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on Frailty & Sarcopenia Research (ICFSR)

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Symposia

S1- U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES (HHS) INITIATIVES TO IMPROVE FUNCTION, PROMOTE HEALTHY AGING AND INDEPENDENT LIVING AMONG OLDER ADULTS. Rosaly Correa-de-Araujo *(National Institute on Aging (NIA), National Institutes of Health (NIH), U.S., Department of Health and Human Services (HHS), Bethesda, Maryland, USA)*

Communication 1: *Aging Research Supported by the National Institute on Aging (NIA),* Marie A. Bernard (National Institute on Aging (NIA), National Institutes of Health (NIH), U.S., Department of Health and Human Services (HHS), Bethesda, Maryland, USA)

In the United States, the population age ≥65 is projected to almost double (98 million) in 2060. Persons reaching 65 years have an average life expectancy of an additional 19.4 years. As we age, our risk for many types of diseases and/or functional impairments/disability increases dramatically. Considerable attention is paid by the U.S. Department of Health and Human Services (HHS) to the health and wellbeing of older Americans. The National Institute on Aging (NIA) leads a broad research portfolio to understand the nature of aging and to extend the healthy, active years of life. Evidence-based research findings support the work of other Federal agencies in the delivery of services and supports including educational programs for this population. This symposium will discuss recent research findings to improve functional status and provide insights on future research priorities including the role of the recently established NIA Central Biorepository. It will also describe the successes and challenges of services and supports evidence-based program models, and educational initiatives implemented in communities across the Nation. Presentation will highlight: A) Discoveries suggesting that extension of lifespan (via calorie restriction and various drugs) is associated with increase in healthspan/better function in animal models – and the CALERIE (Comprehensive Assessment of Long-Term Effects of Reducing Intake of Energy) findings suggesting that some components of the impact of calorie restriction in animals can be found humans. B) Discoveries regarding increasing lifespan without accompanying increase in years lived with physical or cognitive disability, according to supported behavioral and social science research. C) Studies exploring the relationship between age-related cognitive decline/mild cognitive impairment/dementia and various interventions (including exercise), with findings showing that no definitive evidence to support a particular intervention is currently available. D) A perspective on reducing cardiovascular events from ASPREE (Aspirin in Reducing Events in the Elderly); results of SPRINT-MIND (substudy of Systolic Blood Pressure Intervention Trial) on reducing risk of dementia and mild cognitive impairment.

Communication 2: *Aging Research Supported by the National Institute on Aging (NIA): Announcing the NIA Central Biorepository,* Rosaly Correa-de-Araujo ((National Institute on Aging (NIA), National Institutes of Health (NIH), U.S., Department of Health and Human Services (HHS), Bethesda, Maryland, USA)

Presentation will highlight: A) Research aimed at maintaining independence in mobility. Recommendations on clinically meaningful cut-points for muscle mass/function, future directions for potential new interventions to improve muscle function. Testosterone administration for physical functional deficits; effects on frail older men. B) Efficacy of structured physical activity interventions in slowing progression of frailty or preventing mobility disability in high-risk older persons; slow walking speed and physical activity in osteoarthritis. C) Results of workshop on myosteatosis as an important feature of muscle composition in aging and its impact on metabolism and function. Energy metabolism in skeletal muscle as promising novel target for interventions to improve function/symptoms in heart failure. D) STRIDE, an ongoing multifactorial fall injury prevention strategy found efficacious in more tightly controlled settings, under way in real-world health care settings; the model intervention focuses on a partnership between primary care physicians and falls care managers. Vitamin D supplementation in low circulating vitamin D and impaired physical function to reduce falls risk/improve walking speed. E) Research on multiple chronic conditions in old age showing synergistic effects of differing combinations of co-existing conditions on symptoms and functional status. F) Introducing the NIA Central Biorepository, its collections (example, the LIFE Study-Lifestyle Interventions and Independence for Elders) and role on resources sharing to open a wide array of aging research.

