific HbA1c and BP clinical targets in frail people according to European guidelines (EDWPOP 2011) and individualized resistance training program) in frail and pre-frail subjects 70 years with type 2 diabetes in terms of changes in function (FU: 1 year post-randomization) assessed by SPPB. Secondary objectives were changes in quality of life, caregiver burden, Barthel and Lawton index, hospitalization and permanent institutionalization rates and economical assessment. Seven European countries were involved. Country coordinator was selected in each country and was responsible to select 11-12 trial sites (TS) per country which recruited 7-23 participants each. Randomization unit was the TS to avoid the contamination bias. 98 TS were activated once all procedures had been performed and the aproval from the Ethics Committees were received. Good Clinical Practices were followed to carry out the project. Participants and caregivers (if applicable) were invited to sign the informed consent form to can participate in the study. Finally, 1000 participants were included. When one TS included 7 participants was randomized to IG or UCG. TS allocated to IG contacted to country coordinator to provide them the intervention material (exercise machines, diarys, material for educational program, etc). All countries used the same material for intervention. UCG consisted in the level of routine care a patient with diabetes will normally be expected to receive from his/her local healthcare system.

Communication 3: *Main results and conclusions,* Leocadio Rodriguez-Mañas (Geriatric Department, Getafe University Hospital, Getafe, Madrid, Spain)

Results: 963 patients were included in the study along 7 EU countries (Spain, UK, France, Italy, Germany, Belgium, Czech Republic) in 74 Trial Sites. 447 patients were included in sites allocated to intervention and 516 in those receiving usual care. Between the screening and the basal visits 120 patients decided not to participate, being the final sample formed by 834 individuals (494 in UCG and 349 in IG). Mean age was 78.0 ± 5.4 yrs.; 37.8 % were frail; mean years since diagnostic 16.9 ± 14.49; mean HbA1c was 7.27 ± 1.21; mean BMI 29.6 ± 4.96; mean BP 140.0 ± 18.7 mmHg/75.32 ± 11.25 mmHg; mean SPPB was 8.46 ± 2.63; mean Barthel Index 96 ± 7.35 and Lawton Index 6.9 ± 1.67. There were no significant differences in the characteristics of the patients allocated to any of the branches of the trial. After one year of follow up, there was an improvement in SPPB score of 1.19 (from 8.25 at baseline to 9.44 at month 12) in the IG (adjusted $p<0.001$) while this change in the UCG was 0.08 (from 8.63 to 8.71) (NS). The difference between groups was 1.11 ($p < 0.001$). The 2 sensitivity analysis carried out did not show significant changes with the results obtained in the primary analysis. The improvements in SPPB were observed since the week 10 and reached its maximum at week 26 (8 weeks after finishing both the strength training and the educational programs) when the value was 9.51. Since then, SPPB score in the intervention group was maintained, showing a very mild decrease (-0.07). The improvement was observed in the three domains of SPPB (balance, gait speed and chair stand). Episodes of symptomatic hypoglycemia and hospitalization showed a tendency to improvement in IG versus UCG (--4.3%, CI-11.5 to 3.0% and -4.2%, CI -10.2 to 1.7%, respectively) but did not reach statistical significance. No differences were found regarding IADL, ADL, quality of life and care burden Taking into consideration the social perspective, the health benefits did not change, changing the cost items solely. The conclusion obtained according to the health perspective was not altered when we added this social perspective, as intervention was still a dominant option. Thus, switching from usual care to intervention program entails a saving of 610 EUR and a gain of 0.9222 points in SPPB score. More than 15% of individuals improved their SPPB scores at least 1 point. Accordingly, the ICER is negative, indicating that the intervention is a dominant option. When considering QALYs as a health result, intervention program saves 712 EUR in comparison with usual care and obtained 0.0527 additional QALYs. Hence, intervention program dominates again over the usual care. **Conclusion:** A multimodal intervention program, easy to implement and with a good adherence rate, produces clinically significant improvements in older frail and pre-frail patients with Type 2 Diabetes, a benefit that remains along the time. The intervention has, in addition, a good cost-effectiveness relationship, making it available for implementation by health services.

CONFERENCE

C1- SPRINTT CLINICAL TRIAL UPDATE. Emanuele Marzetti[1] Riccardo Calvani[2], Anna Picca[2], Matteo Tosato[1] Matteo Cesari[3,4], Roberto Bernabei[2], Francesco Landi[2] *((1) Department of Geriatrics, Neurosciences and Orthopedics, Teaching Hospital «Agostino Gemelli», Rome, Italy; (2) Department of Geriatrics, Neurosciences and Orthopedics, Catholic University of the Sacred Heart, Rome, Italy; (3) Ospedale Maggiore Policlinico, Milan, Italy; (4) Geriatric Unit, Department of Medical Sciences and Community Health, University of Milan, Milan, Italy)*

The proposition of sarcopenia as a major component of physical indicates that interventions specifically targeting the skeletal muscle may offer preventive and therapeutic advantages against frailty and its clinical correlates. Observational studies and some randomized clinical trials (RCTs) have suggested a positive effect of regular physical activity (PA) (and nutritional interventions) on improving physical function and/or reducing symptoms of disability in healthy older individuals and those at risk for mobility disability. Definite evidence from high-quality, large-scale RCTs is still lacking. To fill this gap in knowledge, the SPRINTT consortium has sponsored a phase III, single-blind, multicenter RCT (ClinicalTrials.gov identifier: NCT02582138) designed to compare the efficacy of a multi-component intervention (MCI) program (physical activity, nutritional counseling/dietary intervention, and information and communication technology [ICT] intervention) versus a healthy aging lifestyle education (HALE) program for preventing mobility disability in non-disabled older persons with physical frailty & sarcopenia (PF&S). The primary outcome is mobility disability, operationalized as inability to walk for 400 m within 15 min, without sitting, help of another person, or the use of a walker. Trial operations are taking place in 16 clinical sites, located in 11 European countries, under the coordination of the Department of Geriatrics at the Catholic University of Rome (Italy) and the support by members of EFPIA (Sanofi-Aventis R&D, Novartis, GlaxoSmithKline, and Servier). 1517 participants (mean age 78 years [SD 5.7], 73.3% women) have been enrolled in the SPRINTT RCT. 1203 had a SPPB score between 3 and 7 (mean SPPB 6.1 [SD1.1]), while 314 participants had a SPPB score of 8 or 9 (mean SPPB 8.7 [SD0.5]). Interestingly, more than 37% of SPRINTT participants have a BMI greater than 30. The main exclusion criteria

were: a) SPPB out of range (49.8%); b) normal muscle mass at DXA (31.2%); and c) failure to complete the 400-m walk test (6.6%). The intervention attendance is quite good. 66% of expected center-based and 74% of home-based physical activity sessions were attended. As for the HALE group, SPRINTT participants were present at more than 70% of the meetings. The dropout rate is around 6%.

C2- INSIGHT INTO THE INTERSECTION BETWEEN SARCOPENIA AND FRAILTY: RELATIONSHIP BETWEEN MUSCLE MASS AND FRAILTY STATUS. Paulo H. M. Chaves[1], Sheila Ingham[2], Antonio Carlos Carvalho[2], Alberto Frisoli[2] *((1) Benjamin Leon Center for Geriatrics Research and Education, Hebert Wertheim College of Medicine, Florida International University; (2) Department of Orthopedics, Federal University of São Paulo, São Paulo, Brazil; (3) Division of Cardiology, Federal University of São Paulo, São Paulo, Brazil; (4) Cardiogeriatric Unit, Division of Cardiology, Federal University of São Paulo, São Paulo, Brazil)*

Introduction: Low muscle mass has been conceptualized to play a role in the pathogenesis of frailty, a major geriatric syndrome. Consistently, low muscle mass has been linked to early clinical manifestations in the natural history of frailty, including weakness and slowness, but not to distal outcomes of frailty, including disability and hospitalization risk. The relationship of muscle mass to frailty status (as opposed to individual frailty phenotype components) in older adults remains to be better characterized, and its evaluation is this study's main objective. **Methods:** Cross-sectional analyses of observational data from the SARCopenia, Osteoporosis, and Vulnerability Outcomes Study (SARCOS), an epidemiologic investigation of older adults in a cardiology outpatient clinic in Sao Paulo, Brazil. Two traditional whole-body dual-energy X-ray absorptiometry estimates of lean mass were considered: appendicular lean mass (ALM) scaled to height squared (ALM/height2), and body mass index (ALM/BMI). Frailty phenotype status (frail, pre-frail, and robust) was defined according to a modified version of the approach proposed by Fried et al. Multinomial logistic regression was used. **Results:** Analytic sample (n=219) had a mean (± standard deviation [SD]) age of 78.2 (±7.2); 56.4% were women. Prevalence of frailty was 14.0%; low muscle mass according to the Foundation of the National Institutes of Health (FNIH) criteria was 64.6% in men (ALM/BMI<0.789), and 47.7% in women (ALM/BMI<0.512). ALM/BMI was associated with frailty status in a linear fashion, with incrementally higher levels of ALM/BMI associated with incrementally lower odds of frailty. In an age- and gender-adjusted model, 1 SD higher ALM/BMI was associated with 63% (25%-82%, p=.006) lower odds of being classified as frail, as opposed to robust. ALM/height2 was not associated with frailty after adjustment. **Conclusion:** The concept and measurement of sarcopenia have been evolving. Our results demonstrated that inferences about the muscle mass–frailty status association may change substantially by ALM estimate, and that ALM/BMI was strongly, linearly, and inversely related to frailty occurrence in older adults. Enhanced understanding about methodologies for muscle mass assessment and clinical classification may help advance knowledge about transition from sarcopenia to frailty, and potentially lead to novel preventive approaches.

C4- SARCOPENIA AND FRAILTY GUIDELINES UPDATE IN ASIA. Hidenori Arai[1], Elsa Dent[2], Chang-Won Won[3], and Liang-Kung Chen[4] *((1) National Center for Geriatrics and Gerontology, Japan; (2) Torrens University of Australia, Australia; (3) Kyung Hee University Hospital, Korea; (4) Taipei Veterans General Hospital, Taiwan)*

Sarcopenia is a major challenge to healthy aging, and affected patients tend to have worse clinical outcomes and higher mortality than those without sarcopenia. The Asian Working Group for Sarcopenia (AWGS) published regional consensus guidelines in 2014, and many research studies from Asia have been published since then. After the introduction of the AWGS consensus, the reported prevalence of sarcopenia estimated by the AWGS criteria ranges between 4.1% and 11.5% of the general older population. Reported risk factors included age, sex, heart disease, hyperlipidemia, daily alcohol consumption, and low protein or vitamin intake, whereas physical activity is a protective factor. Although AWGS 2014 diagnostic cut-offs were generally well accepted, some may require further revision in light of conflicting evidence from outcome-based studies. Due to the great impact of sarcopenia, a life course program for good nutrition and physical activities would be of great benefit. However, various research challenges remain to be resolved in the future and more outcome-based trials are needed to formulate the most optimal strategy for sarcopenia in Asia. In 2016 we organized the clinical guideline committee in the Japanese Association on Sarcopenia and Frailty and tried to publish the guidelines for sarcopenia for Japanese patients. We systematically searched PubMed, the Cochrane Library, and Ichushi-Web for RCTs from January 2000 to December 2016. We meta-analyzed the outcomes with the net difference between-group treatment from baseline to the end of the study. We also developed evidence-based clinical practice guidelines for the identification and management of frailty in older adults. The guidelines were formed using an adapted GRADE methodology, and incorporated an extensive literature search paired with the expert knowledge and experience of international experts in gerontology and geriatrics. Strong recommendations were: (i) frailty should be identified using a validated screening tool; (ii) physical activity should be prescribed that includes a resistance training component; and (iii) polypharmacy should be addressed. These clinical practice guidelines can be used to support healthcare professionals in their recognition, care and management of older persons with sarcopenia and frailty.

C5- A NOVEL NON-PHARMALOGICAL INTERVENTION TO IMPROVE PHYSICAL HEALTH IN OBESE ELDERLY: CITRULLINE WITH HIGH-INTENSITY INTERVAL TRAINING. M Aubertin-Leheudre *(UQAM; Québec-Canada)*

The importance of, the age-related loss of skeletal muscle mass and function, is now widely recognized. The estimated direct health care cost attributable to muscle atrophy in the United States in 2000 was $18.5 billion. However, considering that poly-medication has deleterious effects on health and quality of life, it is therefore appropriate to implement non-pharmacological interventions in order to optimize successful aging. This has led to increasing interest in the influence of adult lifestyle, particularly in the effects of modifiable factors such as physical activity and diet on muscle mass and function in older people, with a view to identifying intervention opportunities both to prevent and manage muscle decline. There is a growing body of evidence that links insufficient intakes of protein, vitamin D, antioxidant nutrients, and n3 long-chain polyunsaturated fatty acids, to poor physical function. Interestingly, ciitrulline (a non-proteinogenic amino acid) supplementation (CIT) was shown, in

both rats and young human adults, to be able to increase muscle protein synthesis and increase lipolysis in adipocytes. In parallel, physical inactivity is also clearly linked to losses of muscle mass and strength, suggesting that increasing levels of physical activity should have protective effects. However, more than half of older adults are sedentary and the first self-reported causes is the lack of time. Thus, High-Intensity Interval Training (HIIT), due to its high effectiveness and short duration, is a promising avenue to prevent also muscle function decline and also metabolic disorders. Therefore, CIT may exert additional beneficial effects when combined with HIIT but their combined effects are unknown in obese older adults. Thus, the general aim of this symposium will be to present and discuss the effectiveness of combined interventional studies (HIIT training with or without citrulline supplementation on muscle function in older adults. More specifically, the speaker will present data from an interventional randomized controlled trial which examined the effects of CIT combined with HIIT on body composition (DXA) muscle strength and physical performance in 72 inactive obese older adults (mean age: 68±5y; 50% of women). Overall, this talk will highlight a new potential non-pharmacological intervention to prevent the loss of muscle function and physical performance in older adults.

C6- A MINIMALIST APPROACH TO POWER TRAINING FOR ENHANCING LATERAL BALANCE FUNCTION AND MOBILITY IN OLDER ADULTS. Mario Inacio[1], Odessa Adison[1,2], Robert Creath[1], Mark W. Rogers[1] *((1) University of Maryland School of Medicine Department of Physical Therapy and Rehabilitation Science, MD, USA; (2) Division of Gerontology and Geriatric Medicine, Baltimore VAMC GRECC)*

In addition to the points made in the rationale and conclusions in the original communication 3 abstract, this study found that just 15 mins of hip abductor-adductor (AB-AD) power training, 3 times per week for eight weeks improved: - hip AB muscle composition (CT derived muscle attenuation and intramuscular adipose tissue (IMAT) infiltration); - hip AB muscle quality and hip AB-AD rate of neuromuscular activation (derived from surface electromyography (EMG)), during standing hip AB-AD isometric maximal voluntary contractions (IMVC); - incidence of the most biomechanically optimized balance recovery stepping strategy (single lateral steps), during lateral waist-pull balance perturbations; - training-induced improvements in the four step square test (FSST), a clinical measure of functional mobility, were associated with reductions in hip AB IMAT.

C8- EUROPEAN AND NORTH AMERICAN PRACTICES ADDRESSING ENDOCRINE ISSUES IN OLDER ADULTS WITH FRAILTY. Willy Marcos Valencia[1,2], Carmen Castillo Gallego[3,4] Ana Alfaro-Acha[4,5,6] *((1) Geriatrics Research, Education and Clinical Center (GRECC), Miami VA Medical Center, Miami (VAMC), FL, USA; (2) Dpt. of Medicine, University of Miami, Miami, FL, USA; (3) Hospital Virgen del Valle, Complejo Hospitalario de Toledo, Spain; (4) CIBER of Frailty and Aging (CIBERFES), Toledo, Spain; (5) Frailty Unit. Dpt. of Geriatric. Hospital Virgen del Valle of Toledo. Spain; (6) GENUD (Growth, Exercise, Nutrition and Development) Research group, University of Toledo. Spain)*

Points: • Older community-dwelling older adults with Frailty phenotype have multiple co-morbidities including endocrine issues. • The phenotype of older adults with impaired mobility is regularly observed in primary care clinics (PCC) but often not assessed; • There is overlap in the phenotypes of patients with frailty syndrome and falls; • Falls syndrome is more prevalent in older adults with frailty, compared to prefrail or robust. • The comprehensive geriatric assessment detects reversible risk factors, but primary care providers are not trained and their practices often cannot accommodate the time. Hence, falls continue to go unrecognized and unassessed. • Older adults at risk for frailty or falls syndromes must undergo a comprehensive geriatric assessment, followed by a multidimensional exercise and nutrition program to optimize successful aging.

C9- THE FUTURE OF FRAILTY MANAGEMENT. Bertrand Fougère[1,2,3], Elsa Dent[4,5] *((1) Gérontopôle, Centre Hospitalier Universitaire de Toulouse, Toulouse, France; (2) Inserm UMR1027, Université de Toulouse III Paul Sabatier, Toulouse, France; (3) Division of Geriatric Medicine, Saint Louis University School of Medicine, St. Louis, Missouri, USA; (4) Torrens University of Australia, 220 Victoria Square, Adelaide, Australia; (5) Baker Heart and Diabetes Institute, Level 4, Commercial Road, Melbourne, Australia)*

Precision Medicine (P4) in the management of Frailty and Sarcopenia (Fougère.B): Precision medicine is an approach that recognizes individual variability in genes, lifestyle and environment for the individual. It recognizes that different persons require different treatment approaches. The 4 pillars of P4 medicine are: Predictive, Preventive, Personalized and Participatory. It requires an interprofessional approach. Frailty lends itself ideally to the P4 approach. We are rapidly learning that both a person's genes and genetic instability lead to frailty. Other factors predicting frailty are telomere attrition, epigenetic alterations, mitochondrial dysfunction and stem cell exhaustion. Precision medicine on muscle quality can also help to understand the substantial variability in individual patient response to health-related outcomes and adapt intervention programs to the individual phenotype of each patient. This will necessarily involve an individualized prescription according to the functional capacity of the person, with specific recommendations about the dose (intensity, volume, and frequency), similar to those of other medications. **Rapid Detection of Frailty in Older Adults (Dent.E):** The FRAIL scale is a useful tool for the rapid detection of frailty, and is suitable for application in multiple settings, including primary care, hospitals and population-wide health screening. Rapid screening of frailty with the FRAIL scale should be paired with a rapid response to frailty, which involves Comprehensive Geriatric Assessment, multidisciplinary case management, and individually tailored care plans.

C12- COGNITIVE FRAILTY: FROM CONCEPTUAL PROPOSAL TO CLINICAL PRACTICE. Liang-Kung Chen[1,3], Hiroyuki Shimada[2], Li-Ning Peng[1,3], Chih-Kuang Liang[1,3], Hidenori Arai[1,2] *((1) National Yang Ming University, Taiwan; (2) National Center for Geriatrics and Gerontology, Japan; (3) Taipei Veterans General Hospital, Taiwan; (4) Kaohsiung Veterans General Hospital, Taiwan)*

Declines in physical and cognitive function are common age-related conditions and the synergistic impact on aging had been reported in the literature. However, previous intervention studies were mostly focused on preventing the occurrence of disabilities in either physical or cognitive domains. Although improvement in physical function may be accompanied by the improvement of cognitive performance as well, more studies are needed to prove the concepts of preventing physical disability and dementia through an integrated approach. In 2013, cognitive frailty was proposed to identify older adults with physical frailty and cognitive impairment to highlight the potential of designing a new approach to promote healthy aging.

Modified criteria have been proposed to improve the early detection rate and to ensure the potential of reversibility. However, to date, no convincing epidemiological studies had been published to demonstrate adverse outcomes of cognitive frailty and the reversibility. The Asian Association for Frailty and Sarcopenia (AAFS) proposed the modified diagnostic criteria for cognitive frailty by using the presence of weakness and/or slowness plus early cognitive impairment in any domain (defined by 1.5 SD below the age, sex, and education-matched norms). By using the diagnostic criteria among cohort studies in Japan and Taiwan, the prevalence of cognitive frailty was between 10-15% and the associations between cognitive frailty with physical disability, incident dementia, and mortality were clearly shown. Moreover, a sub-group study of a nationwide clustered randomized controlled trial clearly showed the significant improvement in physical performance and cognitive performance through an integrated multi-domain intervention study consisting of exercise, cognitive training, nutritional consultation and chronic condition management. In conclusion, modified cognitive frailty by AAFS may identify 10-15% community-living older people with higher vulnerability to physical disability, incident dementia and all-cause mortality. Moreover, a multi-domain integrated intervention program may potentially reverse the vulnerable state.

ORAL COMMUNICATIONS

OC1- THE RELATIONSHIP BETWEEN T-CELL RESPONSES TO CYTOMEGALOVIRUS (CMV) AND ONSET OF FRAILTY IN HIV- AND HIV+ MEN IN THE MULTICENTER AIDS COHORT STUDY (MACS). JB Margolick[1], JH Bream[1], TL Nilles[1], H Li[2], SL Langan[1], S Deng[1] R Wang[3], N Wada[3], SX Leng[2]
((1) Department of Molecular Microbiology and Immunology, Johns Hopkins Bloomberg School of Public Health, USA; (2) Division of Geriatric Medicine and Gerontology, Department of Medicine, Johns Hopkins School of Medicine; (3) Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, USA)

Backgrounds: Both aging and treated HIV-infected populations exhibit low-level chronic immune activation of unknown etiology which correlates with morbidity and mortality. Infection with cytomegalovirus (CMV) is common in both populations but its relation to immune activation is unknown. **Objectives:** To determine whether the T-cell response to CMV is a predictor of the onset of frailty in non-frail men who have sex with men (MSM), either infected with human immunodeficiency virus (HIV+) or not (HIV-), in the MACS. **Methods:** The MACS is a longitudinal cohort study that has followed HIV- and HIV+ MSM semiannually since 1984, with frailty assessments by the Fried criteria (since 2007) and storage of peripheral blood mononuclear cells (PBMC) and serum at all study visits. Nonfrailty was defined as non-satisfaction of the Fried criteria at 2 consecutive study visits. Cryopreserved PBMC from 21 nonfrail MACS participants (11 virologically suppressed HIV+, 10 HIV-) were stimulated with peptides spanning 19 CMV open reading frames and intracellular cytokine responses (percentages of CD4 and CD8 T-cells producing IFN-, TNF-, and/or IL-2) were assessed by flow cytometry. Soluble and cellular markers of immune activation and inflammation were assessed by multiplex electrochemiluminescence and flow cytometry, respectively. Men were followed for up to 7 yr (median 6 yr) after assessment of CMV responses. **Results:** All men had detectable responses to CMV. Proportions of CMV-responsive T-cells correlated strongly (r0.6 or -0.6) and significantly ($p<0.05$) with several immunologic markers, depending on donor HIV status and frailty status. In HIV+ nonfrail men, the CD4 T-cell IL-2 response to CMV correlated strongly (r=0.75) with serum IL-6, a known predictor of frailty. Therefore, we asked whether this response predicted onset of frailty. Men in the upper tertile of the response (>2.5% responding T-cells) had faster time to frailty ($p=0.02$) and a higher proportion of visits with the frailty phenotype (median 30% vs 0%; $p=0.03$) than men in the lower two tertiles, among HIV- men but not among HIV+ men. **Conclusion:** The magnitude of the CD4 IL-2 response significantly predicted onset of frailty in HIV- nonfrail men, but not in HIV+ nonfrail men, in this small study. T-cell responses to CMV may strongly influence chronic immune activation in HIV-uninfected and virologically suppressed HIV-infected men, and may predict frailty in HIV-uninfected men.