Communication 3: *Chronic Disease Self-Management Education (CDSME) Programs and Other Services and Supports Resources Funded by the HHS Administration for Community Living (ACL)* Carol Nohelia Montoya (Florida Health Networks (FHN), North Miami Beach, Florida, USA)

The Administration for Community Living (ACL) funds the delivery of services and supports primarily by states and network hubs of community-based programs, with the main purpose of promoting community integration, healthy aging and independent living. Educational programs also aim to improve chronic or multimorbidity health conditions through behavior change and self-management. Relevant resources are available to help older adults connect to services and supports in their communities. Presentation will highlight: A) The CDSME programs providing older adults and adults with disabilities with education and tools to help them better manage chronic conditions (e.g., diabetes, heart disease, arthritis, chronic pain, and depression). Implemented through competitive grants to state agencies, area agencies on aging, nonprofits, universities, and tribes, funds are used to develop a sustainable infrastructure to deliver evidence-based programs in communities and empower self-care. Major goals: 1) Significantly increase these populations number in underserved areas and participation in evidence-based self-management education and support programs. 2) Implement innovative contracts and partnerships to support CDSME programs.

Embed programs into an integrated, sustainable evidence-based prevention program network hub via centralized, coordinated processes. In 2016 and 2017, 20 forward-funded cooperative agreements (project periods of two-three years) totaled $12.9 million. B) Model services and supports programs and resources available to older adults across the country (The Aging and Disability Resource Centers (ADRCs), the Area Agencies on Aging (AAAs), the Senior Centers and Supportive Services for Older Adults program; the Health, Wellness, and Nutrition programs; and, the Eldercare Locator, a nationwide service, connects older adults and their caregivers with trustworthy local support resources.

S2- NOVEL TARGETS FOR TREATING PHYSICAL AND COGNITIVE SYMPTOMS OF FRAILTY.

Tom Buford *(University of Alabama at Birmingham, Department of Medicine, USA)*

Communication 1: *Neuroinflammation as a contributor to cognitive and physical frailty,* Yenisel Cruz-Almeida (University of Florida, Department of Aging and Geriatric Research, USA)

Frailty is a syndrome that becomes more prevalent with increasing age and is associated with various negative health outcomes including lower quality of life, mortality and disability. Epidemiological evidence implicates systemic inflammation as a contributor to frailty and in part, anti-inflammatory mechanisms underlying various interventions (i.e., exercise) are thought to avoid or delay frailty. In particular, the aging brain is characterized by a shift to an inflammatory state where increased numbers of activated and primed microglia increase pro-inflammatory cytokines and decreases anti-inflammatory molecules leading to a process known as neuroinflammation. Neuroinflammation sensitizes the aged brain to produce an exaggerated response to the presence of an immune stimulus in the periphery or following exposure to a stressor which may produce more severe detriments in cognitive function. Our laboratory uses neuroimaging techniques in vivo to investigate the role of neuroinflammation and its interactions with stressors (i.e., chronic pain), that may impact physical and cognitive function in older individuals. We will present and discuss cross-sectional data investigating associations between neuroinflammatory markers with clinical and experimental pain as well as physical and cognitive function. Further, we will present results from a pilot study investigating the effects of an anti-inflammatory intervention on neuroinflammatory markers, pain and function in at-risk older individuals. Reduction in neuroinflammatory processes in older individuals has the potential to enhance recovery and coping during disease and stress that is common in frail older individuals.

Communication 2: *Weakened skeletal muscle circadian rhythms in older adults with chronic idiopathic fatigue* Todd Manini (University of Florida, Department of Aging and Geriatric Research)

Complaints of fatigue or exhaustion are a hallmark condition of the frailty syndrome. Recent work by our group demonstrates that fatigue is associated with reduced skeletal muscle biomarkers of mitochondrial biogenesis, total content, and function (Wawrzniak et al. 2016). It is plausible that dysregulation in circadian rhythms pathways may play a role in the pathophysiology of fatigue and mitochondrial decrements. The purpose of this work was to evaluate associations between chronic idiopathic fatigue and biomarkers of skeletal muscle circadian rhythms in order to draw inferences in the pathophysiology between fatigue and mitochondrial loss, for informing future intervention-based studies. We hypothesized that idiopathic fatigue is associated with decrements in circadian rhythm biomarkers that parallel the decrements in mitochondrial markers. Forty-eight older adults (72.2 ± 5.3 yrs) volunteered for this study. Participants were excluded for overt fatigue-associated conditions or diseases (e.g. thyroid, heart failure). The Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Scale was used to categorize fatigued (one standard deviation below the age adjusted normative mean score) from non-fatigued (one standard deviation above the age adjusted normative means score) older adults. A single muscle biopsy from the vastus lateralis, between the hours of 0800 and 1000, was collected and muscle samples were prepped for immunoblotting to assess expression key clock proteins Per1, Bmal1 and Rev-Erbα. Results demonstrated that protein expression of Per1 and Rev-Erbα were significantly decreased in the fatigued group ($p<0.05$) whereas the protein expression of Bmal1 was no different between groups. Regression analyses determined that markers of mitochondria were significantly correlated with circadian rhythm biomarkers (Per1 vs. PGC-1α, $r = 0.36$, $p = 0.02$; Rev-Erbα vs. PGC-1α, $r = 0.41$, $p<0.01$). The current analysis illustrates that circadian rhythm biomarkers Per1 and Rev-Erbα, but not Bmal1, expression are lower in fatigued older adults and significantly correlated with PGC-1α expression. The results provide some initial evidence of a relationship between fatigue and mitochondrial decline through circadian rhythm dysregulation. In conclusion, weakening of circadian skeletal muscle rhythms with may contribute to the pathogenesis of skeletal muscle and ultimately complaints of fatigue among older adults.

Communication 3: *The Gut Microbiome as a Target for Physical and Cognitive Frailty,* Tom Buford (University of Alabama at Birmingham, Department of Medicine, USA)

Frailty, in both the physical and cognitive domains, represents and enormous clinical and public health challenge. The rapid aging of the worldwide population makes it imperative to deliver scientific breakthroughs to treat these impairments, thereby increasing older persons' odds of remaining independent. Recently, the gut microbiome has received tremendous interest for its role in influencing human health. Recent evidence indicates that advanced age is associated with changes in the gut microbiome that affect both the density and composition of microbiota. Moreover, recent data also indicate that dysregulation of the microbiome – i.e. dysbiosis is associated with the development of both cognitive impairment and physical frailty. In a series of clinical and pre-clinical studies, our laboratory is investigating the possibility that interventions targeting the gut microbiome hold promise for attenuating symptoms of physical and cognitive frailty. These data, coupled with the extant literature in the area, indicate that the aging process (independent of disease) contributes to gut dysbiosis and intestinal permeability (i.e. "leaky gut"). Moreover, we have also shown that the composition of serum microbiome differs between healthy young and older adults– potentially secondary to intestinal permeability. Notably, each of these changes is associated with systemic indices of chronic inflammation well-established to be associated with physical and cognitive declines. Thus we will conclude the session by discussing recent and ongoing studies targeting the gut microbiome as a therapeutic target for improving physical and cognitive functions among older animals. These strategies appear to hold tremendous promise for both attenuating age-related inflammation and improving physical and/or cognitive functions among older adults.