OC2- MANUAL (STOPWATCH) AND INSTRUMENTAL (GAITRITE) EVALUATION OF 4-METER PREFERRED WALKING SPEED IN OLDER SUBJECTS WITH PHYSICAL FRAILTY. Marcello Maggio, Yari Longobucco, Valentina Angileri, Sara Tagliaferri, Fulvio Lauretani *(Clinic Geriatric Unit Department of Medicine and Surgery, University of Parma, Italy)*

Background: GSK2881078 4m usual gait speed is one of the most used parameters to assess physical frailty and sarcopenia.Timed usual walking speed on 4-meter course is generally assessed by using both a stopwatch (4-meter manual measurement,4-MM) but this method is potentially affected by intra and inter-operators biases.Instrumental techniques using accelerometers may have higher accuracy and GAITRite system is particularly useful on this regard because of its additional ability to determine temporal and spatial parameters of walking. **Objectives:** To compare intra and interclass variability in 4-MM and to test differences between 4-MM and instrumental (GAITRite) modalities to assess 4-meter WS in older subjects with probable physical frailty and sarcopenia. **Methods:** 168 non-disabled community dwellers (n=77men,n=91women) aged 77.31±4.73 and probable physical frailty were asked to walk 4 meters in the GAITRite walkway for three times.The 4-MM (m/s) was performed in parallel by two different operators and measured in GAITRite walkway.Each subject underwent SPPB with a score 9 indicating physical frailty. The correlation between 4-MM and instrumental measurements was tested by Pearson,while the correlation between 3 tests performed by the same tester was evaluated by intraclass correlation coefficient (ICC).The difference between means was tested by regression analysis for non parametric tests. **Results:** The sample(n=168)included 64 frail (SPPB-9)and 104 well performant (SPP-10) individuals.In all subjects,we found a significant difference of the means of the speed assessed by two different operators, (p-=0.03).A strong correlation (r=0.99, $p<0.0001$) between means of the speed assessed by 2 testers (OP1 =1.00088 m/s,OP2= 1.00752), and between 4-MM and GAITrite (1.08172 m/s rOP1-GAITRite=0.92639; rOP2-GAITRite=0.93157). We also found significant difference in the three measures of the same operator ($p<0.0001$). A low ICC between the means of three different measures was found for operator 1 (ICC=0.50) and 2(ICC=0.49). In frail subjects,the means of gait speed of operator 1(1.140 m/s)and 2 (1.143 m/s) were not significantly different but each of these measurements were significantly higher than GAITrite measure (0.97464 m/s, $p<0.0001$). **Conclusion:** In older subjects with probable physical frailty, we detected intra and inter class significant difference in the gait speed measurements performed by manual (stopwatch) approach. Minimal but statistically significant differences were detected between stopwatch and GAITRITE. GAITrite system detected a slower walking speed in older frail subjects suggesting a potential higher 'diagnostic accuracy'.

OC3- FRAILTY AND MULTIMORBIDITY: A SYSTEMATIC REVIEW AND META-ANALYSIS. Davide L Vetrano[1,2], Katie Palmer[3], Alessandra Marengoni[4], Emanuele Marzetti[2], Fabrizia Lattanzio[5], Regina Roller-Wirnsberger[6], Luz Lopez Samaniego[7], Leocadio Rodríguez-Mañas[8], Roberto Bernabei[2], Graziano Onder[2] on behalf of the Joint Action ADVANTAGE WP4 group *((1) Aging Research Center, Department of Neurobiology, Health Care Sciences and Society, Karolinska Institutet and Stockholm University, Stockholm, Sweden; (2) Department of Geriatrics, Catholic University of Rome, Italy; (3) San Camillo Hospital IRCCS, Venice, Italy; (4) Department of Clinical and Experimental Sciences, University of Brescia, Italy; (5) Scientific Direction, Italian National Research Centre on Aging, Ancona, Italy; (6) Department of Internal Medicine, Medical University of Graz, Austria; (7) Andalusian Public Foundation of Progress and Health, Regional Ministry of Health of Andalusia, Spain; (8) Geriatric Department, Hospital Universitario de Getafe, Madrid, Spain)*

Background: Multimorbidity and frailty are expression of the complexity that characterizes health in older people and these constructs have been proposed as potential models of care. However, it is not clear to which extent these conditions overlap, and the evidence on their potential causal links is scanty. **Objectives:** We systematically reviewed the literature, and provide pooled estimations of any evidence regarding a) the coexistence of frailty and multimorbidity, and b) their association in adults and older adults. **Methods:** Systematic review and meta-analysis of observational studies searching PubMed and Web of Science for relevant articles up to September 2017. We retrieved studies providing information on the association between frailty and multimorbidity in adult subjects, regardless of the study setting, study design, or definition of multimorbidity and frailty. Pooled estimates were obtained through random effect models and Mantel-Haenszel weighting. Homogeneity was assessed through the I2 statistics (significant if 50%). The risk of bias was assessed through the Newcastle-Ottawa Scale. Publication bias was assessed with the Egger's and the Begg's tests. This study was a priori registered with PROSPERO (Ref. 57890) and was patronized by the European Joint Action on frailty ADVANTAGE. **Results:** A total of 48 studies involving 78122 participants were selected and 25 were included in one or more meta-analyses. Forty-five studies were cross-sectional and 3 longitudinal, with the majority of them including community-dwelling participants (n=35). Forty-three studies presented a moderate risk of bias, and 5 a low risk. In meta-analyses, the prevalence of multimorbidity in frail individual was 72% (95% Confidence Interval [95% CI] 63% to 81%; I2=91.3%) and the prevalence of frailty among multimorbid individuals was 16% (95% CI 12% to 21%; I2=96.5%). Finally, multimorbidity was associated with frailty in pooled analyses (OR 2.27; 95% CI 1.97 to 2.62; I2 47.7%). The three longitudinal studies suggest a bidirectional causal relationship between multimorbidity and frailty. **Conclusion:** Frailty and multimorbidity are two related conditions in older adults. Most frail individuals are also multimorbid but fewer multimorbid ones present also frailty. Our findings are not conclusive regarding the causal association between the two conditions. Further longitudinal and well-designed studies may help to untangle the relationship between frailty and multimorbidity.

OC4- HEALTH CARE UTILIZATION IN NON-GERIATRIC PATIENTS WITH FRAILTY PHENOTYPE. Miriam Zylberglait Lisigurski, Carmen Cartwright, Sharmila Ravindranathan, Sameer Shaharyar, Osman Perez, Aimee Almanzar, Jasdip Grewal, Saied Alsabagh *(Internal Medicine Residency Training Program. Aventura Hospital and Medical Center, USA)*

Background: The Frailty is associated with increased risk of functional decline, mortality and health care utilization in the elderly population. Data suggests that the frailty phenotype (FP) may be present in non-geriatric individuals, increasing their risk for negative health outcomes. **Objectives:** The aim of the study is to determine the level of health care utilization in non-geriatric patients with FP. **Methods:** Design: Prospective cohort of non-geriatric patients followed for 10 months. Subjects and Setting: Sample of adults (18-65 years) visiting an Academic Primary Care Clinic (August 2016 - January 2017). Measures: We administered the FRAIL Scale, and categorized patients into two groups: robust (0 points), frailty phenotype (1-5 points). Ten months later, information regarding hospital admissions (HA), telephone encounters (TE), emergency room (ER) and primary care (PCP) visits were collected. Data Analysis: We performed descriptive statistics, comparing data between robust and FP patients. Logistic regression analysis was used to ascertain the effect of FP on health care utilization. **Results:** We evaluated 174 participants, mean age of 45+/-12 years, 96(55%) were female. FP was present in 78(45%) participants. Frequency of FP was higher in females (53% vs 35%; p=0.015), no differences in age were found. Charlson Comorbidity score (CCI) was significantly higher in the FP group (1.4+/-1.6 vs 0.9+/-1.3; p=0.024). There was an increased OR for HA 2.3 [95% confidence interval (CI) 1.1-4.9; p=0.045] and >2 TE [OR= 2.4 (95% CI 1.2-4.8; p=0.019)] in the FP group. Having at least one ER visit, had an OR=1.9 (95% CI 0.9 - 3.8; p=0.06), that did not reach statistical significance. PCP visits were not affected by FP. After adjusting for age, gender and CCI, the FP group continue presenting an increased odd for HA, TE and ER, however not reaching statistical significance. **Conclusion:** Frailty phenotype, in non-geriatric community dwelling patients is associated with increased use of the health care system. The results of our study portends that FP warrants prompt targeted interventions that we anticipate will improve healthcare outcomes and potentially reduce health care utilization..

OC5- BLOCKADE OF GDF8 AND ACTIVIN A LEAD TO INCREASES IN THIGH MUSCLE VOLUME IN HEALTHY POSTMENOPAUSAL WOMEN: A SINGLE ASCENDING DOSE STUDY. Stephen Donahue, Shazia Ali, Dinko Gonzalez Trotter, Zhizhi Qing, Joseph Yen, Evelyn Gasparino, Pretty Meier, Marcella Ruddy, Gary Herman *(Regeneron Pharmaceuticals, Inc., Tarrytown, NY, USA)*

Background: In GDF8 (myostatin) and activin A are putative negative regulators of muscle growth. REGN2477 (anti-activin A) and trevogrumab (anti-GDF8) are fully human monoclonal antibodies that specifically bind and block signaling of activin A and GDF8. Preclinical data suggest that blockade of activin A and GDF8 may have greater efficacy in increasing muscle mass than either alone and is proposed to be a possible treatment of muscle diseases. We sought to corroborate this finding in humans. **Objectives:** To assess safety, tolerability, and the impact on muscle size of anti-activin A alone, anti-GDF8 alone, and the combination in healthy postmenopausal women. **Methods:** This was a phase 1, randomized, double-blind, placebo-controlled, single ascending intravenous dose study in 48 subjects. A key objective was to assess thigh muscle volume (TMV) as measured by MRI. Treatments included placebo (n=12), trevogrumab alone (n=6), REGN2477 alone (n=6), and the combination at low

(n=6), medium (n=6), and high (n=12) doses. **Results:** Blockade of GDF8 and activin A together resulted in robust and dose-dependent increases in TMV by MRI, which was corroborated by effects on appendicular lean mass by DXA. TMV increased in the REGN2477+ trevogrumab high dose group by 7.73% as compared with 0.88% in the placebo group (nominal p<0.001) at week 8. Trevogrumab alone also significantly increased TMV. Blockade of both GDF8 and activin A significantly decreased total fat mass (high dose group) compared with placebo. All treatments were generally well tolerated; treatment-emergent adverse events (TEAEs) were mild to moderate in severity except one severe TEAE of radius fracture reported by a placebo subject. There were no serious adverse events, no deaths, and no discontinuations due to TEAEs. **Conclusion:** This study shows for the first time that the selective blockade of GDF8 and activin A, in combination, can increase muscle size in humans and corroborates the role of these proteins as mediators of muscle homeostasis. The results also suggest the promise of REGN2477 and trevogrumab combination as potential therapeutics for the treatment of serious muscle diseases.

OC6- PSOAS MUSCLE AREA IN HEALTHY ADULTS: EFFECT OF NORMAL AGING AND DERIVATION OF REFERENCE VALUES. Samuel Mamane[1], Christos Galatas[2], Wayne Lok[3], Mina Girgis[2], Chams Cherid[3], Louis Mullie[1], Amanda Trnkus[3], Antoinette Colacone[4], Xiaoqing Xue[4], Marc Afilalo[4], Jonathan Afilalo[2,3] (*(1) Division of General Internal Medicine, Jewish General Hospital, McGill University, Montreal, Canada; (2) Division of Cardiology, Jewish General Hospital, McGill University, Montreal, Canada; (3) Division of Epidemiology, Jewish General Hospital, Montreal, Canada; (4) Department of Emergency Medicine, Jewish General Hospital, Montreal, Canada)*

Background: Segmentation of computed tomography (CT) images is increasingly used to estimate skeletal muscle mass. A growing body of evidence has shown the prognostic value of cross-sectional psoas muscle area (PMA) as a readily available biomarker for sarcopenia and frailty in patients with cardiovascular, oncological, and surgical conditions. However, there has yet to be a study measuring PMA in healthy adults, such that normal values and age effects remain unclear. **Objectives:** To derive sex-specific reference values for PMA in a healthy North American population. **Methods:** Consecutive CT scans of the abdominal region acquired at a single emergency department between 1/2014 and 1/2017 were retrospectively identified. Electronic health records were queried to exclude patients with significant acute or chronic medical conditions diagnosed before or after the index CT scan, and to include only those that had a presenting complaint of benign abdominal discomfort. Using the CoreSlicer.com software (version 2.0, Montreal), PMA was measured using the density threshold brush tool from the axial CT image at the level of the top of the L4 vertebrae. All measurements were repeated by 2 independent observers and the mean value was retained. Bland-Altman analysis was used to assess inter-observer reliability. A parametric approach was used to define the 2.5th percentile cutoff in males and females. **Results:** The cohort consisted of 390 healthy adults (162 males, 228 females). In age group 20-39 (N=133), mean PMA was 32.2 ± 6.1 cm2 in males and 19.6 ± 4.0 cm2 in females. In age group 40-59 (N=211), mean PMA was 29.9 ± 5.3 cm2 in males and 17.7 ± 3.7 cm2 in females. In age group 60-79 (N=46), mean PMA was 22.6 ± 3.3 cm2 in males and 15.0 ± 3.5 cm2 in females. The 2.5th percentile cutoff based on the young adult group was 20.3 cm2 in males and 11.8 cm2 in females. Inter-observer measurement mean difference was 0.61 cm2 with 95% limits of agreement of -1.43 to 2.65 cm2. **Conclusion:** PMA is smaller in females and decreases with age, and this is the first study to define sex-specific PMA reference values in a North American population.

OC8- EFFECT OF DELTA-TOCOTRIENOLS AND GREEN TEA POLYPHENOLS ON GLUCOSE HOMEOSTASIS AND SKELETAL MUSCLE IN OBESE MALE MICE WITH INSULIN RESISTANCE. C. Maxwell[1], M. Dietrich[1], M. Karlekar[2], R. Miller[2] *((1) Vanderbilt University, Nashville, TN, USA; (2) Vanderbilt University Medical Center, Nashville, TN, USA)*

Background: Geriatric trauma exemplifies the convergence of aging, frailty and injury with a high prevalence of cognitive impairment (> 40%) and physical frailty (> 50%) among patients admitted to acute care. Since 2013, initiatives at our Level I trauma center have included 1) an 18-month longitudinal examination of the influence of pre-injury frailty on patient outcomes (mortality, functional decline, readmissions to acute care); 2) use of bedside frailty screening as a trigger for early geriatric palliative care; and 3) exploration of older adults and family caregivers perceptions about frailty and the influence on patient outcomes. **Methods:** 1) Prospective longitudinal cohort study (October 2013-March 2015). 395 injured older adults were admitted over a 6-month period and we enrolled and followed 188 patients for one year. 2) Prospective quality improvement project (March-May 2015). Bedside nurses were trained to implement a validated frailty screening process on older adults admitted to our trauma unit. The process included interdisciplinary discussions and referrals for early geriatric palliative care consultations. 3) Qualitative content analysis (June-December 2016). Focus groups (2) were held at a senior living community; and individual interviews were conducted with hospitalized injured older adults (n=25) and family caregivers (n=15). Respondents were shown prognostication data on frailty and outcomes using simple pictographs. Semi-structured interviews were conducted by a trained research assistant. **Results:** 1) 34 patients (18%) died by 6 months, and 47 (25%) by 1 year. Overall, median physical frailty scores did not return to baseline in the majority of survivors at 6-months and 1-year. Multivariate regression analysis revealed that pre-injury cognitive impairment, and pre-injury physical frailty are independently associated with functional status at 6-months and 1-year. Multivariate logistic regression analysis revealed that age (OR=1.09, CI 1.04-1.14), injury severity (OR=1.07, CI 1.02-1.12), and pre-injury physical frailty (OR=1.28, CI 1.14-1.47) are independently associated with overall mortality. 2) 131 patients (age 65 and older) were admitted to the trauma unit and 64 (49%) were screened for pre-injury frailty. Forty-four of 131 (34%) patients received palliative care consultations over the project period, an increase of 150% from four consecutive prior years (2011-2014). 3) Themes emerged among five coded categories: 1) reactions to information, 2) approaching the topic/receptiveness, 3) presence of others, 4) considerations related to a fall, and 5) suggestions about information delivery. Differences among older adults were observed, based on pre-injury frailty status. **Conclusion:** Pre-injury physical frailty is the predominant predictor of poor outcomes among geriatric trauma patients. Trauma teams can implement a screening process for frailty and cognitive impairment into their daily workflow. Positive screens effectively trigger an increase in earlier referrals to palliative care. Communication with patients and families about frailty, injury, and outcomes can be enhanced with simple prognostication aids.

OC9- LEVERAGING NON-PHYSIOLOGICAL ASPECTS OF NMES FOR BENEFICIAL NEUROMUSCULAR ADAPTATIONS IN OLDER ADULTS. David W Russ[1], Eric Leach[1], Brian C Clark[2] *((1) Ohio University Division of Physical Therapy, Athens, OH, US; (2) Ohio Musculoskeletal and Neurological Institute (OMNI) at Ohio University, Athens, OH, USA)*

Backgrounds: Age-related weakness increases risks of disability and mortality 4 and 2-fold, respectively. Accumulating data suggest that dynamic muscle performance parameters (e.g., power, rate of force development) may be more important to maintaining independent function and mobility in older adults than force generation. However no specific type of exercise has been found to consistently improve power more than any other. This may be due to the fact that all volitional exercise protocol involve essentially the same motor unit activation processes. Neuromuscular Electrical Stimulation (NMES) activates motor units in a non-physiological manner. **Objectives:** Our goal was to develop a novel NMES protocol, which we have TRANSIT (Therapeutic Rapid Activation of the Neuromuscular System for Interval Training), and test the potential for it to enhance neuromuscular function in older and younger adults. **Methods:** In a quasi-experimental, repeated measures design (each subject serving as his or her own control), young (n = 9) and older (n= 4) adults received the TRANSIT protocol (3x/wk) to the non-dominant knee extensor muscles. Isometric force, dynamic muscle power, muscle cross-sectional area (CSA), voluntary activation (VA) and electrically-elicited contractile properties were measured pre- and post-training. **Results:** Though muscle quality (isometric force/CSA) did not change for young or older subjects, responses of old and young adults to TRANSIT were quite different in other regards. Younger adults showed small, but significant (3%, p = 0.04) increases in CSA, that largely mirrored changes in isometric force. Older adults showed no significant increase in either CSA or isometric strength. However, improvements in dynamic, isotonic muscle performance of older adults (power, angular velocity) exceeded isometric gains substantially (+10-15%), despite the fact that TRANSIT involved an isometric training paradigm. In addition, changes in contractile responses to stimulation revealed increases in rates of force development (+15-19%) that were not due to improvements in central drive or motivation. As neither group exhibited marked reductions in VA at baseline, TRANSIT did not increase this parameter. However, the one older subject that did show a VA deficit (89%) at baseline did have increased VA post-training (97%). **Conclusion:** Training using the TRANSIT protocol markedly improved dynamic muscle performance in older adults, running counter to the idea of specificity of training. This is unlikely to be the result of improved central drive, as only one participant exhibited any central activation impairment prior to training. Combined with the improved contractile properties of the trained muscles, these data suggest that this method of training with NMES may involve mechanisms not typically responsive to volitional exercise and be of particular benefit to older adults. TRANSIT was well-tolerated by all participants and the method of application involves low joint loads and systemic cardiovascular demand, such that TRANSIT could be effectively used in the presence of common, age-associated comorbidities (e.g., osteoarthritis, cardiovascular disease).