S3- BIOENERGETICS OF FRAILTY: FROM THE ANIMAL MODELS TO THE HUMAN EVIDENCE. Leocadio Rodriguez Mañas[1], José Viña *((1) Director GARN-IAGG Scientific Director of ciberfes, head of the department of geriatrics, hospital universitario de Getafe, Spain; (2) Society for research on free radicals (srfr), chair, department of physiology, universidad de Valencia, Spain)*

Communication 1: *Longitudinal Trajectories of Physical Function in Mice,* Rafael de Cabo (National Institute of Aging Baltimore, USA)

Among the main physiological determinants of the function of the systems and organs, the efficiency of bioenergetics is paramount. It is well-known that one of the most outstanding changes during usual aging is a loss of functional reserve, stemming from an increasing loss of ability to maintain the homeostasis of the systems engaged in providing and maintaining the energy balance. In these systems, mitochondria and several of the processes taking place in this sub-cellular organelle have been involved in the progressive functional deterioration associated with aging. But many of the mechanisms involved (increased oxidative stress, low-grade proinflammation, non-efficient functioning of oxidative phosporylation) have been also claimed as causative mechanisms or pathophysiological pathways in several chronic diseases, including ischaemic heart disease, heart failure, diabetes, COPD or depression (Tchkonia & Kirkland, JAMA 2018 Sep 17. doi: 10.1001/jama.2018.12440 [Epub ahead of print]). More recently a new concept (Damage Associated Molecular Patterns-DAMPs) has emerged allowing for a new approach in the assessment of the relationships between MD and several of their manifestations (Nakahira et al. Antioxid Redox Signal. 2015;23:1329-50; Picca et al. Int J Mol Sci. 2017;18.pii: E933.). Specifically, it offers the possibility of determining the plasma levels of substances directly related to MD (the properly named DAMPs, that include mitochondrial DNA, succinate, TFAM, cardiolipin, N-formyl peptides, ATP among others), but also those involved in inflammatory responses and that can be produced by oxidative insults. Thus, now we have the opportunity of studying the whole bioenergetic status, its consequences and its triggers. This is of particular importance considering that the main potential mechanisms explaining the associations between chronic diseases, life-style, aging and functional impairment share an increase oxidative stress and a low-grade inflammatory status, supposedly linked through MD (Ashar et al. J Mol Med (Berl). 2015;93:177-86; Viña et al. Free Radical Biol Med 2018;124:358-63). Moreover, recent findings have shown that oxidative damage does not correlate with age, especially in the geriatric population, but rather with the frailty state (Inglés M et al., J Am Geriatr Soc 2014;62:1324-8). In this same regard, in animal models superoxide dismutase deficient mice are more frail than controls. But more importantly, we have observed that animals that are protected against oxidative damage by overexpression of antioxidant enzymes, delay the onset of frailty and are more vigorous than controls. These common mechanisms, depending upon some local conditions, will be manifested as impairment of vascular function, brain function or other organ/system function, leading to different clusters of diseases (multimorbidity is not randomly observed, and some clusters of diseases are much more frequent than others) and to be manifested by physical and/or cognitive functional impairment when aging (a process characterised by a loss of functional reserve due to the progressive decline in the efficacy of bioenergetics) emerges and some unhealthy lifestyles are present. For the establishment of these trajectories until recently we did not have useful animal models of frailty allowing to study, in short-term periods of time, the mechanisms involved, as its inter-relations. Fortunately, the development in the last years of several instruments to assess frailty, mimicking some of them the tools used in human beings, have raised the option of studying in depth the role of several mechanisms in healthy and non-healthy aging animal models underlying the functional trajectories (Kane AE et al., Clin Interv Aging. 2016;11:1519–29). According to findings using several of these animal models the effect of physical exercise, nutrition, antioxidants and some chronic diseases have been assessed in delimiting the functional trajectories and the potential interventions focused on their underlying mechanisms, including bioenergetics, and how these different mechanisms can interact among them and with some of the potential interventions.