OC10- SARC-F: DEFINING A VALIDATED CUTOFF FOR PRE-SARCOPENIA FOR RISK ASSESSMENT AMONG COMMUNITY DWELLING OLDER PERSONS. WS Lim[1,2], L Tay[3], A Yeo[2], S Yew[2], N Hafizah[2,4], YY Ding[1,2] *((1) Department of Geriatric Medicine. Tan Tock Seng Hospital. Singapore; (2) Institute of Geriatrics and Active Ageing. Tan Tock Seng Hospital. Singapore; (3) Department of General Medicine (Geriatric Medicine), Sengkang General Hospital. Singapore; (4) Department of Continuing and Community Care. Tan Tock Seng Hospital. Singapore)*

Background: The SARC-F was developed as a rapid screening tool for sarcopenia. A score of 4 or greater is predictive of sarcopenia and poor outcomes. The at-risk state of pre-sarcopenia is characterised by low muscle mass without impact on muscle strength or physical performance. Unlike analogous frailty scales where the cutoff for pre-frailty is established, the SARCF does not have a corresponding cutoff for pre-sarcopenia. **Objectives:** To compare the diagnostic performance, concurrent validity and predictive validity of two cutoffs (1 vs 2) for pre-sarcopenia among older adults without functional or cognitive impairment. **Methods:** Two-hundred community-dwelling older adults (mean age=67.9years) were assessed for frailty using modified Fried criteria; Short Physical Performance Battery (SPPB); Frenchay Activity Index (FAI); activities of daily living (ADL); Mini-Nutrition Assessment (MNA); and appendicular muscle mass using dual-energy X-ray (DXA). Outcomes at 2-years include incident sarcopenia; SPPB<10; FAI<30; incident ADL decline; and incident falls. We performed ROC analysis for sarcopenia diagnosis at baseline for diagnostic performance; 1-way ANOVA with post-hoc comparison for concurrent validity; and logistic regression of 2-year outcomes adjusted for age, gender and body mass index for predictive validity. **Results:** For diagnostic performance, using cutoff 1 identified 54 additional pre-sarcopenia subjects (sensitivity 36.7%, specificity 64.7%) compared with cutoff 2 (sensitivity 11%, specificity 92.3%). The ratios of pre-sarcopenia/sarcopenia cases were 17 and 4 respectively. When stratified into non-sarcopenic, pre-sarcopenic and sarcopenic subgroups, both cutoffs had comparable discriminant ability for frailty and appendicular mass, but cutoff 2 had higher F-values for physical performance (balance, chair-stand, and SPPB total score) and MNA. For predictive validity of 2-year outcomes, both cutoff 2 (OR=9.78,95%CI: 2.96-32.34,P<0.01) and 1 (OR=5.86,95%CI:2.02-17.01,P<0.01) predicted SPPB <10, and showed a trend for FAI<30 (p=0.080 and 0.066 respectively). Both did not predict incident sarcopenia or incident ADL decline. Only cutoff 2 showed a trend for 2-year incident falls (OR=4.56,95%CI:0.96-21.81, P=0.056). **Conclusion:** This is the first study to demonstrate proof-of-concept evidence about the validity of cutoffs for pre-sarcopenia. Using cutoff 2 provides a high specificity case-finding strategy that does not over-detect pre-sarcopenia relative to sarcopenia, and has better discriminatory ability for physical performance and malnutrition. The potential of SARC-F identified pre-sarcopenia as a separate therapeutic entity for early intervention requires further study

OC11- CLINICAL MUSCLE WEAKNESS IS ASSOCIATED WITH MORTALITY IN A NATIONALLY REPRESENTATIVE SAMPLE OF OLDER ADULTS: THE HEALTH AND RETIREMENT STUDY. Kate Duchowny[1], Mark Peterson[2], Philippa Clarke[1,3] *((1) Department of Epidemiology, University of Michigan School of Public Health, Ann Arbor, MI, USA; (2) Department of Physical Medicine and Rehabilitation, University of Michigan, Ann Arbor, MI, USA; (3) Institute for Social Research, University of Michigan, Ann Arbor, M)I, USA*

Backgrounds: Muscle weakness, as measured by handgrip strength, is associated with cardiovascular and all cause-mortality; however, there are wide inconsistences in the magnitude of these effects due to divergent definitions used to define muscle weakness across studies. **Objectives:** The objective of this study was to examine the relationship between previously defined sex/race-specific cutpoints of clinical muscle weakness and early mortality. **Methods:** Data comes from the 2006-2014 Health and Retirement Study. Time-varying clinical muscle weakness, as defined by handgrip strength cutpoints, was the primary exposure. Time to death, ascertained from the National Death Index, was the outcome of interest. The association between time-varying clinical muscle weakness and early mortality across an 8-year observation period was determined using Kaplan-Meir methods and extended Cox regression. **Results:** Out of the 8,495 individuals in the study, 1,799 deaths (21%) occurred during the observation period. Median follow-up time was 8.3 years (SD ±1.9 years). Weak individuals had a steeper decline in their survival trajectory, compared to non-weak individuals (Log-Rank test, p<.001). After adjusting for sociodemographic factors and time-varying smoking history, weak individuals were over 50% more likely to die earlier than non-weak individuals (HR=1.52, 95% CI= 1.15, 1.47). **Conclusion:** This is the first study to use muscle weakness cut-points derived in a nationally-representative sample to identify those individuals who may be at greatest risk for premature mortality. Results underscore the importance of muscle weakness, as defined by handgrip strength, as a key risk factor for premature mortality in older Americans.

OC12- COMBINED EFFECTS OF BIO101 ON ANABOLISM AND MITOCHONDRIAL FUNCTION IN SKELETAL MUSCLE CELLS. Maria Serova[1], Sissi On[1], Blaise Didry-Barca[1], Stanislas Veillet[1], René Lafont[2], Pierre Dilda[1] *((1) Biophytis, UPMC, BC9, Paris, France ; (2) Sorbonne Universités, UPMC Univ Paris 06, Paris-Seine Biology Institute (BIOSIPE), CNRS, Paris, France)*

Background: Skeletal muscle progressive loss of function and atrophy are physiological consequences of aging subsequently leading to a decrease in mobility and poor quality of life. The drug candidate BIO101 previously demonstrated its potential for improving muscle quality and function in different in vitro and in vivo models. BIO101 is the API of Sarconeos currently tested in clinical IIb trial in patients with sarcopenia. **Objectives:** The aim of this study was to characterize the impact of BIO101 on cellular energy metabolism and oxidative stress. **Methods:** Mouse C2C12 myoblasts were induced to differentiate and myotube diameters were measured under fluorescent microscopy. The activation of various signalling pathways was assessed by western blot. Relative levels of mRNA expression were evaluated by qRT-PCR. Intracellular ROS were assessed using the DCFDA dye by flow cytometry. Oxygen consumption was measured using a Seahorse XF Analyzer. Twenty-two-month-old C57BL10 mice were subjected to either vehicle or BIO101 50mg/kg*day for 14 weeks. **Results:** BIO101 treatment induced a significant increase of myofibres diameter (+24%, p<0.001) consistently with a rapid and significant activation of AKT/mTOR and MAPK signalling pathways involved in muscle anabolism and with a significant decrease in myostatin gene expression (-45%; p<0.01). In addition to these anabolic properties, BIO101 stimulated mitochondrial function, specially increasing mitochondrial spare respiratory capacity (+23%, p<0.05). Under glucose starvation and in the presence of fatty acids, BIO101 stimulated basal respiration (+37%, p<0.001) suggesting an increased flexibility in energy metabolism. Furthermore, BIO101 treatment lowered reactive oxygen species levels in cells subjected to an oxidative stress in accordance with an AMPK activation, a key player in mitochondrial biogenesis and antioxidant systems, observed both in vitro and in vivo. **Conclusion:** This study demonstrates that the overall beneficial properties of BIO101 on muscle function rely on both anabolic and mitochondrial effects. Increases in mitochondrial respiratory spare capacity, in energy metabolism flexibility and in antioxidant capacity in response to BIO101 exposure are believed to be responsible for more energy production. These new results are key elements to better understand the effects of BIO101 in improving running ability of old mammals and justify the clinical development of Sarconeos in patients with sarcopenia.

OC13- WEIGHT CHANGE AND RISK OF FNIH SARCOPENIA PROJECT LOW LEAN MASS. John A. Batsis[1,2,3], Rebecca S. Crow, Curtis Petersen[3], Courtney J. Stevens[1], Todd A. Mackenzie[1,2,3], Stephen J. Bartels[1,2,3] *((1) Geisel School of Medicine at Dartmouth, Hanover, New Hampshire, United States; (2) Department of Medicine, Dartmouth Hitchcock Medical Center, Lebanon, New Hampshire, United States; (3) The Dartmouth Institute for Health Policy, Lebanon, New Hampshire, United States)*

Background: The Foundation for the NIH Sarcopenia Project identified cutpoints of low lean mass (LLM) in older adults at risk for physical impairment. Understanding whether weight change over the lifespan impacts the development of LLM is clinically important for identifying individuals at risk for disability. **Objectives:** Ascertain the relationship between self-report weight change and LLM in a United States older adult population. **Methods:** We identified 4,984 subjects 60 years with body composition measures from the National Health and Nutrition Examination Surveys 1999-2004, a cross-sectional survey of non-institutionalized persons in the United States. LLM was defined using appendicular lean mass (ALM): males<19.75kg, females<15.02kg. Self-reported weight was assessed at the time of the survey, at one and 10 years earlier, and at age 25. Weight changes between baseline and each timepoint were categorized as greater/less than 5% or no change (between -5% and +5%; referent). Logistic regression assessed the primary predictor of weight change (gain, loss, no change) on the outcome of LLM, after adjusting for age, sex, race, education, smoking, diabetes, arthritis, coronary artery disease, and cancer. **Results:** Of 4,984 participants (56.5% female), mean age and BMI were 71.1years and 28.2kg/m2. Mean ALM was 19.7kg. Prevalence of LLM was 29.9%. We observed 8.8 and 20.3% participants with LLM gaining and losing 5% weight, respectively in the past year. In the past 10 years, weight gain and loss of 5% was observed in 27.2 and 32.3% of LLM participants. Compared to age 25, 59.9 and 21.1% of LLM participants gained and lost 5% of their weight, respectively. Weight gain over the past year was associated with a lower risk of having LLM (OR 0.57 [0.40,0.82]) compared to individuals losing 5% weight (1.06 [0.85,1.31]. Weight loss (5%) over 10-years had a higher risk of having LLM (OR 1.59 [1.23, 2.07]) while weight gain (5%) had a lower risk (OR 0.46 [0.37,0.56]). Results were robust compared to weight at 25 years (weight gain OR 0.27 [0.20,0.36]; weight loss OR 1.61 [1.13,2.30]). **Conclusion:** Self-reported weight gain suggests a reduced risk of LLM.Future studies

using objective measures are needed to verify these findings and ascertain its relationship with physical function.

OC14- INTER- AND INTRA-READER PRECISION ERRORS OF VOLUME OF MUSCLE AND IMAT OF THE THIGH IN T1-WEIGHTED MAGNETIC RESONANCE IMAGING. Klaus Engelke[1], Dinko González Trotter[2], Ken Gaither[3], Stephen Donahue[2], Shazia Ali[2], Marcella Ruddy[2], Joseph Yen[2], Gary Herman[2], Joyce Harp[2], Thomas Fuerst[3] *((1) Institute of Medical Physics, University of Erlangen & Bioclinica, Inc, Hamburg, Germany; (2) Regeneron Pharmaceuticals, Inc., Tarrytown, NY, USA; (3) Bioclinica, Inc, Portland, OR, USA)*

Background: Quantification of muscle atrophy and adipose tissue (AT) by magnetic resonance imaging (MRI) techniques is a topic of great interest. Clinical applications and active research cover muscle diseases, physical activity, obesity and sarcopenia, all of which rely on reliable and objective measurements. **Objectives:** To determine intra- and inter-operator precision of volume of total thigh muscle, subcutaneous adipose tissue (SAT), fascia, muscle and inter-muscular AT (IMAT, defined as sum of intra and perimuscular AT) in standard T1-weighted MRI sequences. **Methods:** Baseline and one week follow-up images of 48 subjects of a study of safety, tolerability, and pharmacokinetics of Regn2477 alone and in combination with Regn1033 in healthy postmeno-pausal women (Clinical trials.gov: NCT02943239) were used in this investigation. T1 weighted images of both upper legs were obtained (Axial 2D T1-w FSE multi-slice sequence, slice thick-ness 5 mm, slice gap 5 mm). Five slices centered mid-thigh were semi-automatically segmented using slice-based grey level tracing algorithms. The total thigh, the fascia, the entirety of all muscles within the fascia (including intramuscular AT) and IMAT were segmented. Segmentation results were corrected by a trained operator, if necessary. Results of the analyzed five slices were summed for total volume. Precision errors were calculated as root mean square % coefficients of variation (rmsCV%). In-tra-operator precision was calculated using baseline and one week FU visits independently for two operators. Inter-operator precision was assessed independently for both visits. **Results:** Results are shown in the table. Results were pooled for right-left thighs and BL and FU visits, as no differences were observed. Except for IMAT, which represents a much smaller volume, precision errors were below 2-3%, which is an excellent result for a semiautomatic segmentation. Inter-operator IMAT precision errors were about twice as high as intra-operator errors. Mean ± SD Intra-operator 1 Intra-operator 2 Inter-operator mm2/slice rmsCV% rmsCV% rmsCV% Total thigh 182±19 1.63 1.64 0.50 SAT 73±16 2.66 2.70 2.51 Fascia 109±20 1.36 1.48 1.58 Muscle 86±16 2.10 2.21 1.85; IMAT 23±22 5.12 5.78 10.48. **Conclusion:** In standard T1-weighted images precision errors for basic soft tissue parameters are small. However, a separate assessment of intramuscular AT and its differentiation form perimuscular AT is difficult. Here more advanced Dixon sequences are recommended.

OC15- MUSCULAR, VISUOSPATIAL PROCESSING, AND NEUROMOTOR FACTORS AS PREDICTORS OF PHYSICAL FUNCTION IN OLDER ADULTS. Nathan P. Wages[1,2], Leatha A. Clark[1,2,4], Andrew M. Bryant[1,5], Julie A. Suhr[1,5], Todd M. Manini[6], Brian C. Clark[1,2,3] *((1) Ohio Musculoskeletal and Neurological Institute (OMNI), Ohio University, Athens, OH, USA; (2) Department of Biomedical Sciences, Ohio University, Athens, OH, USA; (3) Department of Geriatric Medicine, Ohio University, Athens, OH, USA; (4) Department of Family Medicine, Ohio University, Athens, OH, USA; (5) Department of Psychology, Ohio University, Athens, OH, USA; (6) Department of Aging and Geriatric Research, University of Florida, Gainesville, FL, USA)*

Background: Forty-two percent of the older adult population (i.e., > 65 yrs) report having one or more physical limitations performing essential daily tasks considered necessary for maintaining functional independence in the community. Despite much research associated with age-related reductions in physical independence, the causes of age-related losses in physical function remain unclear. The two most postulated contributors for impaired physical function in the elderly are loss of muscle mass and strength, but there are numerous other factors (e.g., muscle quality, force steadiness, visuospatial processing speed, etc.) that likely contribute as well. **Objectives:** To determine the relative contribution of skeletal musculature, visuospatial processing, and neuromotor factors in explaining the between-subject variance during different physical function tasks in older adults. **Methods:** Fifty-four seniors (77.9±5.9 yrs; range: 68-92 yrs) participated in this study. Multiple regression analyses, using nine predictor variables that represent three domains (skeletal muscle, visuospatial processing, and neuromotor function), were performed for six physical function tasks (Table 1). To minimize the effect of collinearity, only predictor variables that had r 0.60 were included in the models. To evaluate the independent contribution of each predictor, the semi-partial r (sp-r) values were calculated. The sp-r value is interpreted as the variance in the respective physical function task (the dependent variable) uniquely attributable to the given predictor variable (by factoring out shared variance contributions with other predictors). **Results:** Overall, the predictor variables explained between 27-60% of the variance in the performance of the respective physical tasks. Muscle strength and the rate of voluntary force development exhibited the highest sp-r values when considered across all physical function tasks. Refer to Table 1 for complete results. **Conclusion:** These findings suggest that measures of neuromotor function are uniquely related to physical function. They also suggest that visuospatial processing speed is uniquely related to gait and physical function tests requiring a high degree of agility/movement initiation. Interestingly, lean tissue mass was only a strong predictor of stair climb power.

OC16- NEW VIEWS ON SARCOPENIA AND DYNAPENIA - DO WE KNOW THE COHERENCE? A Heber[1,2], K Stöver[3], W. Bloch[1], S. Eichberg[3], K Brixius[1], P Noirez[2] *((1) Institute of Cardiology & Sports Medicine, Department of Molecular & Cellular Sport Medicine, German Sport University Cologne, Germany; (2) Institute of biomedical and epidemiological research in sport, EA7329, Université Paris Descartes, France; (3) Institute of Movement & Sport Gerontology, German Sport University Cologne, Germany)*

Background: It is considered that changes in muscle mass are directly and fully responsible for changes in strength. However, muscle strength is not solely dependent upon muscle size as the decline in muscle strength is much more rapid than the concurrent loss of muscle mass. The link in between loss of skeletal muscle mass (sarcopenia) and muscle strength (dynapenia) is still not fully

understood. **Objectives:** Hypothesizing that sarcopenia and dynapenia are associated with metabolic changes and health status in elderly, resistance training was used to stimulate the muscle tissue. **Methods:** 65-80 year old, healthy men (n=74) were divided in: group I (active), group II (non-active, obese), group III (non-active, sarcopenic obese), group IV (non-active, sarcopenic obese, protein intake). Sarcopenic obesity was measured due to the cut-off points of EWGSOP. Resistance training of the major muscles groups twice a week with 85% 1RM, 3 sets, 8-12 repetitions was performed either 12 (group I) or 16 weeks (group II-IV). Protein supplementation was taken twice per week directly after training (30g Whey protein) and every night (30g Casein) in 300ml 1,5% low fat milk. Handgrip strength (HGS) was measured with a hand dynamometer, leg strength by leg press, skeletal muscle mass (SMI) by bioimpedance analysis and dynapenia by HGS/body weight. **Results:** A significant increase in leg strength after training is indicated in all groups. The SMI in group I decreases significantly after training. Shift in sarcopenic classifications towards 'class I' or 'no sarcopenia' is significant. No changes in SMI or handgrip strength have been observed neither in group II, III nor IV. The level of dynapenia remains unchanged after training. **Conclusion:** The significant increase in leg strength in all groups supports the documented effect of resistance training in elderly. The increase of strength while observing a skeletal muscle mass decline or no mass change validated the finding that age related muscle strength is weakly associated with the loss of muscle mass. However, resistant training lead to a significant decrease in muscle mass of healthy elderly.

OC17- 25-HYDROXYVITAMIN D AND SARCOPENIA IN OLDER ADULTS: THE HEALTH ABC STUDY.

Denise K. Houston[1], Janet A. Tooze[1], Marjolein Visser[2], Frances A. Tylavsky[3], Anne B. Newman[4], Tamara B. Harris[5], Stephen B. Kritchevsky[1] *((1) Wake Forest School of Medicine, Winston Salem, NC, USA; (2) Vrije Universiteit, Amsterdam, The Netherlands; (3) University of Tennessee Health Science Center, Memphis, TN, USA; (4) University of Pittsburgh, Pittsburgh, PA, USA; (5) National Institute on Aging, Bethesda, MD, USA)*

Background: 25-hydroxyvitamin D (25(OH)D) has been shown to play a role in muscle strength and physical function; however, the effects of 25(OH)D on muscle mass are less clear. **Objectives:** We examined the association between 25(OH)D and prevalent and incident sarcopenia in community-dwelling older adults in the Health ABC study. **Methods:** Health ABC participants were initially well-functioning, community-dwelling black and white men and women aged 70-79 years from Pittsburgh, PA, and Memphis, TN, USA (n=2,696; mean (SD) age, 73.6 (2.8) years; 51% female; 39% black). Serum 25(OH)D was categorized as <20 ng/mL, 20-<30 ng/mL, and 30 ng/mL. Body composition was assessed by DXA. Usual gait speed was assessed over a 6m walk. Sarcopenia was defined as low appendicular lean mass divided by height squared (7.23 in men, 5.67 in women) and slow gait speed (<1.0 m/sec) at baseline, 2- and 4-year follow-up using the International Working Group on Sarcopenia definition. The association between 25(OH)D categories and prevalent sarcopenia was examined using logistic regression; incident sarcopenia over 4 years of follow-up was examined using Cox regression. All models were adjusted for demographics, behavioral characteristics, BMI, chronic conditions, and season. **Results:** The mean (SD) 25(OH)D was 25.7 (10.3) ng/mL, with 33%, 35%, and 32% of participants having 25(OH)D <20, 20-<30, and 30 ng/mL, respectively. At baseline, 99 (3.7%) participants had prevalent sarcopenia. Compared to participants with 25(OH)D 30 ng/mL, participants with 25(OH)D <20 ng/mL, but not 20-<30 ng/mL, had greater odds of prevalent sarcopenia (OR (95%CI): 1.94 (1.05-3.56) and 1.48 (0.86-2.55), respectively). After excluding participants with prevalent sarcopenia and those lacking follow-up (n=351), 247 (11.0%) participants developed sarcopenia over 4 years of follow-up. However, there was no association between 25(OH)D and incident sarcopenia over 4 years of follow-up (HR (95% CI): 1.01 (0.71-1.45) and 0.77 (0.57-1.05) in participants with 25(OH)D <20 and 20-<30 ng/mL, respectively, compared to participants with 25(OH)D 30 ng/mL). **Conclusion:** Low 25(OH)D was associated with greater prevalence of sarcopenia at baseline but not incidence of sarcopenia over 4 years of follow-up among initially well-functioning, community-dwelling older adults. Further research is needed to determine the role of 25(OH)D on sarcopenia.

OC18- HIGH ENDOGENOUS BCAA LEVELS ARE ASSOCIATED WITH MUSCLE STRENGTH AND SIGNATURES OF MYOSTEATOSIS: FRIENDS OR FOES?

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Background: Branched chained amino acid (BCAA) supplementation seems to exert beneficial effects on physical functionality. However, endogenous BCAA metabolism in obesity and its relationship with ectopic lipid deposition in the skeletal muscle (namely, myosteatosis) and muscle strength has been poorly investigated to date. **Objectives:** The aim of our study was to investigate the relationship between endogenous BCAA levels and muscle strength, muscle quality and signatures of myosteatosis in adult subjects with obesity. **Methods:** Participants were enrolled among patients admitted to the High Specialization Center for the Care of Obesity, Sapienza University, Rome, Italy. Inclusion criteria were age between 18 and 65 years, and BMI 30kg/m2. Body composition (body fat, total lean body mass- LBM, and appendicular lean mass- ALM) was assessed through DXA and magnetic resonance imaging with spectroscopy was used to evaluate the signatures of sarcopenia and myosteatosis (thigh muscle cross sectional area- CSA, intramyocellular lipid content- IMCL, and intramuscolar adipose tissue- IMAT). Muscle strength was assessed through the handgrip strength (HGST) test. HGST was normalized to LBM to obtain an indicator of muscle quality. FFA levels were measured. The HOMA-IR was calculated as an index of insulin resistance. In addition, study participants were divided into two groups based on the median values of ALM (below the median: low muscularity group vs. above the median: high muscolarity group). **Results:** A total of 80 participants were included (women, n= 65, men, n=15), age: 48.3 ± 12.6 years, BMI: 37.69 ± 4.94 kg/m^2. Participants in the low muscularity group showed significantly lower plasma BCAA levels than their high muscolarity counterparts after adjustment for age and sex ($p<0.05$). A significant positive correlation emerged between plasma BCAA levels and HGST ($r=0.26$, $p=0.036$), muscle quality ($r=0.32$, $p=0.013$); surprisingly, BCAA levels were also correlated with IMCL ($r=0.30$, $p=0.036$), and with a segmental index of sarcopenic obesity: the IMAT/ thigh muscle CSA ratio ($r=0.26$, $p=0.04$). Multiple regression analysis confirmed those associations and revealed a negative association between BCAA concentrationas and FFA levels after adjustment for HOMA-IR and body fat (all p values < 0.05). **Conclusion:** In adult subjects with obesity endogenous BCAA levels exhibited a positive association with muscle strength but as well as with some phenotypic aspects of myosteatosis. The discrepant role potentially played by BCAAs in muscle strength generation and lipid

metabolism in skeletal muscle needs to be further elucidated by future research.