Communication 2: *The isocaloric Ketogenic Diet reduces frailty and extends longevity in mice: potential mechanisms,* Gino Cortopassi (Molecular Biosciences, UC Davis,USA)

Among the most studied interventions assessed to modify longevity, caloric restriction has shown some controversial results in primates but quite consistent ones in rodents, mostly related to changes in bioenergetics through modifications in mitochondrial functioning and in the generation and management of oxidative stress through a shift away from glycolysis toward beta-oxidation. However, the role of caloric restriction in modifying health-span, embracing the effect of the intervention on the so called aged-associated diseases and functional trajectories are less studied. Recently, the effect of calorie restriction, without malnutrition, has been assessed in terms of determining not only longevity but also on health-span in mice. C57BL/6 mice were assigned to a ketogenic, low-carbohydrate, or control diet at 12 months of age and were either allowed to live their natural lifespan or tested for physiological function after 1 or 14 months of dietary intervention. The ketogenic diet (KD) significantly increased median lifespan and survival compared to controls. In aged mice, only those consuming a KD displayed preservation of physiological function. The KD increased protein acetylation levels and regulated mTORC1 signaling in a tissue-dependent manner. This study demonstrates that a KD extends longevity and health-span in mice.

Communication 3: *The role of bioenergetics in human frailty,* Jeremy D. Walston (Johns Hopkins Asthma and Allergy Center, Baltimore, USA)

Jointly to these findings in animal models, several studies in older and middle-aged people stress the role of bioenergetics and some of their related systems and mechanism producing and regulating functional impairment including frailty. This is the case of the metabolic changes, which have long been hypothesized to in part drive frailty and late life decline. Early studies using the frailty phenotype model have demonstrated strong associations between frailty and glucose intolerance, suggesting a dysregulated response to energy intact in frail, older adults. Subsequent studies in a frail mouse model with chronic inflammation has helped to demonstrate strong relationships between aging, physical frailty and energy metabolism changes in mitochondria. Over the past few years, metabolomic measurements have proposed and applied to the measurement of more specific energy-related molecules that may be altered in frailty. We will provide a broad overview of previously performed human studies related to energy metabolism and frailty, more specific studies of frail mouse mitochondrial and bioenergetics changes, and discussion of future directions and the potential importance of metabolomic approaches to better focus on specific energy-related signatures that may be altered in frailty.

S4- A GLOBAL CALL TO ACTION TO IMPROVE CARE FOR OLDER ADULTS WITH FRAGILITY FRACTURES. Jay Magaziner *(Division of Gerontology, Department of Epidemiology and Public Health, School of Medicine, University of Maryland, Baltimore, MD, USA)*

Communication 1: *Mobilizing the Globe: A Call to Action for Treating and Managing Hip Fractures*, Jay Magaziner (Division of Gerontology, Department of Epidemiology and Public Health, School of Medicine, University of Maryland, Baltimore, MD, USA)

Communication 2: *Sarcopenia as a Target for Care After Hip Fracture*, Denise Orwig (Division of Gerontology, Department of Epidemiology and Public Health, School of Medicine, University of Maryland, Baltimore, MD, USA)

Communication 3: *Promising Interventions Targeting Sarcopenia in Hip Fracture Patients*, Ellen Binder (Division of Geriatrics and Gerontology, Department of Medicine, Washington University School of Medicine, St Louis, MO, USA)

S5- THE ROLE OF MITOCHONDRIAL FUNCTION IN CONDITIONS OF ACCELERATED AGING: IMPLICATIONS FOR NUTRITIONAL THERAPY. R. Fielding *(Boston, MA, USA)*

Communication 1: *Novel aspects of mitochondrial biology and its implications for healthy aging*, Pinchas Cohen (University of Southern California, Los Angeles, USA))

Communication 2: *Benefits of increasing glutathione concentrations with cysteine and glycine supplementation demonstrated in HIV patients*, Rajagopal V Sekhar (Baylor College of Medicine , Houston, USA)

S6- SPECIAL CONSIDERATIONS OF THE CANCER PATIENT WITH SARCOPENIA AND FRAILTY. Bette Caan *(Senior Research Scientist Division of Research, Kaiser Permanente of Northern California, USA)*

Communication 1: *The Aging Cancer Patient: Assessing Frailty, Sarcopenia and Accelerated Aging in the Geriatric Oncology Setting*, Grant Williams (The Institute for Cancer Outcomes and Survivorship, University of Alabama at Birmingham, USA)

Dr. Williams is a geriatric oncologist whose research focuses on sarcopenia in the geriatric oncology setting. His presentation will discuss assessments of frailty, sarcopenia and accelerated aging that are developing in the geriatric oncology setting. His presentation will provide evidence of how incorporation of these assessments into comprehensive geriatric assessments can predict the risk of morbidity, mortality and treatment-related toxicity in older adults. The presentation will discuss a variety of measures of muscle health and their correlation with functional status, as well as other frailty measures and promising biomarkers of aging such as DNA methylation, IL-6, CRP, and D-Dimer.

Communication 2: *Maintaining muscle health in cancer survivors: when and how to intervene*, Kristin Campbell (Faculty of Medicine, University of British Columbia, USA)

Dr. Campbell is a physical therapist and research scientist who helped develop the first published exercise guidelines for cancer survivors from the American College of Sports Medicine. She will discuss the anabolic potential in cancer patients, and how and when to intervene among cancer patients. The presentation will include the design of ongoing trials of resistance training and aerobic exercise and specific considerations for cancer exercise among patients at different points along the cancer continuum, including those on active treatment or with metastatic disease. The presentation will also discuss current recommendations and guidelines for cancer patients in the context of sarcopenia and frailty.

Communication 3: *Sarcopenia in oncology: prediction and assessment tools for clinical practice*, Elizabeth Cespedes Feliciano (Kaiser Permanente Northern California, USA)

Dr. Feliciano is a research scientist at Kaiser Permanente Northern California, one of the largest and oldest managed care organizations in the United States. Dr. Feliciano will discuss emerging methods to assess sarcopenia in oncology practice, including abbreviated assessments of linear area and automated assessments of muscle mass from clinically-acquired CT scans and their use in predicting clinical outcomes such as mortality, surgical complication, and chemotherapy toxicity in cancer patients. In addition, she will discuss where within oncology practice such tools could be useful to refer patients to supportive interventions.

S7- OSTEOSARCOPENIA OBESITY: ENOUGH EVIDENCE FOR A DISTINCT ENTITY? Islene Araujo de Carvalho[1], Roger Fielding[2] *((1) Senior Policy and Strategy Advisor at Ageing and Life Course Department, WHO, Genève, Suisse; (2) Boston, MA, USA))*

The co-existence of impaired bone health (osteopenia/osteoporosis), reduced muscle mass and strength (sarcopenia), and increased adiposity (obesity) in middle-aged and older people has been identified in recent studies, leading to a proposal for the existence of osteosarcopenic obesity (OSO) as a syndrome. Evidence for the pathophysiological overlap of these conditions is mounting, although a causal relationship is yet to be established. Each component condition occurs frequently with increasing age, and with shared risk factors in many instances, thus, an overlap of these three conditions is not surprising. However, whether the concurrent existence of sarcopenia, osteoporosis and obesity leads to an increased risk of adverse musculoskeletal outcomes and mortality above and beyond the risks associated with the sum of the component parts remains to be proven and is a question of research interest. In this symposium, we review evidence for the current operational definition of OSO, prevalence, pathophysiology, outcomes and exploratory approaches to the management of OSO components. To expand knowledge and understanding in this area, there is a need for consensus on a definition of OSO which will allow for identification, further epidemiological studies and comparisons between studies. Additionally, studies should assess whether the clinical outcomes associated with OSO are worse than the mere addition of those linked with its components. This will help to determine whether defining a person as having this condition will eventually result in a more effective treatment than addressing each of the three conditions separately.