OC23- SOCIOECONOMIC GRADIENTS IN FRAILTY, DISABILITY, AND DEATH PROCESS: RESULTS FROM THE JAPAN GERONTOLOGICAL EVALUATION STUDY. Takaaki Ikeda[1,2], Jun Aida[2], Toru Tsuboya[2], Yusuke Matsuyama[3,4], Shihoko Koyama[2,5], Kemmyo Sugiyama, Katsunori Kondo[6,7], Ken Osaka[2] *((1) Department of Rehabilitation, Sendai Seiyo Gakuin College, Sendai, Japan; (2) Department of International and Community Oral Health, Tohoku University Graduate School of Dentistry, Sendai, Japan; (3) Department of Global Health Promotion, Tokyo Medical and Dental University, Tokyo, Japan; (4) Research Fellow of Japan Society for the Promotion of Science, Tokyo, Japan; (5) Tohoku Medical Megabank Organization, Tohoku University, Sendai, Japan; (6) Center for Preventive Medical Sciences, Chiba University, Chiba, Japan; (7) Center for Gerontology and Social Science, National Center for Geriatrics and Gerontology, Aichi, Japan)*

Background: A few studies examined the impact of socioeconomic status (SES) on frailty/disability process and the results were inconsistent. **Objectives:** This study aimed to determine the impact of SES on changes in (pre-)frailty, disability, and all-cause mortality. **Design:** Prospective cohort study. **Setting:** Twenty-Three Japanese municipalities between 2010 and 2013. **Participants:** Functionally independent community-dwelling elderlies aged 65 (n = 65,952). **Measurements:** The baseline survey was conducted between 2010 and 2012, and self-reported questionnaires were mailed to 141,452 community-dwelling elderlies (response rate 65.2%). The follow-up survey was conducted in 2013 (follow-up rate 81.7%). Discrete health stages were classified into five groups; robustness, pre-frailty, frailty, disability, and death. A frailty index was used to detect frailty status and higher scores indicated higher severity of frailty (robustness, 0-3 points, pre-frailty, 4-7 points; and frailty, 8-25 points, respectively). The onset of functional disability was defined as disability. We conducted three multinomial logistic regression models stratified by initial disability status (robustness, pre-frailty, and frailty). Educational attainment and equalized household income were separately added to the models, adjusting for covariates, including age and sex. **Results:** The prevalence of pre-frailty and frailty were 34.0% and 24.2% at the baseline, respectively. Participants with the highest educational level were less likely to experience changes in pre-frailty, frailty, and disability from robustness (to pre-frailty, the odds ratio (OR), 0.70, 95% confidence interval (CI), 0.64-0.77; to frailty, OR, 0.58, 95 % CI, 0.47-0.71; and to disability, OR, 0.77, 95% CI, 0.64-0.93, respectively). Meanwhile, participants with the highest income level were less likely to experience whole adverse health status switching from robustness (to pre-frailty, OR, 0.62, 95% CI, 0.54-0.70; to frailty, OR, 0.36, 95% CI, 0.25-0.52; to disability, OR, 0.63, 95% CI, 0.44-0.89; and to death, OR, 0.57, 95% CI, 0.40-0.82, respectively). Further, they were less likely to experience change in frailty and more likely to recover to robustness from pre-frailty (to frailty, OR, 0.83, 95% CI, 0.67-1.02, and to robustness, OR, 1.23, 95% CI, 1.05-1.43, respectively). Additionally, they were more likely to recover to robustness from frailty (OR, 1.35, 95% CI, 0.96-1.90). **Conclusion:** Socioeconomic gradients were observed on health status switching among older individuals in Japan.

OC24- INTERLEUKIN-6 AND PERCEIVED FATIGABILITY AMONG ADULTS IN MID-TO-LATE LIFE. Amal A. Wanigatunga[1,2], Ravi Varadhan[2,3], Eleanor M. Simonsick[4], Stephanie Studenski[4], Luigi Ferrucci[4], Jennifer A. Schrack[1,2] *((1) Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA; (2) Center on Aging and Health, Johns Hopkins University and Medical Institutions, Baltimore, Maryland, USA; (3) Department of Biostatistics, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA; (4) Intramural Research Program, National Institute on Aging, Baltimore, Maryland, USA)*

Backgrounds: Chronically elevated interleukin-6 (IL-6) levels contribute to functional decline via multiple pathways that often lead to frailty. Lesser known is the relationship between IL-6 and activity-related fatigue (fatigability), another frailty component. **Objectives:** To characterize the association of IL-6 and perceived fatigability at baseline and longitudinally. **Methods:** A total of 985 men and women from the Baltimore Longitudinal Study of Aging (BLSA; mean age of 70 +/- 10 years) were evaluated every 1-4 years (mean follow-up of 3 (range 1-8) years). IL-6 was measured in fasting blood serum samples collected at each visit and log-transformed for analyses. Several baseline IL-6 cut-points, ranging from 2.5-4.1 pg/mL, were explored to examine categorical IL-6 associations with perceived fatigability over time. Perceived fatigability was reported by the participant based on the Borg rating of perceived exertion (RPE; scored 6 to 20 where higher scores represent higher exertion) after a 5-minute, 0.67 m/s, 0% grade treadmill walk. Associations between IL-6 (baseline and repeated measures) and perceived fatigability were assessed using generalized estimating equations, adjusting for demographics, behavioral factors, and comorbid conditions. **Results:** In fully adjusted models, each 1 unit higher baseline log IL-6 was associated a 0.42 higher RPE (p=0.03). This relationship tended to remain constant over time (baseline log IL-6 by time interaction p=0.15). The sample median (3.7 pg/mL) was used to define high and low IL-6 levels. The high group reported 0.26 higher RPE (p=0.03) averaged over time (time interaction p=0.41) than the low group. Annual changes in logged IL-6 were not associated with annual changes in perceived fatigability (0.10 RPE, p=0.53). **Conclusion:** Higher baseline IL-6 was associated with higher perceived fatigability in adults in mid-to-late life. Those with IL-6 levels >3.7 pg/ml had significantly greater perceived fatigability than those with lower IL-6 levels an association that remained stable over time. Our findings suggest that after chronic IL-6 elevation becomes substantially high, subsequent increases do not materially affect fatigability. Future studies should evaluate whether subsequent reductions in IL-6 dampen the perception of activity-related fatigue. Additionally, further validation of the 3.7 pg/mL IL-6 is cut-point necessary to determine clinical utility..

OC25- IDENTIFYING FRAILTY USING THE ELECTRONIC MEDICAL RECORD WITHIN A MEDICARE ACCOUNTABLE CARE ORGANIZATION. Nicholas M. Pajewski[1], Kristin Lenoir[2], Brian J. Wells[2], Jeff D. Williamson[3], Kathryn E. Callahan[3] *((1) Division of Public Health Sciences, Wake Forest School of Medicine, Winston-Salem, NC, USA; (2) Clinical and Translational Science Institute, Wake Forest School of Medicine, Winston-Salem, NC, USA; (3) Section on Gerontology and Geriatric Medicine, Department of Internal Medicine, Wake Forest School of Medicine, Winston-Salem, NC, USA)*

Background: Recent evidence suggests that frail and pre-frail older adults may benefit from targeted interventions, and that frailty

itself may be reversible. Despite the existence of several validated definitions, measures of frailty have not been consistently incorporated into primary care. Based on the model of deficit accumulation, investigators in England have developed an Electronic Medical Record (EMR) frailty index (eFI) for the National Health Service. However, there is no measure of frailty, including the eFI, that has yet been adapted for routine use in US health care systems. **Objectives:** To build an eFI for patients in a Medicare Shared Savings Plan Accountable Care Organization (MSSP-ACO) at our institution. **Methods:** We extracted encounter, diagnosis code, laboratory, and medication data from the EMR for 7,935 MSSP-ACO patients (95 years of age as of 7/1/2015). We used a 2 year look-back period to estimate an eFI (46 total deficits), and examined the association of the eFI with incident events over the following year. **Results:** The MSSP-ACO cohort was 57.8% female, 86.3% white, with a mean age of 76.5 (SD=6.9) years. The eFI could be calculated for 6,689 (84.3%) patients. Of these 16.1%, 51.5%, and 32.4% were classified as fit (eFI>0.10) pre-frail (0.10<eFI>0.21), or frail (eFI>0.21), respectively. Accounting for age, sex, race/ethnicity and comorbidity (Charlson Index), the eFI was an independent predictor of all-cause mortality (Explained Relative Risk = 7.6%). Allowing for the competing risk of death, patients classified as frail (compared to fit patients) exhibited increased risk for emergency department visits (Relative Risk (RR)=1.85, 95% CI: 1.47 to 2.32), inpatient hospitalizations (RR=1.82, 95% CI: 1.34 to 2.47), and injurious falls (RR = 1.75, 95% CI: 0.38 to 7.99). **Conclusion:** Our results indicate that EMR data captured during routine primary care can identify frail and at-risk older adults. While further work is needed to refine and validate the eFI, incorporating functional data from Medicare Annual Wellness Visits, implementation of the eFI could facilitate the identification of a subgroup of older patients at risk for the negative health consequences of frailty, for whom health systems may target care coordination and other health care resources.

OC26- MULTIMODAL INTERVENTIONS TO PREVENT AND MANAGE COGNITIVE FRAILTY. Manuel Montero-Odasso[1,2,3], Quincy J. Almeida[4], Richard Camicioli[5], Karen Li[6], Teresa Liu-Ambrose[7], Laura Middleton[8], Louis Bherer[6,9] *((1) Department of Medicine, Division of Geriatric Medicine, Schulich School of Medicine & Dentistry, University of Western Ontario, London, ON, Canada; (2) Department of Epidemiology and Biostatistics, Schulich School of Medicine & Dentistry, University of Western Ontario, London, ON, Canada; (3) Gait and Brain Lab, Parkwood Institute, Lawson Health Research Institute, London, ON, Canada; (4) Sun Life Financial Movement Disorders Research Centre, Wilfrid Laurier University, Canada; (5) Geriatric and Cognitive Neurology, University of Alberta, Canada; (6) Department of Psychology and PERFORM Centre, Concordia University, Canada; (7) Department of Physical Therapy, University of British Columbia, Centre for Hip Health and Mobility, and Djavad Mowafaghian, Centre for Brain Health, Vancouver Coastal Research Institute, University of British Columbia, Canada; (8) Department of Kinesiology, University of Waterloo, Canada; (9) Faculty of Medicine, University of Montreal, Montréal, Canada)*

Background: Cognitive frailty has been postulated to increase the risk of dementia and to be treatable by exercise. Exercise training is beneficial for cognition even in frail older adults and in those with low mobility. Animals and humans studies have demonstrated that aerobic exercise may have neuroprotective and neurorestorative effects. The rationale of combining aerobic and progressive resistance training as a multimodal exercise intervention is supported by research that has revealed potential beneficial effects on insulin-like growth factor-1, insulin sensitivity, and anti-inflammatory and brain-derived neurotrophic factor pathways, which are related to both sarcopenia and cognitive decline. Multimodal exercise interventions have shown positive effects on muscle/lean mass, cognition and brain volume. In addition, cognitive training (e.g., computer based cognitive process training) has been linked to improvements in brain plasticity, cognition, mobility and postural control. **Objectives:** The SYNERGIC Trial (SYNnchronizing Exercises, Remedies in GaIt and Cognition) is a multisite clinical trial aimed to improve cognition and delay progression to dementia syndromes in older adults with cognitive frailty, using a combination of multimodal interventions. **Methods:** A total of 200 participants with cognitive frailty will be assigned to active or sham interventions. Active interventions include combined aerobic and resistance training, cognitive training, and vitamin D supplementation. Control interventions consist of balance and toning exercises, control cognitive training, and placebo vitamin D. **Results:** Preliminary results show that the effect of combined aerobic and resistance training improved ADAS-Cog 13 (combined training: 15.51 ±5.47; balance and toning: 26.93 ±8.39; p= 0.006) and ADAS-Cog plus scores (combined training: 0.22 ± 0.56; balance and toning: 0.45 ±0.36; p= 0.394) after 6 months of intervention, compared to balance and toning exercises. An active cognitive training also improved ADAS-Cog 13 (active cognitive training: 14.47 ±3.96; control cognitive training 20.01 ±8.62; p=0.046) and ADAS-Cog plus scores (active cognitive training: 0.15 ±0.57; control cognitive training: 0.35 ±0.50; p= 0.070) after 6 months of intervention, compared to control cognitive training. **Conclusion:** Conclusion: Our preliminary results show that a multimodal intervention with physical and cognitive training is feasible and may have a synergistic effect in improving cognitive function in participants with cognitive frailty.

OC27- AGE-RELATED DECLINE IN D3CR MUSCLE MASS (BUT NOT DXA LEAN MASS) IS CORRELATED WITH DECLINE IN WALKING SPEED. Peggy M. Cawthon[1,2], Katherine Peters[1], Eric S. Orwoll[3], Andrew Hoffman[4], Steven R. Cummings[1,2], Marc Hellerstein[5], William J. Evans[5,6] *((1) California Pacific Medical Center Research Institute, San Francisco, CA, USA; (2) University of California, San Francisco, CA, USA; (3) Oregon Health and Sciences University, Portland, OR, USA; (4) Stanford University, Stanford, CA, USA; (5) University of California, Berkeley, CA USA; (6) Duke University Durham, NC, USA)*

Background: Strength, walking speed and lean mass decline with age, yet declines in lean mass by DXA are modest. Direct measures of change in muscle mass by the D3Cr dilution method may be more strongly related to changes in physical performance than are changes in DXA lean mass. **Objectives:** To determine the association between change in D3Cr muscle mass and DXA lean mass with the change in grip strength and walking speed over 6 meters. **Methods:** At the Year 14 Visit of the Osteoporotic Fractures in Men (MrOS) Study, 1,382 men had D3Cr muscle mass, grip strength, walking speed, and lean mass by DXA. A convenience sample (N=41, mean age 83.3±3.9 years) returned for repeat assessments an average 1.6 years later. We calculated percent change in all measures, and tested whether this change differed from 0 using one sample t-tests. We calculated the correlation between change of D3Cr muscle mass, DXA lean mass, grip strength, walking speed, and weight. We analyzed D3Cr muscle mass alone, or divided by weight; and DXA lean mass as total lean, appendicular lean mass (ALM) alone, ALM/height2 and ALM/weight. **Results:** There was no change in weight or any DXA lean mass measure (Figure, p for change not equal to zero >0.05 for all). In contrast, D3Cr muscle mass (alone or divided by weight), grip strength and walking speed all declined by 4.1-5.1% over 1.6

years (Figure; p for change not equal to zero <0.05 for all). Decline in D3Cr muscle mass/weight was modestly correlated with the decline in gait speed (r=0.33, p=0.037) and the change in ALM/ht2 ((r=0.48, p=0.002) but not the decline in grip strength (r=0.06, p=0.70). The change in ALM/ht2 was not correlated with change in walking speed (r=-0.10, p=0.55) or the change in grip strength (r=0.18, p=0.22). **Conclusion:** Declines in D3Cr muscle mass mirror changes in strength and walking speed, while changes in DXA lean mass do not. These results provide preliminary evidence that the D3Cr dilution method to assess muscle mass may more closely reflect functional changes than DXA assessments of body composition.

OC28- HIGH AND LOW RESPONSE TO HIGH INTENSITY INTERVAL TRAINING CORRELATES WITH DISTINCT MUSCLE MIRNA MRNA PROFILES. Kenneth L. Seldeen[1], Le Yang[2], Jonathan Bard[3], Merced Leiker[1], Norma Nowak[3], Yijun Sun[2], Bruce R. Troen[1] *((1) Division of Geriatrics and Palliative Medicine, Jacobs School of Medicine and Biomedical Sciences, University at Buffalo and Research Service, Veterans Affairs Western New York Healthcare System, Buffalo, NY, USA; (2) Department of Microbiology and Immunology, School of Medicine and Biomedical Sciences, University at Buffalo, Buffalo, NY, USA; (3) New York State Center of Excellence in Bioinformatics and Life Sciences and Department of Biochemistry, School of Medicine and Biomedical Sciences, University at Buffalo, Buffalo, NY, USA)*

Background: Frailty is a prevalent condition that increases risk for co-morbidities, loss of independence, and mortality. Exercise is emerging as an effective intervention for frailty, although participation in older populations is low and is therefore driving the need for new exercise modalities that might appeal to this demographic. We recently reported (Seldeen et al (2017) Journal of Gerontology) that a 3 day a week, 10 minute high intensity interval training (HIIT) regimen improved muscle mass and physical performance, and reduced frailty in aged mice (from 24-28 months of age, human equivalent of 65-75 years). **Objectives:** To identify the underlying mechanisms that facilitate the response to exercise, we examined differences in miRNA and mRNA profiles between both HIIT and sedentary (SED) mice as well as between mice that exhibited a high and low improvement in physical performance in response to HIIT. **Methods:** Micro-RNA was isolated from anterior tibialis muscles of male C57BL/6 mice that were sedentary or had been administered 4-months of HIIT, and then subjected to Next-Gen miRNA sequencing. Bioinformatics included principle component analysis and differential expression and were correlated to SED versus HIIT and high versus low responders based upon a composite physical performance score derived from treadmill, grip strength, open field activity, and gait speed. **Results:** We identified 13 differentially expressed miRNAs between SED and HIIT mice, including known regulators of metabolism, muscle, and mitochondria (mir-1A, Let-7J, mir-206, mir-146a, mir-23a, mir-185, and mir-6538). Other affected pathways include adipocyte regulation (mir-122) and inflammation (mir-709). We further examined differences between mice with the high and low responses to HIIT and found 19 differentially expressed miRNAs. Many miRNA fell in pathways associated with muscle and mitochondrial metabolism (mir-6538, mir-483, mir-3968, mir-146b, mir-23b, mir-652, mir-27a, mir-23a, mir-183, mir-200b, mir-203, mir-200c, and mir-205). Principal component analysis also identified unique clustering between SED and HIIT groups as well as between high and low responders to HIIT. Our ongoing investigations include examining differences in mRNA expression and miRNA-mRNA pathway analysis. **Conclusion:** A thrice weekly, 10 minute HIIT regimen induces distinctive miRNA profiles in muscles of aged mice. Furthermore, specific miRNA profiles correlate with greater response to the HIIT intervention.

OC29- HOW DOES FRAILTY INFLUENCE WHO GETS DEMENTIA? Lindsay Wallace[1], Olga Theou[1], Judith Godin[1], Melissa Andrew[1,2], Kenneth Rockwood[1,2] *((1) Department of Medicine, Dalhousie University, Halifax, Canada; (2) Centre for Health Care of the Elderly, Nova Scotia Health Authority, Halifax, Canada)*

Background: The neuropathological features of Alzheimer's disease (AD) are not always well correlated with clinical dementia. In contrast, dementia and frailty are closely linked as both are strongly related to age and vulnerability to adverse health outcomes. Possibly, frailty interacts with neuropathological features of AD to increase vulnerability to cognitive impairment and dementia. **Objectives:** To examine how frailty moderates relationships between neuropathology, cognition, and dementia status. **Methods:** This was a cross-sectional analysis of data from the Rush Memory and Aging Project, a clinico-pathological study of older Americans. Participants had annual clinical and neuropsychological evaluations and, at time of death, an autopsy. AD neuropathology was quantified by counts of neuritic plaques, diffuse plaques, and neurofibrillary tangles. Frailty was operationalized using the deficit accumulation approach, with a frailty index constructed from 41 health variables including function, comorbidities, symptoms, and signs. Cognition was operationalized using the 30-item Mini Mental State Examination (MMSE) and dementia status was ascertained by clinical consensus. Regression models tested the relationships between frailty, neuropathology, and cognition. Process syntax was applied in SPSS to evaluate moderation effects. **Results:** 700 adults were included in this analysis (83.2±5.9 years, 68.9% female). At time of death, 52.7% met criteria for dementia. Frail participants were more likely to have dementia, and worse MMSE scores (p<0.05). Interestingly, degree of AD neuropathology did not significantly differ between frail and non-frail groups. Regressions demonstrated a significant interaction between frailty and neuropathology in the prediction of both dementia status and MMSE score. When probed, these interactions demonstrated: 1) as frailty increases, the relationship between neuropathology and dementia status weakens; and 2) as frailty increases the relationship between neuropathology and cognition strengthens. **Conclusion:** Our results suggest that frailty reduces the degree of structural deficit (neuropathology) necessary to produce functional deficit (worse MMSE score). That this relationship does not hold with dementia status as the outcome suggests that dementia depends on other constructs (i.e. activities of daily living, mobility, etc.) and not just cognition. These results challenge the notion that AD is a result of single mechanism failure and brings forth the treatment of frailty as a preventive measure for dementia.