S8- GAP BETWEEN THEORY AND PRACTICE: A 360 DEGREE CONSIDERATION OF OPPORTUNITIES REMAINING IN FRAILTY MEASUREMENT. Karen Bandeen-Roche, Hurley Dorrier *(Johns Hopkins Bloomberg School of Public Health, Baltimore, USA)*

Communication 1: *Disparate Measurement as well as Status? Frailty Criteria Manifest Differently in Blacks and Whites,* Karen Bandeen-Roche (Johns Hopkins Bloomberg School of Public Health, Baltimore, USA)

Background: Recent research in the National Health and Aging Trends Study has found systematic racial differences in the measurement of phenotypic frailty. For example, four out of five phenotypic criteria were found to be more prevalent among black than white Americans, as was phenotypic frailty itself, but the exhaustion criterion was met 35% less frequently in blacks than whites. Analyses comparing individuals of like underlying frailty status reiterated this finding. **Objectives:** To evaluate potentially disparate measurement of phenotypic frailty by age, sex and other demographic variables and consequences of this for identifying vulnerable older adults, and to illustrate a methodology for conducting this inquiry. **Methods:** Using data from the National Health and Aging Trends Study baseline, latent class and item response models were applied to test whether phenotypic criteria assess frailty differentially for individuals of different demographic characteristics, after accounting for underlying frailty status. Predictive accuracy of frailty for adverse events, morbidity and mortality were compared across demographic groups, and across frailty definitions with varying degrees of tailoring to account for measurement differences. **Results:** Males tended to under-report self-reported frailty criteria: odds of "weight loss," "exhaustion," and "low physical activity" were estimated to be lower, respectively by 29% (95% CI 14%-40%), 27% (95% CI 11%-39%), and 42% (95% CI 30%-52%) than female counterparts of the same latent frailty status. Frailty status was equivalently associated with mortality for men and women. More striking differences emerged with respect to age: while each criterion was estimated to become more prevalent with increasing age—after accounting for overall frailty status, such a trend was notably stronger for slowness than for any of the other criteria—reaching more than tenfold increased prevalence in the oldest versus the youngest old. The hazard ratio for the association of frailty status with mortality attenuated considerably with older age—with more than a twofold distinction between older adults aged 65-69 and those 85 years and older. **Conclusion:** Strategies to increase comparability of frailty measurements across demographic groups may be needed if frailty assessment is to improve health equitably for all older adults.

Communication 2: *Derivation of a measure of physiological multisystem dysregulation: Results from WHAS and Health ABC,* Alden L. Gross (Johns Hopkins Bloomberg School of Public Health, Baltimore, USA)

Background: Physical frailty is thought to be a manifestation of multisystem dysregulation at the physiological level. The objectives of this study were to operationalize a theory-driven measure of multisystem physiological dysregulation using biomarkers from multiple systems, and to empirically test for measurement differences in the measure by key background characteristics (age, race, and study membership). **Methods:** We used data from the Women's Health and Aging Studies (WHAS) I and II (N=649), and replicated findings in the Health ABC study (N=1,514). We identified 12 biomarkers representing multiple systems including stress response (e.g., inflammation and endocrine system) and energy regulation. We estimated a series of confirmatory factor analyses (CFA) to evaluate the interplay between individual physiological systems and underlying multisystem dysregulation. Models corresponded to a unidimensional CFA of biomarkers, a second-order CFA of biomarkers in which multisystemic dysregulation leads to dysregulation in particular physiological systems and in turn abnormalities in individual biomarkers, and a bifactor CFA in which specific factors for physiological systems and multisystemic dysregulation each independently contribute to variability in individual biomarkers. We tested for measurement invariance of the factor by age, race, and study membership (WHAS I, WHAS II, Health ABC). **Results:** A bifactor CFA fit the data well in both WHAS and Health ABC (RMSEAs<0.03; CFI>0.95). The factor structure was invariant across age, sex, and study membership. Findings were replicated in Health ABC. **Conclusions:** Biomarker data from two epidemiologic studies lend support for the construct of multisystem physiological dysregulation. Contributions of independent physiological systems should also be acknowledged empirically in models of physiological multisystem dysregulation.