OC30- THE ROLE OF HOMOCYSTEINE AND B VITAMINS IN TELOMERE LENGTH: RESULTS FROM THE CROSS-SECTIONAL AND INTERVENTIONAL TRIALS. Irene Pusceddu[1,2], Markus Herrmann[3], Marcus Kleber[4], Susanne H. Kirsch[2], Christian Werner[5], Graciela Delgado[4], Ulrich Hübner[2], Marion Bodis[2], Angela M. Di Pierro[1], Silvia Giuliani[1], Ulrich Laufs[5], Stefan Wagenpfeil[6], Jürgen Geisel[2], Winfried März[4], Wolfgang Herrmann[1] *((1) Department of Clinical Pathology, District Hospital Bolzano, Italy; (2) Department of Clinical Chemistry and Laboratory, Medicine, Saarland University Hospital, Germany; (3) Clinical Instituite for Medical and Chemical Laboratory Diagnostics Medical University of Graz; (4) University of Mannheim, Germany; (5) Department of Cardiology, Saarland University Hospital, Germany; (6) Department of Biometry and Epidemiology, Saarland University Hospital,*

Germany)

Background: Telomeres are essential for the maintenance of genomic integrity. Telomere dysfunction has been proposed as a biomarker for age-related diseases. Vitamin B12, B6 and folic acid are essential cofactors for genomic integrity as they are involved in the synthesis of nucleotides and protein/DNA methylation. B vitamin deficiencies are risk factors for the development of age-related diseases. **Objectives:** Evaluate the effects of B vitamins on telomere biology in healthy, cardiovascular and elderly subjects. **Methods:** LURIC study (3316 cardiovascular patients), STVS study (350 healthy subjects) and KNOVIB study (supplementation of 60 elderly for 1 year (group A n=31 vitamin B12, B6, folate, vitamin D and calcium; group B n=29 vitamin D and calcium)). Relative telomere length (RTL), telomerase activity, LINE-1 methylation, vitamin B6, B9, B12, homocysteine (HCY), 5-methyltetrahydrofolate (5-methylTHF), 5,10-methenylTHF, S-adenosylmethionine (SAM), dimethylglycine (DMG), metylmalonic acid (MMA), choline, IL-6, and advanced glycation endproducts (AGEs) were quantified. **Results:** STVS study: HCY correlated negatively with age-corrected RTL; higher levels of AGEs were identified in subjects with higher HCY concentrations; subjects with telomerase activity above the median were characterized by a higher concentrations of vitamin B12. LURIC study: age-corrected RTL was negatively correlated with HCY and positively with vitamin B6. IL-6 was higher in the presence of vitamin B deficiency, and IL-6 correlated negatively with age-corrected RTL. KNOVIB study: one-year of B and D vitamins supplementation significantly changed the pattern of correlation between RTL and B vitamin metabolites (MMA, 5-methyl-THF, choline and DMG). Vitamins supplementation in group B reduced LINE-1-methylation and LINE-1-methylation correlated inversely with RTL. In group B, subjects with HCY >12µmol/L had lower mean LINE-1-methylation. **Conclusion:** These results provide evidence for an association between vitamin B6, B12, folic acid, HCY and RTL. Hyperhomocysteinemia is able to negatively affect RTL in healthy, in cardiovascular patients and in elderly. On one hand hyperhomocysteinemia is able to induce an inflammatory and oxidant status that in turn induces telomere attrition. On the other hand hyperhomocysteinemia induces DNA hypomethylation that in turn induces telomere dysfunction. In fact, literature data indicates that DNA hypomethylation is associated with elongated and dysfunctional telomeres. Further analyses are needed to confirm these results.

OC31- MIRNAS AND PROCOLLAGEN TYPE III N-TERMINAL PEPTIDE (P3NP) IN ELDERLY.

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Background: MicroRNAs (miRNAs) are short non coding RNAs with key roles in cellular regulation, aging and aging related conditions and their disruption has been linked to a variety of diseases. Procollagen type III N-terminal peptide (P3NP) is a marker of muscle growth, which has been also linked with muscle repair and fibrosis. Since muscle growth, repair and fibrosis have all been connected with sarcopenia, understanding factors that regulate the production of P3NP may shed light in the pathogenesis of this important condition with aging. **Objectives**: We hypothesized that specific miRNA can regulate the production, deposition and biological activity of P3NP. To test this hypothesis we studied the relationship between plasma levels of 77 miRNA and P3NP in community-dwelling elderly subjects 65 years old and older. **Methods:** Plasma miRNAs determination by quantitative PCR was supported by EU-FP7 Health Project FRAILOMIC 305483. Serum P3NP was determined by radioimmunoassay. The Least Absolute Shrinkage and Selection Operator (LASSO) statistical approach was used to interrogate 77 miRNAs for their association with serum P3NP in frail (n=91) and non frail (n=189) InCHIANTI study participants aging 65 years old and older. Frailty was defined according to Fried's criteria. The reduced set of explanatory miRNAs variables selected by LASSO model was used to perform a regression multivariate analysis of miRNAs (adjusted for sex and age) versus P3NP to test whether association were similar in frail and non-frail participants. **Results:** Data on 280 InCHIANTI participants (Frail/Robust ratio: 1/3; Age =76.6; 110M, 170F) were analyzed. MiR.193b.3b was a significant correlate of P3NP in both groups. Different set of miRNAs were indentified with LASSO in frail and not frail subjects considering P3NP as outcome. After multivariate regression analysis, miR.221.3p, miR.210, miR.148a.3p (all with $p<0.01$) and miR.188.3p ($p<0.05$) were significantly associated to P3NP among frail participants. Female sex was a significant correlate of P3NP in frail subjects only ($p<0.05$). **Conclusion:** Our findings further support the notion that miRNAs may be involved in the genesis of sarcopenia perhaps through the intermediate function of P3NP.

OC32- PRE-HOSPITAL FRAILTY AND INCIDENT DISABILITY AFTER CRITICAL ILLNESS HOSPITALIZATIONS IN OLDER ADULTS.

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Backgrounds: For older adults, critical illness is a sentinel event often associated with new disabilities which often preclude returning home and can impact trajectory of recovery. **Objectives:** We aimed to 1) describe the levels of disability in Activities of Daily living at hospital discharge in non-disabled critically ill adults who were treated for acute illness in an Intensive Care Unit and 2) to estimate the association between pre-hospital frailty and post-hospitalization disability in this population. **Methods:** This is a prospective observational cohort study of adults (age>50) admitted into Intensive Care Units (ICUs) across two university hospitals in Bronx, New York. Informed Consent was obtained within 3 days of ICU admission from the patient/surrogate. Frailty was identified using the Clinical Frailty Scale, a judgment based frailty assessment tool previously validated in adult ICU patients. At study enrollment, a baseline questionnaire was administered to patient/surrogate asking about basic demographic information including frailty markers, pre-hospital disability status (assistance/supervision in completing the seven Activities of Daily Living (ADLs). Laboratory and clinical data were collected on ICU admission and severity of illness on admission was calculated using the Sequential Organ Failure Assessment score on admission and on day 5 (120 hours). The patients were followed through hospital discharge and their vital status/disability level was collected at hospital discharge. **Results:** In a cohort of 302 adults with age (mean (standard deviation, SD) 67.2 (10.5), 195 (64.6%) of whom reported being independent in all 7 ADLS prior to the hospitalization. Of these 195 patients: only 62 (31.8%) had no disability at discharge; 24 (12.3%) had mild disability levels (1-2 ADL impairments); 15 (7.7%) had moderate disability (3-5 ADL impairment); 48 (24.6%) reported severe disability (greater than 5 ADL impairments and 44 (22.6%) died. Those patients without pre-hospital disability who survived the hospital with incident disability were significantly older than those who survived without disability (mean age (SD) 67.8 (11.0) versus 65.1 (9.6), $p=0.05$). Patients with pre-hospital frailty were more

likely to survive hospitalization with an incident disability (76.3% versus 50.9%, p=0.006). Those who had an Increase in SOFA score over the first 5 days of hospitalization were also more likely to survive with incident disability (73.0% versus 54.2%, p-value 0.045). In the final multivariable model, pre-hospital frailty was associated with surviving the hospitalization with incident disability independent of age, baseline SOFA score and increase in SOFA scores (adjusted Odds Ratio (95% Confidence Interval) 2.7 (1.10-6.60), p=0.003). Similar effect estimated were obtained if death was included in outcome as the worst disability (adjusted OR for frailty (95% CI 2.5 (1.07-6.03), p=0.035). **Conclusion:** In a cohort of critically ill older adults, new disability at hospital discharge was common and pre-hospital frailty diagnosed in the ICU was an important predictor of this patient-centered outcome.

OC33- MICROBIOTA AND METABOLIC DANGER SENSING CONTRIBUTE TO SARCOPENIA. Jonathan D. Schertzer *(McMaster University, Canada Hamilton ON, Canada)*

Background: The external environment influences chronic disease risk, including sarcopenia. However, the stimuli and biological sensors that underpin decreased skeletal muscle strength and slowing of movement during aging are ill-defined. Increased inflammation during ageing or 'Inflammaging' has been proposed as a contributor to sarcopenia, but the participatory immune components are ill-defined. **Objectives:** We aimed to determine if immune detection of commensal bacteria, specific components of bacteria or metabolic stress contributed to the progression of sarcopenia in mice. We hypothesized that germ free mice (devoid of any bacteria) and mice lacking immune sensors for the bacterial cell wall would be partially protected from age-related inflammation and sarcopenia. We also hypothesized that mice lacking an immune sensor of general metabolic danger, the NLRP3 inflammasome would be protected from sarcopenia. **Methods:** We tested 10 month old (adult) and 24 month old (aged) C57 Bl6 male mice for hindlimb muscle structural and functional indicators of sarcopenia. We tested wild type (WT) mice versus mice devoid of peptidoglycan sensing via Nod1 (Nod1-null) and mice lacking NLRP3 inflammasome (NLRP3-null). We also tested germ free WT mice versus conventionally housed, specific pathogen free mice. **Results:** We found that Germ free mice had worse indicators of sarcopenia compared to conventional mice. We found that Nod1-null mice had worse indicators of sarcopenia compared to WT mice. We found that NLRP3-null mice had an attenuation of sarcopenic indicators compared to WT mice. **Conclusion:** Surprisingly, our results in old germ free mice reveal that commensal bacteria actually protect against aspects of sarcopenia. Further, deletion of immune proteins that detect specific components of the bacterial cell wall such as peptidoglycan worsen sarcopenia. Conversely, deletion of a general metabolic danger sensor (NLRP3) protects against sarcopenia. These results warrant caution in strategies targeting the microbiome in sarcopenia and highlight the importance of immunometabolism in age-related muscle frailty.

OC34- COMPARING OBJECTIVE AND SELF-REPORTED MEASURES OF FRAILTY AMONG COMMUNITY-DWELLING OLDER ADULTS: A PILOT STUDY. Brian Buta[1,2], Scott Zheng[1], Bukola Adeosun[2], Jackie Langdon[2], Jeremy Walston[1,2], Karen Bandeen-Roche[1,2,3], Qian-Li Xue[1,2] *((1) Center on Aging and Health, Johns Hopkins University School of Medicine, Baltimore, MD, USA; (2) Division of Geriatric Medicine & Gerontology, Johns Hopkins University School of Medicine, Baltimore, MD, USA; (3) Department of Biostatistics, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA)*

Background: For a self-reported version of the frailty phenotype to be useful for frailty syndrome detection in clinical settings, establishing its convergent validity against the standard phenotype is an important first step. **Objectives:** We examined self-reported questions identified from the research literature that have previously shown agreement with their objective counterparts found in the frailty phenotype. We sought to determine whether these subjective measures may have better agreement with objective measures than self-reported questions used to date. We hypothesized that agreement between objective measures in the frailty phenotype and self-reported measures can be improved by: a) dynamic questions that aim to account for changes in grip strength and walking speed; and b) multiple self-report questions instead of single questions for weakness and slowness criteria. **Methods:** We completed a prospective pilot study and analyses comparing the standard frailty phenotype to a self-reported phenotype with self-reported measures of weakness and slowness, using Cohen's kappa coefficient. Participants, ages 65 years and older, were recruited from an aging registry in a geriatric clinical studies unit at Johns Hopkins in Baltimore, Maryland (N=94). Standard frailty phenotype (walking speed, grip strength, weight loss, activity and exhaustion questions) and self-reported measures of slowness and weakness were collected. **Results:** Self-reported walking speed questions had fair to moderate agreement with objective walking speed (kappa range=0.36-0.43). For self-reported grip strength questions, there was only slight agreement with measured grip strength (kappa range=0.02-0.17). The dynamic self-reported measures of walking speed and grip strength had fair (kappa=0.37) and slight (kappa=0.17) correlations, respectively, with objective tests. The levels of agreement improved to moderate for walking speed (kappa=0.57) and to fair for grip strength (kappa=0.20) by combining multiple self-report questions in comparison to objective measurements. **Conclusion:** This pilot study provides novel information about correlations between objective and subjective frailty measurements. Our results reiterate the difficulty of approximating the physical frailty phenotype by a modified frailty phenotype substituting self-reported questions of slowness and weakness. A self-reported frailty phenotype with high agreement to the standard phenotype could be a valuable tool in clinical settings.

OC35- GEROPROTECTORS FOR MULTIMORBIDITY AND FRAILTY: ROADMAP TO CLINICAL TRANSLATION. I Bellantuono[1], D Ehninger[2], S Howlett[3], R Muller[4], P Potter[5], H Stemplewski[6], T Tchkonia[7], AU Trendelenburg[8], R Vandenbroucke[9], R van Os[10], N van Riel[11] *((1) MRC Arthritis Research UK Centre for Integrated research into Musculoskeletal Ageing, University of Sheffield, UK; (2) German Centre for Neurodegenerative Disease, Bonn, Germany; (3) Department of Pharmacology, Dalhousie University, NS, Canada; (4) Insttute of Biomechanics, ETH, Zurich, Switzerland; (5) Mammalian Genetics Unit, MRC Harwell, Oxford, UK; (6) Medicine and Healthcare Products Regulatory Agency, London, UK; (7) Mayo Foundation for Medical Education and Research, Rochester, USA; (8) Novartis Institute for Biomedical*

Research, Cambridge, USA; (9) VIB UGENT Centre for Inflammation Research, University of Ghen, Belgium; (10) Laboratory of Ageing Biology and Stem Cells, European Research Institute for the Biology of Ageing (ERIBA), University; Medical Centre Groningen, University of Groningen, The Netherlands; (11) Academic Medical Centre, University of Amsterdam, The Netherlands)

Background: Human life expectancy has been increasing steadily over the last century but this has resulted in an increasing incidence of age-related chronic diseases. Patients often present with more than one disease at the same time (multimorbidity) and become frail. Multimorbidity and frailty are complex to treat, and strongly associated with disability and hospitalization. Current treatments also address each disease individually, which can lead to the complications associated with polypharmacy. New effective interventions for multimorbidity and frailty are urgently required. Geroprotectors are a new class of drugs, which target fundamental mechanisms of ageing common to multiple age-related diseases and shows promise in delaying the onset of multimorbidity and/or boosting resilience in frail older people. However, there are barriers to their clinical translation. **Objectives:** To address the lack of a clear strategy to exploit the potential of geroprotectors twenty-four experts from the European network MouseAGE and associated partners of international reputation convened in Madrid. The aim was to reach consensus and issue recommendations to speed up the clinical testing of these drugs. **Methods:** Consensus was achieved by roundtable discussion **Results:** The group has made a number of recommendations. There is a need for a regulatory framework for the use of drugs targeting frailty or multimorbidity as these are not recognised indications by regulatory bodies at present. However, groups of patients with other indications such as cancer, hip fracture, older patients undergoing surgery and associated frailty may offer opportunities to perform proof of concept studies with these drugs. There is a paucity of animal models, which reproduce accurately those indications, and therefore there is a need to characterise in depth such models for generating preclinical data supporting an application for first in man studies. Clearly defined, validated, measurable outcomes in preclinical studies, which accurately reflects outcomes in patients are required for swift clinical translation. **Conclusion:** Geroprotectors offers new therapeutic opportunities for frailty and multimorbidity. The MouseAGE network has agreed on a strategy which should speed up their translation to patients' benefit.

OC36- A NOVEL APP FOR ASSESSING THE INDIVIDUAL'S FUNCTIONS AND INTRINSIC CAPACITY. Jean-Pierre Michel *(French Academy of Medicine, Paris, France)*

Background: Recent progresses in technology communications open doors to perform quick and scientifically reliable self-comprehensive assessment using i-Phones or androids and tablets **Objectives:** Intrinsic capacity, an essential individual component of «healthy ageing» insists on functional abilities. The novel app assesses your health and functioning. It could be done on your own or on request of your physician, while being in the waiting room. **Methods:** The app includes a first and attractive game (less than 8 minutes) with short questions and tests which results are immediately calculated and presented in a nice and attractive way; they concern your robustness/ frailty status, muscle strength and balance but also your mental agility and memory retention . The results are easily understandable and completed by short and simple comments. The second part of the application includes more personalized questions (N = 7), before proposing you to perform 5 measures a) functional (including nutrition and sarcopenia risks as well as precise measurements of your balance, normal gait speed, functional reserve) and b) cognitive measurements based on previously validated scientific studies. **Results:** Using this application will help the user as well as the physician to immediately focus on known or new discovered health/functioning inabilities. This was the cases for the 10 adults (from 45 to 85 y.o.) who were already tested. Then physical, balance and cognitive exercises are proposed. The regular follow up of the measurements results will show you that it is never too late to intervene to reverse the frailty process or low down the age related functional decline. Indeed the medical control and follow-up of the assessment will be important in case of needed personalized interventions and treatments. **Conclusion** The effectiveness of this very easy and quick assessment and measurements followed by individualized and specific interventions will surprise the user but also the family members and convince the physician that functional abilities could «add life to years».

OC37- MUSCLE ARCHITECTURE: A USEFUL TOOL TO IDENTIFY FUNCTIONAL DECLINE IN INPATIENT OLDER PEOPLE? Livia P. Carvalho[1,2], Dominic Martel[1,2], Marco V. Narici[3], Marc Bonnefoy[4], Mylène Aubertin-Leheudre[1,2] *((1) Department of Physical Activity Sciences, Université du Québec à Montréal, Montreal, QC, Canada; (2) Centre de Recherche de l'Institut de Gériatrie de Montréal (CRIUGM), Université de Montréal, Montreal, QC, Canada; (3) MRC-ARUK Centre for Musculoskeletal Ageing Research, School of Medicine, University of Nottingham, Derby, UK; (4) Centre Hospitalier Universitaire de Lyon Sud, Lyon, France)*

Backgrounds: Muscle mass and strength losses are known to be key factors in the development of long-term physical disability. These declines are even more significant in older people during hospitalizations, increasing their risk of falls, fractures, loss of quality of life further on. However, psychophysical conditions (pain, demotivation, depression and temporary physical incapacities) during hospitalization can be important barriers to the evaluation and monitoring of the functional status of these patients. Performance measurements such as the Short Physical Performance Battery (SPPB) may be difficult to assess. Therefore, identifying a new objective and clinical tool to detect the loss of functional capacity in this population at high risk of developing physical disabilities is of utmost clinical relevance. Changes in muscle architecture (MA) have been shown to be associated with sarcopenia (Narici et al. 2003; Ticinesi et al. 2017). **Objectives:** Our study aimed at: 1) Comparing MA, muscle mass and strength measurements in hospitalized older adults with different functional levels, 2) evaluating the association between these measurements and; 2) verifying whether SPPBscore could be estimated from MA measurements. **Methods:** Forty-four hospitalized older adults were divided in 2 groups: Pre-Disabled (PDis, SPPBscore: 6-9 (n=21), 81±7years old, SPPBscore:7.6±1.1) and Disabled (Dis, SPPBscore:<6 (n=23), 83±7years old, SPPBscore:3.6±1.6). Participants were submitted to the following evaluations: SPPB, body mass (BM) and composition (bioimpedance), handgrip strength (HS, dynamometer) and MA (ultrasound, Pennation angle [PA], muscle thickness [MT], Fiber length [FL] and subcutaneous fat [SCF]). **Results:** Relative muscle strength (HS/BM) (0.28±0.08 vs 0.34±0.09), PA (10.6±1.8 vs 12.3±1.9), and MT (16.4±0.4 vs 19.2 0.4mm) were significantly different between Dis and PDis, respectively. Associations between PA and the SPPBscore (r=0.37) or walking speed (r=0.38); between SCF and walking speed (r=-0.36); as well as between MT and SPPBscore (r=0.29) or walking speed (r=0.31) were observed. Linear regression analysis demonstrated that 14% (r2=0.135) of the variance in the SPPBscore is explained by PA (p=0.02, SEM=2.2). **Conclusion:** Muscle architecture seems related to functional capacities and could be a potentially useful and objective

screening tool for clinicians to tailor care during hospitalization. Further and longitudinal studies are needed to confirm our observation in hospitalized older population.

OC38- THE EFFECT OF INTENTIONAL WEIGHT LOSS ON BIOMARKERS OF MORTALITY IN OLDER ADULTS WITH OBESITY. Lauren Shaver,[1], Daniel Beavers[2], Stephen Kritchevsky[3], Kristen Beavers[1] *((1) Health and Exercise Science; (2) Biostatistics; (3) Internal Medicine, Wake Forest University, Winston-Salem, NC., USA)*

Background: Intentional weight loss (WL) in older adults modestly reduces mortality risk. Observational cohorts have identified several biomarkers of mortality, but their responsiveness to intentional WL is unknown. **Objectives:** To determine the impact of intentional WL on a compilation of biomarkers, including the previously published Healthy Aging Index (composite score range: 0-10; healthiest-unhealthiest). **Methods:** 96 older adults (70.3±3.7 years) with obesity (35.4±3.3 kg/m2) were randomized into a 6-month WL (n=47) or weight stability (WS; n=49) program. Weight, HAI composite score and its component variables [systolic blood pressure, forced vital capacity (FVC), creatinine, fasting plasma glucose (FBG), Montreal Cognitive Assessment], as well as other candidate biomarkers [gait speed, grip strength, interleukin-6 (IL-6), Digit Symbol Substitution Test (DSST), forced expiratory volume in 1 second (FEV1), C-reactive protein (CRP), heart rate (HR), and cystatin-C], were measured at baseline and follow-up. **Results:** Average baseline HAI score was 3.2±1.6. WL participants lost an average of 6.6±0.4 kg (8.6±0.4%), while weight remained stable in the WS group [(-0.2±0.5 kg); 6-month p<0.01]. Treatment effect estimates, adjusted for gender and baseline value, revealed a significant reduction in HAI score in the WL group [WL: -0.80 (-1.18, -0.41) vs WS: -0.17 (-0.57, 0.23); p=0.02], driven by reduced FBG [WL: -4.31 (-8.22, -0.40) mg/dL vs WS: 1.47 (-2.61, 5.55) mg/dL; p=0.03] and marginally increased FVC [WL: 0.11 (-0.02, 0.23) L vs WS: -0.04 (-0.17,0.09) L; p=0.08]. Of the candidate biomarkers, a significant treatment effect was only observed for cystatin-C [WL: -2.57 (-4.41, -0.73) ng/mL vs WS: 0.10 (-1.79, 1.99) ng/mL; p=0.04]. In groups combined, a 1 kg reduction in weight was associated with a 0.07 (0.01, 0.14) reduction in the HAI score (p=0.03), which is associated with 13% lower mortality risk in observational studies. **Conclusion:** Intentional WL in older adults reduces mortality risk, largely due to improvements in metabolic and pulmonary factors. This work identifies cystatin-c as an additional biologic target for reduced mortality risk with WL in older adults.

OC42- FRAILTY, INFLAMMATION, AND MORTALITY AMONG PATIENTS WITH END-STAGE RENAL DISEASE. Mara A. McAdams-DeMarco[1,2], Hao Ying[1], Alvin G. Thomas[1], Fatima Warsame[1], Ashton A. Shaffer[1,2], Christine E. Haugen[1], Jacqueline M. Garonzik-Wang[1], Niraj M. Desai[1], Ravi Varadhan[3], Jeremy Walston[4], Silas P. Norman[5], Dorry L. Segev[1,2] *((1) Department of Surgery, Johns Hopkins University School of Medicine, Baltimore, MD, USA; (2) Department of Epidemiology, Johns Hopkins School of Public Health, Baltimore, MD, USA; (3) Department of Oncology, Sidney Kimmel Comprehensive Cancer Center, Baltimore, MD, USA; (4) Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD, USA; (5) Department of Internal Medicine, Division of Nephrology, University of Michigan School of Medicine, Ann Arbor, MI, USA)*

Background: Among community-dwelling older adults, frailty is associated with heightened inflammation and subsequent mortality. Although frailty is common among end-stage renal disease (ESRD) patients on the kidney transplant (KT) waitlist, the role of frailty and inflammation in this population remains unclear. We quantified the association between frailty, inflammation, and mortality in ESRD patients on the KT waitlist, and tested whether frailty and/or inflammation improves risk prediction beyond clinical factors available in registry-based models. **Objectives:** To quantify the association between frailty and mortality among ESRD patients on the transplant waitlist. To test whether frailty and/or inflammation improves risk prediction beyond clinical factors. **Methods:** We studied 1,975 prevalent ESRD patients on the KT waitlist (11/1/09-2/28/17) in a multi-center cohort study of measured frailty in patients undergoing transplant evaluation; serum inflammatory markers (interleukin-6 [IL-6], soluble tumor necrosis factor- receptor-1 [sTNFR1], and C-reactive protein [CRP]) were analyzed in 605 of these participants. We compared the C-statistic of an established registry-based prediction model adding frailty and/or inflammation (1SD change in log IL-6, sTNFR1, CRP, or an aggregate inflammatory index). **Results:** The mean age was 53.7 and 18.4% were frail. Frail candidates had elevated serum IL-6 (P<0.001), sTNFR1 (P=0.02), CRP (P=0.01), and a higher inflammatory index (P<0.001). The registry-based model had moderate predictive ability (C-statistic=0.655). Frailty was associated with increased mortality risk (frail HR=2.19, 95%CI:1.26-3.79) but did not improve mortality risk prediction (C-statistic=0.646; P=0.65). Like frailty, IL-6 (HR=2.13, 95%CI:1.41-3.22), sTNFR1 (HR=1.70, 95%CI:1.12-2.59), CRP (HR=1.68, 95%CI:1.06-2.67), and the inflammatory index (HR=2.09, 95%CI:1.38-3.16) were all associated with increased mortality risk. But unlike frailty, adding IL-6 (C-statistic=0.777; P=0.02), CRP (C-statistic=0.728; P=0.02), or the inflammatory index (C-statistic=0.777; P=0.02) substantially improved mortality risk prediction. **Conclusion:** Among adult ESRD patients on the KT waitlist, frailty and inflammation were associated with increased waitlist mortality risk, but only inflammatory markers significantly improved mortality risk prediction. Heightened inflammation may be the biological link between frailty and mortality in KT candidates.

OC43- ROLE OF THE SERUM METABOLOME AND GUT MICROBIOME ON LEAN MASS, MUSCLE COMPOSITION, AND PHYSICAL FUNCTION IN OLDERADULTS. Roger A. Fielding *(Tufts University HNRCA, Bosto, USA)*

Background: In older adults (70+ years), reduced lean mass and muscle composition are associated with increased disability, hospitalization, morbidity, and mortality. Because older adults are the fastest growing global subpopulation, identification of mechanisms that underlie these outcomes will be important for addressing the public health priority of healthy aging. With use of an untargeted metabolomic approach, I recently reported significant associations between gut bacteria-related metabolites with lean mass and muscle composition in older adults (average age, 78y), evidence that suggests a role for the gut microbiome on these outcomes. To test this hypothesis, we analyzed whether the gut microbiome is significantly different when comparing older adults with low or high levels of appendicular lean mass (ALM). Moreover, we investigated the role of dietary fiber on these associations. **Objectives:** To identify associations between dietary fiber with the gut microbiome that differentiate older adults with high lean mass from low lean mass **Methods:** Untargeted serum metabolomics (HPLC/MS, GC/MS) on 73 older adults (average age, 78y) 16S rRNA gene profiling on 189 older adults (average age, 85+ years). **Results:** 15 bacterial OTUs were significantly different when comparing older adults with a high ALM percentage (average, 74%), when compared with low (64%). Six

of these OTUs are associated with dietary fiber intake, including fiber from fruits and vegetables, beans, or grains. These 6 OTUs were not associated with age, smoking, or a physical activity score, evidence that suggests a fiber-specific role on affecting both the microbiome and lean mass and older adults. Separately, 60 serum metabolites, including urea and uremic metabolites were associated with muscle composition in older adults. Elevated urea and uremic metabolites suggest roles for an altered gut microbiome (39 metabolites), for increased intestinal permeability (10 metabolites), and increased systemic microbial burden (12 metabolites). **Conclusion:** Based on these data, interventions aimed at increased dietary fiber may be an important means for positively affecting the gut microbiome-muscle axis in older adults. Separately, future studies aimed at testing the hypothesis that the gut microbiome, intestinal permeability, and circulating microbial burden are involved in mechanisms that affect muscle composition in older adults are of interest.

OC44- AGING-ASSOCIATED CHANGES IN SKELETAL MUSCLE MORPHOLOGY ASSESSED BY INTRAMUSCULAR ADIPOSE AND CONNECTIVE TISSUE. Jaclyn Sesso[1], Yoko Kato[1], Jeremy Walston[1], Karen Bandeen-Roche[1], Joao AC Lima[1], Bharath Ambale Venkatesh[2] *((1) Johns Hopkins University, Baltimore, MD, USA; (2) Radiology, Johns Hopkins University, Baltimore, MD, USA)*

Background: Increasingly, intramuscular adipose tissue (IMAT) is identified as a major contributing factor to mobility dysfunction in older adults, a key component of frailty. IMAT is known to increase with both aging and disuse. IMAT has also been linked to increased pro-inflammatory cytokines that contribute to local metabolic dysregulation and feed into the cycle of muscle catabolism leading to functional decline of the muscle. **Objectives:** This study aims to explore these changes in healthy older adults through chemical shift-based water-fat separation magnetic resonance imaging (MRI) which has the capability to assess muscle fat percentage. **Methods:** We assessed changes in skeletal muscle morphology in 15 healthy volunteers (11 men and 4 women) between the ages of 21 and 80. Questionnaires and medical records were checked to ensure there was no prior history of associated disease conditions such as peripheral artery disease, sarcopenia, or frailty. Patients were scanned on a Toshiba 3T Galan system with a 64-channel phased array coil and a body coil to assess calf musculature. Dual-echo 3D Dixon techniques were employed to assess fat distribution and percent fat quantification. Users defined regions-of interest for each of the three muscle regions the tibialis anterior, the soleus and the gastrocnemius, and excluded areas of extensive connective tissue and nerves from the fat fraction map (fat*100/(fat+water)). An average of the fat% from the 3 ROIs was used to calculate mean muscle fat% (FPm), and the standard deviation of the fat% among all the ROIs was also calculated (FPsd). Linear regression analysis was used to assess the association of age, gender and body mass index (BMI) on FPm and FPsd. **Results:** Higher FPm ($r = 0.50$, $p = 0.07$) and FPsd ($r= 0.61$, $p = 0.02$) were associated with older age. Similarly, higher BMI was associated with higher FPm ($r = 0.61$, $p = 0.02$) and FPsd ($r = 0.47$, $p = 0.08$). Calf muscle FPm and FPsd were not associated with gender. **Conclusion:** Aging was associated with increased skeletal muscle fat. MRI based skeletal muscle morphology as measured by fat fraction has the potential to be useful in the study of aging and frailty.

OC45- THE TEMPORAL RELATIONSHIP BETWEEN CHANGE IN MUSCLE MASS AND CHANGE IN MUSCLE STRENGTH. Nancy Chiles Shaffer, Qu Tian, Stephanie Studenski *(Longitudinal Studies Section, Translational Gerontology Branch, National Institute on Aging, National Institutes of Health, Baltimore, MD, USA)*

Background: Muscle mass and muscle strength decrease over the lifespan, with a greater rate of decline in strength compared to mass in men and women. The temporal relationship between changes in mass and strength is unclear; mass loss as sarcopenia is often considered a cause of weakness while inactive or denervated muscle is known to shrink. Thus, the question becomes: with usual aging, does mass loss lead to strength loss or vice versa? Understanding the temporal sequence with aging might inform novel strategies to promote strength and physical function, and prevent sarcopenia. **Objectives:** Assess the temporal relationship between changes in muscle mass and muscle strength in the Baltimore Longitudinal Study of Aging (BLSA). **Methods:** We identified an inception cohort without baseline low muscle mass or strength (defined as: ALM<14.12 kg in women and <21.38 kg in men, and grip strength <19.99 kg in women and <31.83 kg in men, per previous BLSA analyses) with at least three repeated measures of appendicular lean mass (ALM) and grip strength over time. ALM from dual-energy X-ray absorptiometry and grip strength from hand dynamometry, assessed every 2 years, measured muscle mass and muscle strength. Autoregressive cross-lagged structural equation models assessed the temporal sequence of change in muscle mass and muscle strength. Due to known sex differences in muscle mass and strength, all analyses were sex-stratified, and adjusted for baseline age and body mass index. **Results:** Among 214 women (mean age=66 (range 29-94), 43% Black, 8 mean years of follow-up) and 193 men (mean age 69 (range 36-89), 25% Black, 7 mean years of follow-up), as expected, ALM predicted future ALM and grip strength predicted future grip strength. ALM predicted subsequent grip strength (coeff, $p<.001$) and grip strength predicted subsequent ALM (coeff $p< .001$) in women and men. **Conclusion:** With aging, the temporal relationship between changes in mass and strength is bidirectional. Interventions that solely promote muscle mass may unnecessarily miss out on the chance to attend to the non-muscle factors that affect strength with age. These factors might not only help promote preserved physical function but might also help delay muscle mass loss.

OC47- NORMATIVE VALUES OF KNEE EXTENSORS ISOKINETIC STRENGTH FOR OLDER WOMEN AND IMPLICATIONS ON PHYSICAL FUNCTION. Ricardo M. Lima[1], Juscelia Cristina Pereira[1], Silvia Gonçalves Ricci Neri[1], Baruch Vainshelboim[2], André Bonadias Gadelha[1], Martim Bottaro[1] *((1) Faculty of Physical Education, University of Brasília, Brasília, Distrito Federal, Brazil; (2) Master of Cancer Care Program, School of Health Sciences, Saint Francis University, Loretto, PA, USA)*

Background: Lower limbs strength is required for everyday activities and its evaluation has been especially emphasized in older people. Isokinetic testing is a gold standard method to assess muscle strength, however, lack of reference values limits its usefulness when inspecting results. **Objectives:** To develop reference values of knee extensors isokinetic strength for older women, and examine its functional implications. **Methods:** A total of 453 elderly women aged 60 to 84 years (67.4±5.8) participated in this study. Knee extensors isokinetic strength was measured using the Biodex System dynamometer at 60°s-1. Timed Up and Go (TUG) test and the Five Times Sit to Stand Test (5tSTS) were used for functional

evaluation. Subjects were categorized into age groups of five-years range. Age-specific percentiles for muscle strength were identified for classification purposes. ANOVA and Chi-square tests were performed for functional performance comparisons, with statistical significance set at p<.05. **Results:** Mean strength values significantly decreased with advancing age (p<.05). Below percentile 20th, between 20th and 40th, between 40th and 60th, between 60th and 80th and higher than percentile 80th, were respectively labeled as «poor», «below average», «average», «above average», and «excellent». Age-specific quadriceps strength classification for absolute (Nm) and relative to body weight (Nm/kg) values are provided. Volunteers in the lower strata of the proposed classification showed significantly reduced performance in both the TUG and 5tSTS tests (p<.01).

Table 1
Classification of dominant knee extensors isokinetic strength at 60o/s (Nm/kg)

	Age groups (years)				
Classification	60-64	65-69	70-74	75-79	80-84
Poor	<1.26	<1.11	<1.08	<1.05	<0.95
Below Average	1.26-1.45	1.11-1.34	1.08-1.29	1.05-1.17	0.95-1.08
Average	1.46-1.61	1.35-1.52	1.30-1.43	1.18-1.28	1.09-1.17
Above Average	1.62-1.80	1.53-1.70	1.44-1.61	1.29-1.50	1.18-1.36
Excellent	>1.80	>1.70	>1.61	>1.50	>1.36

Conclusion: This study provides normative values of isokinetic knee extensors strength in older women. The proposed classification had the ability to detect reduced physical function among those classified in the lower strata, indicating a potential application when interpreting results of isokinetic tests, which may serve as a clinical screening reference for Sarcopenia. Future studies should ascertain these findings in different women populations.

OC48- A SPECIFIC PROFILE OF CIRCULATING AMINO ACIDS CHARACTERIZES OLDER PERSONS WITH PHYSICAL FRAILTY AND SARCOPENIA: RESULTS FROM THE BIOSPHERE STUDY.

Anna Picca, Federico Marini, Alessandra Biancolillo, Emanuele Marzetti, Jacopo Gervasoni, Silvia Persichilli, Aniello Primiano, Francesco Landi, Roberto Bernabei, Riccardo Calvani *(Catholic University of the Sacred Heart, Rome, Italy)*

Backgrounds: Muscle loss (sarcopenia) and decreasing homeostatic reserve (frailty) are hallmarks of aging. Several circulating markers have been associated with these conditions in older persons. However, a «gold standard» biomarker able to predict functional impairment in older adults is currently unavailable. Muscle is crucial for several metabolic processes, including protein/aminoacid metabolism. Perturbations in protein/aminoacid metabolism may play a role in the development of physical frailty and sarcopenia (PF&S). The simultaneous analysis of an array of circulating aminoacid/metabolites may help gain relevant insights in the pathophysiology of PF&S. **Objectives:** To characterize the profile of circulating amino acids in older people with and without PF&S. **Methods:** More than five hundred persons aged 70+ years were screened. Of these, sixty (20 men and 40 women; mean age 76.9±4.8 years) were diagnosed with PF&S. Thirty (14 men and 16 women) non-sarcopenic, non-frail persons were enrolled in the control group. A panel of 37 serum amino acids and derivatives was assessed by UPLC-MS. Partial Least Squares Discriminant Analysis (PLS-DA) was used to characterize the amino acid profile of people with and without PF&S. **Results:** The optimal complexity of the PLS-DA model was found to be four latent variables. The proportion of correct classification was 70.4 ± 3.6 for persons with PF&S, 88.3 ± 3.9 for non-PF&S individuals. The statistical reliability of the PLS-DA model was established by a double cross-validation procedure and randomization tests. People with PF&S were characterized by higher levels of aspartic and glutamic acid, gamma-aminobutyric acid and taurine, sarcosine, citrulline, and ethanolamine. Conversely, the profile of non-PF&S controls was defined by higher levels of alpha-aminobutyric acid, histidine, and methionine. **Conclusion:** Distinct profiles of circulating amino acids and derivatives from several metabolic patterns characterize older individuals with or without PF&S. The dissection of these patterns may provide novel insights into the role played by protein/amino acid perturbations in the disabling cascade and possible new targets for interventions.

OC49- BODY COMPOSITION REMODELING AND INCIDENT MOBILITY LIMITATIONS IN AFRICAN ANCESTRY MEN.

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Background: Mobility limitations are common in older adults, with higher prevalence in African Americans compared to whites, and are associated with disability, institutionalization and death. Aging is associated with losses of lean mass and a shift to central adiposity, which are more pronounced in African Americans. **Objectives:** We aimed to examine the association of baseline body composition and body composition remodeling with incident mobility limitations in older men of African Ancestry from the Caribbean island of Tobago. **Methods:** Seven-year changes in body composition were measured using peripheral computed tomography (pQCT) of the calf and whole-body dual x-ray absorptiometry (DXA) in 505 African Ancestry men aged 60 years and free of self-reported mobility limitations at baseline. At baseline and the 6-year follow-up visit, mobility limitations were defined by self-report of any difficulty walking 2-3 blocks or climbing up 10 steps due to a health/physical problem. Men with prevalent mobility limitation at baseline were excluded from analyses and incident mobility limitations at follow-up were used as the primary outcome variable for subsequent analysis. Odds of developing mobility limitations associated with baseline and change in body composition were quantified using separate logistic regression models. **Results:** Seventy-five men (14.9%) developed incident mobility limitations over 6.2±0.6 years. Baseline body composition was not associated with incident mobility limitations. After adjustment for covariates, gaining total and intermuscular fat were associated with incident mobility limitations a (OR: 1.60; 95% CI: 1.21-2.13; OR: 1.51; 95% CI: 1.18-1.94). Changes in DXA lean mass were not related to mobility limitations; however, maintaining pQCT calf muscle area was protective against mobility limitations (OR: 0.65; 95% CI: 0.48-0.87). **Conclusion:** Increases in body fat, and particularly intermuscular fat, and decreases in calf skeletal muscle were associated with a higher risk of developing mobility limitations. Our findings emphasize the importance of body composition remodeling in the development of mobility limitations among African ancestry men.

OC50- CO-APPLICATION OF LMHFV AND HMB RETARDS SARCOPENIA BY REDUCING INTRAMYOCELLULAR FAT INFILTRATION IN SARCOPENIC MICE.
J. Wang, SKH Chow, RMY Wong, YN Chim, KS Leung, WH Cheung *(Department of Orthopaedics and Traumatology, Faculty of Medicine, the Chinese University of Hong Kong, Hong Kong)*

Background: The European Working Group on Sarcopenia in Older People (EWGSOP) defined sarcopenia as «a syndrome characterised by progressive and generalised loss of skeletal muscle mass and strength with a risk of adverse outcomes such as physical disability, poor quality of life and death». Intramyocellular fat infiltration is postulated to play a role on age-related sarcopenia, which leads to dynapenia. Low Magnitude High Frequency Vibration (LMHFV) is a non-invasive biophysical intervention which has been considered as a potential approach to improve musculoskeletal system. «-hydroxy-»-methylbutyric (HMB) is a metabolite of leucine. Studies have shown that HMB had positive effects on sarcopenia. **Objectives:** We hypothesized that co-application of LMHFV and HMB can reduce fat infiltration in sarcopenic senescence-accelerated mouse (SAM) P8 mice. **Methods:** A total of 96 7-month SAMP8 male mice were randomly divided into 4 groups: Control (CTL), LMHFV treatment only (VIB), HMB only (HMB) and the combined treatment (COM) group. LMHFV (35Hz, 0.3g; 20min/day) and HMB (500mg/kg/day, 5days/week) treatments were given to the corresponding groups at month 7 of age. Grip strength and mice body composition were assessed at 1, 2, 3 months post-intervention (equivalent to age month 8, 9, 10) were compared among groups. Oil red O staining (ORO) of muscle samples was performed. Grip strength was measured by force gauge (Mark-10 Corporation, USA). Body composition and bone mineral density (BMD) were detected by dual energy X-ray absorptiometry (DXA) (Faxitron, USA). Data analysis was done with one-way ANOVA and independent t-test; the significant level was set at p=0.05. **Results:** The grip strength of HMB group, VIB group and COM group were significantly higher than the CTL group (p=0.012; p=0.004 and 0.000 respectively, one-way ANOVA) at month 10. The difference of grip strength at both month 8 and month 9 was not significant. Fat mass percentage of the HMB group (9.23% drop), VIB group (9.82% drop) and the COM group (9.46% drop) was significantly lower than the control group at month 9 (p=0.011; p=0.007; p=0.009 respectively, one-way ANOVA). The percentage change in fat mass was not significant between groups at month 8 and month 10. Both the VIB and COM group presented significantly lower ORO area at month 10 (p=0.022; p=0.005 respectively, one-way ANOVA). At month 8 and 9, no significant differences of ORO area were seen among groups. At month 8, COM group showed significantly higher (p=0.004, one-way ANOVA) BMD than the CTL group. At month 9, BMD of both HMB and COM group were significantly higher (p=0.019 and p=0.004 respectively, one-way ANOVA) than the CTL group. **Conclusion:** Co-application of LMHFV and HMB could improve muscle function by reducing fat infiltration, which suggested this combined treatment could be used as an intervention for age-related sarcopenia. Acknowledgement: General Research Fund (Ref: 14103314)

OC51- SARA-OBS, AN OBSERVATIONAL STUDY DEDICATED TO CHARACTERIZE AGE RELATED SARCOPENIA POPULATION SUITABLE FOR INTERVENTIONAL STUDIES.
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Backgrounds: Sarcopenia, a key underlying cause of age related physical disability is characterized by the loss of muscle mass and function. Sarcopenia can encompass Sarcopenic obesity (SO), a condition affecting older obese individuals defined by fat mass increase associated with the loss of muscle mass and function. The SARA clinical program is built around BIO101, the oral investigational new drug developed by Biophytis and is hosted by SARA-Data, an innovative platform for clinical trials management. SARA program includes SARA-PK phase1, completed in 2016, SARA-OBS, the ongoing 6-month observational study and SARA-INT, the 6-month interventional study. **Objectives:** - Characterize the target population that will be subsequently studied in SARA-INT, the Phase 2 study in EU and US. - Estimate the prevalence of sarcopenia including sarcopenic obesity in a representative sample of older persons in US and Europe with poor physical function according to the FNIH criteria (Studenski et al., 2014); - Define baseline characteristics of main and secondary criteria. **Methods:** SARA-OBS study consists of two main visits (baseline and 6-month) to evaluate the main (400-meter gait speed), and secondary endpoints (6-minute walk, body composition, SPPB, grip strength and physical activity through actimetry). **Patient:** Reported Outcomes and biomarkers of sarcopenia are also studied. Patients of SARA-OBS study are selected within centers in US and EU (France, Belgium and Italy), based on the FNIH criteria (Studenski at al., 2014; SPPB 8 and ALM/BMI < 0.512 in women and < 0.789 in men or ALM <19.75 kg in men and <15.02 kg in women. **Results:** SARA-OBS baseline characteristics including main criterium (400 m gait speed) and key secondary criteria will be presented. The overlapping between alternative definition of sarcopenia will be discussed, e.g. grip strength newly proposed cut-points. **Conclusion:** The SARA-OBS study will contribute to a better characterization of Age-related Sarcopenia in a community dwelling older patients at risk of mobility disability. SARA-OBS patients will be used in SARA-INT, to evaluate safety and efficacy of BIO101.

OC52- ASSOCIATION OF CIRCULATING MIRNAS WITH SARCOPENIA: THE SARCOPENIA AND PHYSICAL IMPAIRMENT WITH ADVANCING AGE STUDY (SARCOPHAGE).
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Backgrounds: Sarcopenia, the age-related decline in skeletal muscle mass and function, is a major health issue in geriatric medicine. With aging, skeletal muscle gene expression is significantly dysregulated suggesting that epigenetic alterations may play a crucial role in the skeletal muscle aging process. The small non-coding microRNAs (miRs) are endogenous regulators of gene expression. They bind to complementary sequence on target messenger RNA transcripts resulting in translational repression or target degradation. The remarkable miR stability in biofluids suggests they could become non-invasive disease biomarkers. **Objectives:** We studied the

differential expression of circulating miRs in subjects with and without sarcopenia in the SarcoPhage cohort. **Methods:** The study group included Belgian subjects belonging to the population-based cohort SarcoPhage (n = 534). Expression levels of serum miR were measured in 19 healthy subjects without sarcopenia (77.1 ± 6 years, 9 men) and in 18 subjects with sarcopenia (79.6 ± 6.8 years, 9 men). Both groups were matched for age (p = 0.23) and sex. The evaluation of sarcopenia was performed according to the European Working Group on Sarcopenia in Older People (EWGSOP): low muscle mass plus either low muscle strength or low physical performance. According to the manufacturer's protocol (EXIQON, Denmark) for the Next Generation Sequencing method, RNA sequencing was performed from 400 µl of serum (Illumina platform). **Results:** We identified 383 miRs with an expression level '1 TPM (Tags per million) and 196 with an expression level' 10 TPM. When we compared the two groups, 43 miRs showed differential expression (p<0.05) between controls and sarcopenia patients. After Benjamini-Hochberg False Discovery Rate (FDR) correction hsa-miR-668-3p and hsa-miR-200a-3p exhibited significantly different concentrations in sarcopenia patients and controls (p<0.05, FDR at 5%) (see Table).

Names	Log Fold change	p-Value	FDR	Healthy average TMM*	Sarcopenia average TMM*
hsa-miR-668-3p	3.29	1.76E-06	0.001018	3.82	0.23
hsa-miR-200a-3p	1.53	5.74E-05	0.016988	146.33	50.5

* measurements were expressed as Trimmed mean of M-values normalization method (TMM)

Conclusion: With a NGS screening approach, we identified 2 miRs that are differentially expressed in patients suffering from sarcopenia compared to healthy subjects. The next step will be the measurement of these specific miRs in the entire cohort to determine the clinical utility of these markers.

OC53- HIGH PROTEIN INTAKE AND THE MAINTENANCE OF SKELETAL MUSCLE DURING ENERGY DEFICIT COMBINED WITH REDUCED DAILY ACTIVITY IN OLDER ADULTS. Sara Y Oikawa, Chris McGlory, Nelson I Saddler, Adrienne K Morgan, Lisa K Souza, Gianni Parise, Stuart M Phillips *(Department of Kinesiology, McMaster University, Hamilton, Canada.)*

Background: Losses of skeletal muscle with age are accelerated during periods of inactivity such as hospitalization or convalescence from illness/injury. These periods are often accompanied by a reduction in appetite and energy deficit, which can accelerate muscle loss. Protein supplementation may offset skeletal muscle loss during inactivity and energy deficit; however, the effect of protein supplement-type in combination with mixed meals on muscle retention is unknown. **Objectives:** The purpose of this study was to determine the effects of 2wks of step-reduction (SR), during energy-restriction (ER), on the loss of skeletal muscle mass and strength in older-adults consuming either a whey protein- (WP) or collagen peptide- (CP) supplemented diet. **Methods:** Participants (16 men, 69±3yr, 15 women, 68±4 yr) were provided with a controlled-diet containing 1.6g/kg/day of protein (HP), 55±9% of protein from diet sources and 45±9% of protein via twice-daily (30g bid) supplement of WP or CP. **Participants:** underwent 2wk of SR (<750 steps/day) while maintaining HP in combination with mild ER (-500kcal) before returning to habitual-activity for 1wk: recovery (RC). Body composition was measured by DXA for determination of leg-lean-mass (LLM), a fasted blood sample was taken to characterize insulin sensitivity, inflammatory cytokines, and a muscle biopsy for the measurement of muscle fiber cross sectional area (CSA). Participants also performed an isometric maximum voluntary contraction (MVC) to determine knee-extensor torque. **Results:** Following SR, there was a loss in LLM in both groups (p<0.001) that was recovered following RC (p<0.001). There were no differences between groups (p>0.05) for LLM or following SR (p>0.05) on CSA (type I or II fibers). There were no differences between groups for any measure of insulin sensitivity or inflammatory cytokines (p>0.05). Fasted glucose and insulin were elevated following SR (p<0.001) and did not recover at RC (p<0.001). MVC was reduced following SR in both groups (p<0.001) and was recovered at RC but this was only in men (p=0.046). **Conclusion:** In conclusion, a high protein diet restores leg muscle mass following reduced activity when combined with return to habitual activity regardless of protein supplement source. Older women may be more susceptible to loss of muscle function with inactivity than men.

OC54- SARCOPENIA AND EXERCISE INTOLERANCE IN THE OLD: NEW TREATMENTS THAT COMBINE DIET AND EXERCISE TO BUILD STRENGTH AND ENDURANCE. Kevin Conley[1], Sophia Z. Liu[1], Amir S. Ali[1], Baback Roshanravan[1,2], Eric G. Shankland[1] *((1) Departments of Radiology; (2) Medicine, University of Washington, Seattle, WA, USA)*

Background: Reduced muscle size and strength (sarcopenia), exercise tolerance and mobility are debilitating aspects of aging. Exercise training has been the gold-standard for improving the muscle strength or endurance lost with age but not both together. Astaxanthin is a natural product that combined with vitamin E has both anti-inflammatory and anti-oxidant properties that may improve muscle adaptation to exercise training to improve strength and endurance in the elderly. **Objectives:** To conduct a randomized, double-blind, placebo-controlled study of the impact of daily oral astaxanthin treatment (astaxanthin; 12 mg/day, vitamin E; 10 mg/day, zinc; x mg/day) with interval treadmill incline training in the elderly. **Methods:** Healthy males and females (n=41), age 65-82 yrs, undertook 3 months (3x/week for 40-60 min) of interval incline treadmill walking protocol (target 85% HRmax). The following was determined before and after training: training exercise time, 6 min walk distance, tibialis anterior (TA) muscle maximum voluntary contraction (MVC, strength) and muscle cross-sectional area (CSA by MRI). **Results:** Increases in MVC by 14.4% (±6.2%, mean±SEM, P<0.02, paired t-test), CSA by 2.7% (±1.0%, P<0.01) and specific force by 11.6% (MVC/CSA, ±6.0%, P=0.053) were found with Ax treatment but no change was evident in these properties with placebo treatment (MVC, 2.9%±5.6%; CSA, 0.6%±1.2%; MVC/CSA, 2.4±5.7%; P>0.6 for all). Greater endurance (exercise time in incline walking, >140%) and distance in 6 min walk (>8%) accompanied training in both treatments. **Conclusion:** An astaxanthin formulation uniquely improved TA muscle strength and size with the exercise endurance and walking distance increases that came with treadmill walking training. These muscle improvements are consistent with anti-inflammatory and anti-oxidant function of the astaxanthin formulation. Thus, the formulation in combination with a functional training program uniquely improved muscle strength, endurance and mobility in the elderly.

OC55- DOES COMBINED OSTEOPENIA AND SARCOPENIA CONFER GREATER RISK OF FRACTURE THAN EITHER CONDITION ALONE IN OLDER MEN? THE CONCORD HEALTH AND AGEING IN MEN PROJECT. Vasant Hirani[1], David Scott[2], Robert Cummin[3], Markus Seibel[4] *((1) Discipline of Dietetics, School of Life and Environmental Science and the Charles Perkins Centre, The University of Sydney Centre for Education and Research on Ageing, Concord Hospital, University of Sydney, New South Wales, Sydney, Australia. The ARC Centre of Excellence in Population Ageing Research, University of Sydney, New South Wales, Sydney, Australia; (2) School of Clinical Sciences at Monash Health, Monash University, Clayton, Victoria, Australia, Australian Institute for Musculoskeletal Science, Department of Medicine, Western Health, The University of Melbourne, St Albans, Victoria, Australia; (3) School of Public Health, University of Sydney, New South Wales, Sydney, Australia. Centre for Education and Research on Ageing, Concord Hospital, University of Sydney, New South Wales, Sydney, Australia. The ARC Centre of Excellence in Population Ageing Research, University of Sydney, New South Wales, Sydney, Australia; (4) Bone Research Program, ANZAC Research Institute, The University of Sydney, and Dept of Endocrinology & Metabolism, Concord Hospital, Sydney, New South Wales, Australia)*

Background: It is unclear whether older men with both osteopenia/osteoporosis and sarcopenia («osteosarcopenia») are at greater risk of incident falls and fractures than older men with either condition alone. **Objectives:** The primary aim of this secondary analysis of a longitudinal study of community-dwelling older men was to determine whether, compared with assessing sarcopenia and osteopenia/osteoporosis as distinct entities, combining these two risk factors into one entity (osteosarcopenia) provides a better determination of falls and fracture risk. **Methods:** 1,575 community-dwelling men aged 70 years from the Concord Health and Ageing in Men Project (CHAMP) study had appendicular lean mass, total hip and lumbar spine bone mineral density (BMD) determined by dual-energy X-ray absorptiometry, and hand grip strength and gait speed were also assessed. Osteosarcopenia was defined as a BMD T-score <-1.0SD and sarcopenia according to the European Working Group on Sarcopenia definition. Participants were contacted every 4 months for 6±2 years to ascertain incident fractures (confirmed by radiographic reports) and for 2 years for incident falls. **Results:** The prevalence of osteosarcopenia was 8%, while 34% of participants had osteopenia/osteoporosis alone and 7% had sarcopenia alone. Osteosarcopenic men had significantly increased fall rates (incidence rate ratio: 1.40; 95% CI: 1.02, 1.93) and fracture rates (hazard ratio: 1.85; 95% CI: 1.06, 3.23 compared with non-osteopenic/osteoporotic non-sarcopenic men. However, there was no statistical interaction between sarcopenia and osteopenia/osteoporosis, with no difference in fall or fracture rates for osteosarcopenic men compared with osteopenic/osteoporotic alone and sarcopenic alone men (all P>0.05). In continuous analyses of osteosarcopenia components, only higher baseline total hip BMD was predictive of reduced likelihood of fracture (odds ratio: 0.02; 0.01, 0.07 per g/cm2). **Conclusion:** Community-dwelling older men with both low bone and muscle mass do not appear to have increased rates of falls and fractures compared with those with only one of these conditions. These findings suggest that the concept of\»osteosarcopenia\» is of no clinical value.

OC56- HUMAN MULTILINEAGE-INDUCIBLE CELLS MEDIATE THE REPAIR AND REJUVENATION OF TISSUES DERIVED FROM ALL EMBRYONIC LAYERS IN IMMUNOCOMPETENT RODENTS THROUGH MULTIPLE MECHANISMS. Paul C. Schiller *(Prime Cell Biomedical Inc. Miami Beach, USA)*

Background: Cell therapies have played a central role in promoting health in many disease conditions. Developmentally immature cells, or stem cells, have been classically thought of as mediators of tissue repair primarily by replacing dysfunctional cells. It has become evident that adult progenitor cells, i.e., mesenchymal stem/stromal cells (MSCs), mediate tissue repair by mechanisms other than cell replacement. MSCs are highly heterogeneous and show therapeutic effects that vary from donor to donor and depend on donor age and tissue. **Objectives:** Identify and characterize a human early progenitor cell with broad therapeutic and rejuvenating potential useful in the clinical setting. **Methods:** Develop isolation and expansion conditions mimicking the stem cell niche. Isolated cells were assessed for homogeneity, differentiation potential, ability for tissue repair in different disease/injury animal models, immune status, and potential for regulating cell death and senescence. **Results:** Multilineage-inducible cells have been isolated from several species and exhibit similar therapeutic potentials. They express unique molecular and functional profiles that clearly distinguish them from the classical MSCs. Human MI cells are highly homogeneous among donors and have proven effective in repairing and restoring normal function in tissues derived from all three embryonic germ layers in animal models of disease. Human cells can achieve this in animal models without the need of immunosuppression, strongly indicating their immune privileged status. These cells have been highly effective in animal models of inflammatory bowel disease (repairing endoderm-derived intestinal tissue), bone repair and augmentation (mesoderm-derived), and central nervous system (ectoderm-derived) models of injury (focal and global ischemia) and degeneration (Parkinson's disease). They achieve these effects by several mechanisms including, cell replacement, immunomodulation (host tissue immune profile from a pro-inflammatory to an anti-inflammatory status), preventing host cell apoptosis, preventing host cell dysfunction and senescence by modulating cellular mechanisms involved in the accumulation of dysfunctional proteins, such as those forming plaques and tangles known to mediate neurodegenerative diseases and age-related conditions that contribute to physiological deficits. **Conclusion:** Multilineage-inducible cells have a strong potential to mediate tissue repair and organismal rejuvenation in the clinic under an allogeneic setting by modulating mechanism proven to mediate cellular senescence and organismal aging.

OC57- INNOVATING ANIMAL MODELS OF FRAILTY: FRAILTY INDEX AND MORTALITY IN PET DOGS WITH EXCEPTIONAL LONGEVITY. David J. Waters[1,2], Emily Chiang[2], Cheri Suckow[2], Aimee Maras[2] *((1) Center on Aging and the Life Course, Purdue University, West Lafayette, IN, USA; (2) Center for Exceptional Longevity Studies, Gerald P. Murphy Cancer Foundation, West Lafayette, IN, USA)*

Background: People are living longer lives, but persons with the same chronological age display considerable heterogeneity in their accumulation of deficits. Frailty index (FI) operationalizes frailty as the proportion of health deficits present in each individual, providing vital insights into the aging process and its consequences in terms of mortality risk and healthy life-expectancy. **Objectives:** To advance our understanding of frailty and the aging process and

to minimize adverse health consequences associated with increased life-expectancy by using a novel animal model of highly-successful human aging. **Methods:** To achieve this objective, we launched the first systematic scientific study of the oldest-living pet dogs in North America, gathering detailed data on exceptionally long-lived dogs that are physiologically equivalent to human centenarians. Frailty index was constructed assessing accumulation of 34 deficits using information from personal interviews with dog owners and validated through in-person examination by a veterinarian. Cox proportional hazard was used to determine relationship between increasing FI and mortality risk. To better understand differences in individual response to deficit accumulation, we analyzed whether duration of lifetime ovary (estrogen) exposure protected females from adverse impact of increasing FI on mortality. **Results:** Median frailty index (FI) did not differ significantly between males and females (0.44 and 0.41, respectively). For both male and female dogs, the maximum limit of FI, defined as 95th percentile of FI values, was 0.59-0.65, compared to 0.70 reported in humans by Rockwood and colleagues. In 51 male canine centenarians, each 0.1 unit increase in FI was associated with age-adjusted hazard ratio (HR) of 1.5 (95%CI,1.1-2.2)(P=0.027). In 88 females, the relationship was equally strong, with each 0.1 unit increase in FI associated with age-adjusted HR of 1.8 (95%CI,1.3-2.5) (P=0.0008). Higher lifetime endogenous estrogen exposure did not buffer females from the adverse impact of deficit accumulation on mortality. **Conclusion:** This is the first report of using frailty index to describe and dissect the heterogeneity of deficit accumulation in pet dogs with exceptional longevity, a model of highly-successful aging. Future research using the dog model will focus on testing interventions that can delay the onset of deficit accumulation and mitigate adverse consequences of frailty.

OC58- A DOUBLE-BLIND PLACEBO CONTROLLED TRIAL INTO THE EFFECTS OF TESTOSTERONE PROVISION UPON BODY COMPOSITION, GLYCAEMIC CONTROL AND INTRA-MUSCULAR SIGNALING PATHWAYS DURING RESISTANCE EXERCISE TRAINING IN OLDER MEN. Nima Gharahdaghi, Supreeth S Rudrappa, Bethan E Phillips, Iskandar Idris, Matthew S Brook, Daniel J Wilkinson, Nathaniel J Szewczyk, Kenneth Smith, Philip J Atherton *(MRC-ARUK Centre of Excellence and NIHR BRC, School of Medicine, University of Nottingham, UK)*

Background: The andropause is associated with declines in serum testosterone (T), an associated loss of skeletal muscle mass and function (i.e. sarcopenia) and insulin resistance. Two of the major interventions purported to offset sarcopenia are T therapy and Resistance Exercise Training (RET). Nonetheless, the global physiological impacts and mechanisms of T therapy adjuvant to RET remain poorly defined in older individuals. **Objectives:** To determine the impacts of RET plus T (vs. placebo) in older individuals. **Methods:** Eighteen non-hypogonadic healthy older men, 65-75y, BMI 30 kg.m-2 (serum T>8.3nmol.l-1) were assigned in a random double-blinded fashion to receive bi-weekly: placebo (P, n=9) or T (Sustanon 250-mg, n=9) injections over 6-weeks of whole-body RET (leg-extension, leg-press, leg-curl, lat-pull-down, shoulder-press and bench-press (3-sets, 8-10 reps at 80% 1-RM)). Subjects underwent Dual-energy X-ray Absorptiometry (DXA) to assess body-composition, ultrasound scans of m.vastus lateralis architecture, isometric dynamometer knee-extensor Maximal Voluntary Contraction (MVC) testing, Oral Glucose Tolerance Testing (OGTT) and finally, m.vastus biopsies were taken to quantify insulin and anabolic signaling pathways via immunoblotting. **Results:** T adjuvant to RET, augmented whole-body (53002±5240g to 56068±5262g vs. 54132±6331g to 54860±5870g, P<0.0001, ES=0.58) and appendicular lean mass (23887±3190g to 25571±3336g vs. 24591±3752g to 24811±3390g, P<0.0001, ES=0.52) while decreasing body fat (1194g vs. 209g, P=0.01, ES=0.29). T also augmented m.vastus lateralis thickness (2.36±0.21cm to 2.61±0.13cm vs. 2.31±0.3cm to 2.45±0.28cm, P<0.0001, ES=0.73) and fascicle-length (7.18±0.8cm to 7.9±0.75cm vs. 7.7±0.19cm to 8.11±0.1cm, P=0.0008, ES=0.92) in addition to strength gains e.g. 1-RM leg-extension (69.89±15.11kg to 125.6±15.82kg vs. 61.22±29.58kg to 103.1±46.88kg, P=0.0003, ES=0.64) and MVC (166.6±32.7Nm to 210±38.33Nm vs. 164.8±51.25Nm to 194.6±44.23Nm, P=0.0119). Additionally, T augmented insulin sensitivity (e.g. Cederholm index: 54.08±12.77 to 65.41±18.1 mg'L2'mmol'L'1'mU'1'min'1 vs. 46.95±10.99 to 52.05±12.29 mg'L2'mmol'L'1'mU'1'min'1, P=0.028, ES=0.86). Finally, acute RE-induced phosphorylation of AKTser473 (0.088±0.07 to 0.2±0.1 vs. 0.034±0.02 to 0.089±0.06, P=0.008, ES=1.1) and mTORC1ser2448 (0.027±0.01 to 0.12±0.06 vs. 0.05±0.03 to 0.085±0.05, P=0.041, ES=0.59) was enhanced with T. **Conclusion:** T adjuvant to RET, enhanced phosphorylation of insulin and anabolic-related signaling pathways perhaps explaining augmented muscle hypertrophy and insulin sensitivity. Thus, T coupled to RET, is an effective short-term intervention to improve muscle mass, function and glycaemic control in older aged men.

OC59- DISRUPTION OF IL-6 IN A FRAIL MOUSE MODEL DELAYS PHYSICAL FUNCTION DECLINE IN OLDER ANIMALS. Lina Ma, Huanle Yang, Jackie Langdon, Reyhan Westbrook, Ruth Marx-Rattner, Jeremy Walston, Peter Abadir *(Division of Geriatric Medicine and Gerontology, Johns Hopkins University, Baltimore, USA)*

Background: Chronic inflammation (CI) is strongly associated with functional decline, chronic disease states, reduced health span, and mortality in mouse models and humans. Interleukin 6 (IL-6) is one of the markers of CI that is strongly and consistently associated with age-related adverse health outcomes, however the specific role of IL-6 has not been well defined. **Objectives:** to dissect the role of IL-6 in development of age related functional decline in the frail mouse model (IL-10tm/tm mice). **Methods:** We developed a double knockout mouse strain (DKO) on a C57BL/6 background that lacks both IL-6 and IL-10. We compared young (3 months) and old (18-23 months) DKO mice to age- and gender-matched IL-10tm/tm and C57BL/6 wild-type (WT) mice (n=5-9 per group). Treadmill tests including maximum running distance (MRD) and number of visits (NOV) were compared. Changes in inflammatory mediators, mitochondrial energetics and muscle type composition were also compared. **Results:** Old male DKO mice performed better than frail mice (IL-10tm/tm) in both MRD adjusted for body weight (MRD/weight) and NOV in 90 mins ($p = 0.023$ and 0.003, respectively). Old female DKO mice performed better than WT mice ($p=0.019$) as indicated by NOV in 15 mins on the treadmill. However, these differences were observed only on the first day of a three days of treadmill testing. Two-way ANOVA revealed MRD/weight was significantly higher in DKO mice in both old male ($p = 0.017$) and female ($p = 0.028$) in all three days. Post-mortem tissue analysis showed old female DKO mice had reduced mass in kidney, quadriceps, extensor digitorum longus, gastrocnemius and tibialis anterior compared to WT mice (all $p < 0.01$). Young male DKO mice had elevated levels of serum TNFaR1 ($p < 0.05$) and a significant increase in the energetically demanding, fast type 2 muscle fibers in quadriceps ($p = 0.002$), compared to WT mice. **Conclusion:** The mouse model of chronic inflammation in the absence of IL6 exhibits a better functional performance in the short term, but does not display increased physical reserve in subsequent testing. Further analysis to determine the exact biological basis of this enhanced

functional performance is in progress.

OC60- THE ROLE OF DIMINISHING ENERGY RESERVES IN INCREASING FATIGABILITY IN MID-TO-LATE LIFE. Jennifer A. Schrack[1], Amal A. Wanigatunga[1], Pablo Martinez-Amezcua[1], Vadim Zipunnikov[2], Stephanie A. Studenski[3], Eleanor M. Simonsick[3] *((1) Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, USA; (2) Department of Biostatistics, Johns Hopkins Bloomberg School of Public Health, Baltimore, USA; (3) National Institute on Aging, USA)*

Background: Poor energy efficiency is linked to declining health and functional status and increasing likelihood of frailty. Declining energy efficiency may manifest as reduced energy reserves and rising perceived fatigability (activity-related fatigue), but the association between perceived fatigability and energy efficiency has not been empirically evaluated. **Objectives:** To examine the longitudinal association between the energetic cost of walking as a percentage of peak energy availability and perceived fatigability in a cohort of well-functioning adults. **Methods:** 995 participants of the Baltimore Longitudinal Study of Aging (BLSA; mean baseline age 68 + 13 years) were evaluated between 2007-2017 (mean visits: 1.8, range 1-6). The energetic cost of walking (walking VO2; ml/kg/min) was assessed during a 5-minute, 0.67 m/s, 0% grade treadmill test (Medgraphics CPX-D), and perceived fatigability was defined using the Borg rating of perceived exertion (RPE; range 6-20) immediately after. Peak energy availability (peak VO2; ml/kg/min) was assessed during 400m of fast-paced walking using a portable indirect calorimeter (Cosmed K4b2, Italy). The longitudinal association between energy reserves, (a ratio of walking VO2/peak VO2) and perceived fatigability was estimated using generalized estimating equations, adjusted for demographics, body composition and history of chronic conditions. **Results:** In adjusted models, a one-unit (0.1) annual increase in the cost-capacity ratio resulted in a 0.4-unit increase in RPE ($p < 0.001$, $z=12.1$). Other significant contributors to rising fatigability included age ($p < 0.001$, $z=8.3$), and fat mass ($p < 0.001$, $z=4.7$). The addition of an interaction term between age and cost-capacity ratio suggested that the combination of age and increasing costs in relation to capacity ($p < 0.001$, $z=4.6$) were more important contributors to rising fatigability over time than age ($p = 0.50$) or cost alone ($p = 0.02$, $z=-2.4$). **Conclusion:** Rising energy costs in relation to capacity were strongly associated with increasing RPE with aging. These findings suggest that perceived fatigability may act as an early indicator of decreasing energy reserves, which could be used for timely identification of individuals who may benefit from interventions to curb future threats to mobility and risk of frailty. Future investigation in clinical populations is warranted.

Late Breaking News

OC19- RELATIONSHIP OF INCIDENT FALLS WITH BALANCE DEFICITS AND BODY COMPOSITION IN MALE AND FEMALE COMMUNITY-DWELLING ELDERS. DL Waters[1], CR Qualls[2], M Cesari[3,4], Y Rolland[5], B Vellas[5,6] *((1) Department of Medicine and School of Physiotherapy, University of Otago, Dunedin, New Zealand; (2) Department of Mathematics & Statistics and School of Medicine, University of New Mexico, Albuquerque, USA; and Biomedical Research Institute of New Mexico, Albuquerque, USA; (3) Fondazione Ca? Granda ? Ospedale Maggiore Policlinico, Milan, Italy; (4) Department of Clinical and Community Sciences, Univesity of Milan, Italy; (5) Centre Hospitalier Universitaire de Toulouse, Toulouse, France; (6) Department of Internal and Geriatrics Medicine, Gerontopole, CHU de Toulouse, UMR 1027 INSERM, University Toulouse III, Toulouse, France)*

Background: Sarcopenia and obesity are reported risk factors for falls, although the data are not consistent. In most studies, falls incidence is often reported retrospectively rather than prospectively and do not make sex comparisons. **Objectives:** We investigated whether falls would be associated with the balance and gait deficits and body composition, and whether these relationships were sex-specific. **Methods:** Secondary analysis of 4-year follow-up data from 307 participants (M, n=122, 75.8 yr SD5.5; F, n=183, 74.6yr SD6.1) of the New Mexico Aging Process Study. All outcomes were assessed annually. Falls were assessed using bimonthly falls calendars. Gait and balance were assessed using the Tinetti test. Lean body mass (LBM), appendicular skeletal muscle mass (ASM), fat free mass (FFM), total fat mass (FM) were assessed by DXA. Hazard ratios (HR) for 2 point worsening in gait and balance score and falls were calculated by Cox proportional hazard for men and women. **Results:** Baseline balance deficits, and not body composition, was the strongest predictor of falls. Worsening balance had significant sex interactions with LBM (Male-HR 0.97, 95%CI 0.59-1.80; Female-HR 1.82, 95%CI 1.07-2.91 p=0.02), ASM (Male-HR 0.92, 95%CI 0.55-1.73; Female-HR 2.01, 95%CI 1.11-3.03 p=0.01), and FFM (Male-HR 0.96, 95%CI 0.61-1.83; Female-HR 1.93, 95%CI 1.16-3.18, p=0.01). The body composition relationship with balance deficits was U-shaped with the strongest predictors being low lean mass in males and high fat mass in females. **Conclusion:** This 4-year prospective investigation of the relationships between falls, body composition, balance and gait, found no direct association between falls and body composition. However, there were sex-specific relationships between body composition and worsening balance, and worsening balance with increased falls risk. Sex differences need to be further explored and taken into consideration for interventions to improve worsening balance and body composition aimed at preventing falls.

OC20- JNK REGULATES MUSCLE HYPERTROPHY VIA MYOSTATIN/SMAD INHIBITION. Sarah Lessard[1], Tara MacDonald[1], Prerana Pathak[1], Myoung Sook Han[2], Vernon Coffey[3], Donato Rivas[4], Michael Hirshman[1], Roger Davis[2], Laurie Goodyear[1] *((1) Joslin Diabetes Center; (2) University of Massachusetts Medical School; (3) Bond University; (4) Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University)*

Background: Resistance exercise leads to hypertrophic remodeling events in skeletal muscle that increase muscle mass and strength, making this exercise modality a good therapy for combating muscle wasting. However, advanced age and chronic disease can impair the adaptive response of muscle to exercise, or physically limit the ability of an individual to undertake exercise training regimens. **Objectives:** We aimed to identify novel molecular mechanisms that mediate muscle hypertrophy in response to increased load or resistance exercise to discover novel therapeutic targets for increasing muscle mass. **Methods:** We performed bioinformatics analysis in animal models that identified the c-Jun N-terminal kinase (JNK) as a potential mediator of muscle hypertrophy with overload and exercise. We then employed a multi-disciplinary approach, including tissue culture systems, animal models, and human subjects, to determine the effect of JNK hyper-activation and loss of function on muscle fiber hypertrophy. **Results:** Using muscle-specific JNK knockout mice, we determined that JNK is necessary for overload-induced increases in muscle mass and myofiber cross-sectional area. Next, we identified phosphorylation of the transcription factor SMAD2 at specific linker region residues (Ser245/250/255) as a mechanism for JNK-

mediated muscle fiber hypertrophy. SMAD2 is a known effector of the Transforming Growth Factor' family ligand, Myostatin, which is a potent inhibitor of muscle hypertrophy. Our data in cells and animal models demonstrate that JNK-mediated SMAD phosphorylation has an inhibitory effect on Myostatin activity. Therefore, we propose that overload- or exercise-induced JNK activation leads to increased muscle mass via Myostatin/SMAD inhibition. In line with this hypothesis, we show that JNK/SMAD signaling is activated by hypertrophy-inducing resistance exercise, but not endurance exercise, in humans. **Conclusion:** This work identifies a JNK/SMAD signaling axis as a novel therapeutic target to increase muscle mass.

OC21- METABOLOMICS OF FRAILTY SEVERITY AMONG BLACK MEN IN THE HEALTH ABC STUDY. Megan M. Marron[1], Rachel A. Murphy[2], Tamara B. Harris[3], Stacy G. Wendell[1], Robert Boudreau[1], Anne B. Newman[1] *((1) Department of Epidemiology, University of Pittsburgh, Pittsburgh, PA, USA; (2) Centre of Excellence in Cancer Prevention, School of Population and Public Health, University of British Columbia, Vancouver, Canada; (3) Laboratory of Epidemiology and Population Sciences, Intramural Research Program, National Institute on Aging, Bethesda, MD, USA; (4) Departments of Medicine and Clinical and Translational Science, University of Pittsburgh, Pittsburgh, PA, USA)*

Background: Frailty is an important public health issue at both the individual- and societal-level. It is more prevalent with older age and associated with a higher risk of multiple adverse health outcomes, such as falls, hospitalization, and mortality. Currently, the understanding of the pathophysiology of frailty is incomplete. Metabolomics is a promising tool to further our understanding of the biology of frailty, to discern how to prevent or slow the progression of frailty during late-life. **Objectives**: We sought to identify metabolites that correlate with frailty severity among older black men from the Health, Aging, and Body Composition (Health ABC) study and determine significant biological pathways that contribute to frailty. **Methods:** The Health ABC study was a prospective cohort of N=3075 ambulatory older black and white men and women from Pittsburgh, PA and Memphis, TN. Metabolomics (350 metabolites) was performed by the Broad Institute using fasting plasma samples drawn at the second visit (1998-1999) from a random subset of n=319 Health ABC black men aged 70-81. Frailty severity was measured using the modified Fried Frailty Phenotype, based on unintentional weight loss, weakness, low energy, slowness, and low levels of physical activity. **Results:** Thirty-seven metabolites were correlated with frailty severity (p-value<0.05), while adjusting for age and study site, of which 14 remained significant after adjusting for multiple comparisons using a 0.30 false discovery rate. Among the 14 metabolites, 6 were negatively correlated (tryptophan, methionine, tyrosine, C14:0 sphingomyelin, 1-methylnicotinamide, and asparagine) and 8 were positively correlated (glucoronate, N-carbamoyl-beta-alanine, isocitrate, creatinine, C4-OH carnitine, cystathionine, hydroxyphenylacetate, and putrescine). Applying a pathway analysis using MetaboAnalyst, we found significantly more metabolites were involved in nitrogen metabolism and aminoacyl-transfer RNA biosynthesis than what you would expect by chance among the 14 metabolites that were correlated with frailty severity. The pathway analysis was repeated using all 37 metabolites that were correlated with frailty at a 0.05 significance level, which supported our evidence for the nitrogen metabolism and amino acyl-transfer RNA biosynsthesis pathways, as well as for the citrate cycle. **Conclusion:** Nitrogen metabolism, aminoacyl-transfer RNA biosynthesis, and the citrate cycle may be involved in the pathophysiology of frailty in late-life.

OC22- APPROACHES TO ASSESSMENT OF SARCOPENIA ON COMPUTED TOMOGRAPHY (CT): A SYSTEMATIC REVIEW. Sean P. Boyle[1], Robert D. Boutin[1], Leon Lenchik[2], Behrang Amini[3] *((1) University of California, Davis, USA; (2) Wake Forest School of Medicine, USA; (3) The University of Texas M.D. Anderson Cancer Center, USA)*

Background: There is increasing use of computed tomography (CT) for the assessment of sarcopenia; however, there is no consensus on protocols used for CT assessment of sarcopenia. **Objectives:** To evaluate all relevant studies that used CT muscle measurements to assess sarcopenia to identify the differences between protocols used. **Methods:** A comprehensive search of PubMed from 1983-2017 was performed to identify peer-reviewed studies that used CT muscle measurements to assess sarcopenia. Abstracts and, as needed, text of the search results were reviewed to make the final selection. Review articles were excluded. The CT protocols were summarized and compared with emphasis on: anatomic landmark(s), analysis software, thresholding and segmentation, muscle(s) measured, key measurement (i.e., muscle attenuation, cross-sectional area [CSA], volume), derived variables, and cut-points for sarcopenia. **Results:** From the described search, 654 articles were identified and 369 studies met inclusion criteria for this systematic review. L3 level was the most common landmark, used in 151 (40%) studies. Slice-O-Matic was the most commonly used software (n=86, 23%), followed by other commercial packages (n=65, 18%). Attenuation thresholding was used in 267 (72%) studies. 235 (64%) studies used semi-automated segmentation, while 29 (8%) studies used some combination of manual, semi-automated, and automated segmentation. The most commonly measured muscle groups were all visible muscles at the selected abdominal anatomic landmark (n=145, 39%), followed by all visible muscles of some part of the lower extremity (n=114, 31%). The psoas muscle was measured in 52 (14%) studies. Muscle CSA was the most common metric (n=323, 88%), followed by muscle attenuation (n=134, 36%), and volume (n=61, 17%). 153 (41%) studies assessed more than 1 of the preceding measures. The most common derived variable was the skeletal muscle index (n= 139, 38%). 47 (13%) studies used a sarcopenia cut-point based on their own data, while 89 (24%) used a previously reported cut-point. **Conclusion:** There is considerable variation in the CT protocols used for assessment of sarcopenia. There is urgent need to develop consensus for CT protocols to better standardize the study of sarcopenia.

OC39- SMALL-MOLECULE APPROACHES TO ATTENUATE THE E3 LIGASE MURF1 AND SKELETAL MUSCLE ATROPHY AND DYSFUNCTION. Siegfried Labeit[1], Scott Bowen[2], Lee H. Sweeney[3], Volker Adams[4] *((1) University of Heidelberg, Germany; (2) University of Leeds, UK; (3) University of Florida, USA; (4) TU Dresden Germany)*

Background: MuRF1 is a muscle-specific ubiquitin E3 ligase that is activated in skeletal muscle wasting. Yet there remains a paucity of therapeutic interventions that directly inhibit MuRF1 function. **Objectives:** In this presentation, we will discuss the development of novel compounds targeting the central B-box-coiled coil domain of MuRF1 in order to inhibit muscle wasting in cardiac cachexia. The underlying objective is to obtain tools by chemical biology to attenuate muscle wasting. **Methods:** As screening approach, an ALPHA based high -throughput screen was applied to select novel compounds from an unbiased library. As a wasting model, we used a monocrotaline induced cardiac cachexia murine model. **Results:** Selected compounds under active study inhibit MuRF1-titin complexation with IC50 values < 25 μM; of which 3 were found to also inhibit MuRF1 E3 ligase

activity, with 1 further showing low toxicity on cultured myotubes. This last compound, EMBL chemical core ID#704946, also prevented atrophy in myotubes induced by dexamethasone and attenuated fiber atrophy and contractile dysfunction in mice during cardiac cachexia. Proteomic studies provide novel mechanistic insights on the downregulated stress pathways that are attenuated by ID#704946 treatment. These include a normalization of proteins associated with apoptosis (BAX), with protein synthesis co-factors, and metabolic enzymes. **Conclusion:** Small molecules directed to MuRF1´s central myofibrillar protein recognition domain may be useful for drug development approaches. Our current data show at least for one compounds an attenuation of in vivo muscle wasting and contractile dysfunction in a mouse model for cardiac cachexia.

OC40- RELATIONSHIP BETWEEN PATIENT-REPORTED OUTCOME MEASURES AND LEG EXTENSOR MUSCLE WEAKNESS IN OLDER ADULTS. Janet E. Simon[1,2] Todd M. Manini[3], Anoop Balachandran[3], Leatha A. Clark[1,4,5], Simon Moskowitz[1], Brian C. Clark[1,4,6] *((1) Ohio Musculoskeletal and Neurological Institute, Ohio University, Athens OH, USA; (2) School of Applied Health Sciences and Wellness, Ohio University, Athens, OH, USA; (3) Institute on Aging and the Department of Aging and Geriatric Research, University of Florida, Gainesville, FL, USA; (4) Department of Biomedical Sciences, Ohio University, Athens, OH, USA; (5) Department of Family Medicine, Ohio University, Athens, OH, USA; (6) Department of Geriatric Medicine, Ohio University, Athens, OH, USA)*

Background: A loss of voluntary muscle strength predisposes older adults to a 4-fold increase in functional limitations and a 2-fold increase in mortality. The importance of the patients' points of view on their health status and use of health care is widely recognized. However, it is unclear how well patient-reported measures are associated with clinically-relevant muscle weakness. **Objectives:** To determine the degree to which patient-reports of physical limitations and fatigue can classify isokinetic leg extensor weakness in older adults. **Methods:** Fifty-seven older adults (77.6±5.9 years, 72.4±15.6 kg, 36 women and 21 men) underwent an isokinetic (60 degrees/sec) maximal leg extensor strength test of the non-dominant limb. Individuals were grouped into strong, intermediate, and weak groups based on previously established isokinetic leg extensor strength/body weight ratio cut-points that identify older adults at risk for mobility limitations. All participants completed 15 questions from the Patient-Reported Outcomes Measurement Information System (PROMIS) Lower Extremity Function, Fatigue, and Upper Extremity Function scales. A discriminant function analysis was conducted to assess the discriminant capability of the PROMIS questions on isokinetic leg extensor strength strata. **Results:** The discriminant function analysis was statistically significant, =0.52, 2=30.7, p=0.04. High scores on the discriminant function were associated with the questions related to difficulty 'climbing step over step', 'getting up off the floor', 'getting in and out of a car', 'going up and down stairs', and 'forcing myself to get up because I was physically too weak' (r=0.43-0.54, p<0.05). Overall, 59.6% of cases were classified correctly with 42.9% of cases in the strong group, 76.2% in the intermediate group, and 54.5% in the weak group classified correctly. **Conclusion:** These data suggest that the PROMIS questions had limited predictive ability only correctly classifying approximately 60% of all individuals. Specifically, worse classification was observed in individuals in the strong and weak groups. While these data should be interpreted within the context of the relatively small sample size and the specific strength cut-points, they do suggest that existing patient-reported outcomes loosely map onto objectively measured lower extremity muscle strength. These results suggest that new patient-reported outcomes are needed to better distinguish clinically-significant weakness.

OC41- HIGHER EXPRESSION OF MIR-19B-3P ASSOCIATED WITH INCREASED FAT-FREE MASS FOLLOWING 6 MONTHS OF RESISTANCE EXERCISE IN OLDER MEN AND WOMEN. Donato A Rivas, Roger A. Fielding, Lee M. Margolis *(USDA Human Nutrition Research Center on Aging at Tufts University, USA)*

Background: Anabolic stimulation by resistance exercise (RE) may delay the progression of muscle loss and prolong independence among community-dwelling elders. However, a high degree of variability in the responses to RE has been observed. Differences in expression of microRNA (miRNA) in skeletal muscle have been identified as a potential mechanism regulating gains in muscle to RE training. Whether discrepancies in circulating miRNA expression profiles can also predict responses in body composition and function after RE training remain unclear. **Objectives:** Determine if alterations in c-miRNA expression can distinguish the responses in body composition and function in mobility-limited older-adults following 6-mo of RE. **Methods:** Seventy three mobility-limited elders (70?85 years, men; n = 30, women; n = 43) completed a 6-mo progressive high-intensity RE training program. Body composition was assessed by DXA before and after training. Participants were dichotomized by gain (Gainers; n = 40) or loss (Losers; n =33) of lower-body limb mass. Total RNA was extracted from serum from 44 participants (22 per group) using miRVANA PARIS kit. 17 miRNA highly associated with skeletal muscle homeostasis were analyzed using TaqMan MicroRNA Assays following multiplex RT and preamplification. **Results:** After training Losers experienced declines (P<0.05) in body mass (-1.0 ± 2.4 kg), primarily from fat mass (-0.73 ± 1.6 kg), while Gainers increased (P<0.05) body mass (1.3 ± 1.9 kg), due to increased fat-free mass (1.1 ± 1.2 kg). Six c-miRs (miR-1-3p, miR-19b-3p, miR-92a, miR-126-5p, miR-133a-3p, and miR-133b) were differentially (P<0.05) expressed between Losers and Gainers. Bioinformatics analysis identified the anabolic PI3k-Akt pathway as the most commonly targeted pathway of these 6 miRNA. Additionally, miR-19b-3p, was positively associated with changes in fat-free mass for Gainers (r = 0.615, P<0.05) and change in fat mass (r = 0.570, P<0.05) for Losers. **Conclusion:** Divergent responses in body composition between Gainers and Losers were most highly predicted by expression of miR-19b-3p. These findings may indicate that circulating miR-19b-3p may be a valuable biomarker to predict the variability in the response to RE.

OC46- THE DIAGNOSTIC SIGNIFICANCE OF PQCT AND DXA IN GERIATRIC PATIENTS. Michael Drey[1], Michaela Henkel[1], Sophie Petermeise[1], Uta Ferrari[1], Marietta Rottenkolber[1], Ralf Schmidmaier[1,2] *((1) Geriatric Department, Klinikum der Universität München, Munich, Germany; (2) Endocrinological Department, Klinikum der Universität München, Munich, Germany)*

Background: The loss of bone and muscle mass increases the risk of osteoporotic fractures. Especially in geriatric patients the Dual-Energy X-ray Absorptiometry (DXA) is often confounded by degenerative changes. **Objectives:** The purpose of this study was to compare associations of DXA and peripheral quantitative computed tomography (pQCT) measurements with major fractures. **Methods:** Bone mineral density (BMD) and muscle area (MA) of 168 patients aged 65 years and older (mean: 76.3±6.5) were measured with pQCT at distal forearm additionally to an osteoporosis basic assessment consisting of anamnesis, blood test and DXA of lumbar spine

and femur. Prior fractures were categorized in major osteoporotic fractures. Logistic regression was used to show the association of BMD ascertained with DXA and pQCT as well as muscle area with major fractures. **Results:** Only pQCT-BMD and pQCT-MA were significantly associated with major fractures (total and trabecular BMD OR 0.555 and 0.487, p<0.001; muscle area OR 0.701, p=0.031), whereas DXA-BMD was without significant association. These associations remained significant after adjustment for age, sex, BMI, physical activity and other risk factors. Hip fractures were significantly associated with cortical pQCT-BMD (OR 0.520, p=0.010) and total hip DXA-BMD (BMD OR 0.520, p=0.048 and T-Score OR 0.527, p=0.028). In the adjusted model for patients >75 years only the pQCT-MA was significantly associated (OR 0.187, p=0.026) with major fractures. **Conclusion:** Measurement of bone and muscle with pQCT seems to have advantage over DXA in fracture prediction in geriatric patients. This supports the significance of the hazardous duet of osteosarcopenia, especially in geriatric patients.