Communication 3: *Measuring Frailty Status in Older Adults with Acute Myocardial Infarction in Population-based Studies: Feasibility to Capture Prevalence and Effect Measure Modification,* Abdulla Damluji (Johns Hopkins University, Baltimore, USA)

Background: While clinical assessment of frailty is used to predict mortality and disability in the context of cardiovascular disease, these domains are not routinely measured in clinical practice and in large population-based studies. **Objective:** We aimed to estimate the prevalence of frailty by age, sex, and race in a large population-based cohort of older adults with acute myocardial infarction (AMI), and to test whether frailty modifies the relationship between treatment with percutaneous coronary intervention (PCI) and in-hospital mortality. **Methods:** We used the Premier Healthcare Database to identify hospitalizations of older adults with primary diagnoses of AMI. We classified individuals as frail or not using the validated Claims-based Frailty Index (CFI) algorithm, with which we generated a frailty score for each patient using 21 variables derived from inpatient and outpatient data from 6 months prior to the first AMI admission. To evaluate whether frailty is an effect measure modifier, univariable logistic regression analysis of percutaneous revascularization with PCI on in-hospital mortality during index admission was performed stratified by baseline frailty status. **Results:** From 2000 to 2016, we identified 469,390 encounters for patients >= 75 years admitted with first AMI. In the overall cohort, the prevalence of frailty tended to be higher in (1) very old adults, (2) among females than male counterparts (24% vs. 14%, p <0.001), and (3) among African Americans, and lowest among Caucasians (Blacks 43%, Hispanics 35%, Other 39%, Caucasians 12%, p <0.001). In each age stratum, frailty was associated with in-hospital mortality. Frail men and frail women had similar rates of in-hospital mortality. While frail older adults benefited from PCI with in-hospital mortality reduction of 41% (OR 0.59, CI 0.55-0.63), non-frail patients benefited more from PCI, approaching 51% (OR 0.49, CI 0.47-0.50). **Conclusions:** In the U.S., frailty is more common among females and patients who belong to ethnic minorities during first AMI hospitalization. While this vulnerable patient group is at an increased risk for hospital mortality, judicious use of revascularization with PCI in frail older patients still confers survival benefit.

S9- SELECTION OF RELEVANT OUTCOMES IN SARCOPENIA: A DISCRETE CHOICE EXPERIMENT.

Jean-Yves Reginster[1,2] ((1) Department of Public Health, Epidemiology and Health Economics, University of Liège, Liège, Belgium; (2) WHO Collaborating Centre for Public Health Aspects of Musculo-Skeletal Health and Aging)

Communication 1: *Identification and prioritization of important outcomes for patients in sarcopenia* Charlotte Beaudart[1,2], Olivier Bruyère[1,2], Jean-Yves Reginster[1,2] Jürgen Bauer[3], Cyrus Cooper[4,5], Alfonso J. Cruz-Jentoft[6], Charlotte Dupuy[7], Francesco Landi[8], Médéa Locquet[1,2], Stefania Maggi[9], Rene Rizzoli[10], Yves Rolland[7], N. Vaquero[6], Mickael Hiligsmann[11] ((1) Department of Public Health, Epidemiology and Health Economics, University of Liège, Liège, Belgium; (2) WHO Collaborating Centre for Public Health Aspects of Musculo-Skeletal Health and Aging; (3) Center for Geriatric Medicine, University of Heidelberg, Heidelberg, Germany; (4) MRC Lifecourse Epidemiology Unit, University of Southampton, Southampton, England, UK; (5) NIHR Musculoskeletal Biomedical Research Unit, University of Oxford, Oxford, UK; (6) Servicio de Geriatría, Hospital Universitario Ramón y Cajal (IRYCIS), Madrid, Spain; (7) Gérontopôle of Toulouse, University of Toulouse III, CHU Purpan, Toulouse, France; (8) Department of Geriatrics, Neurosciences and Orthopedics, Catholic University of the Sacred Heart Rome, Milano, Italy; (9) National Research Council, Neuroscience Institute, Aging Branch, Padua, Italy; (10) Service of Bone Diseases, Geneva University Hospitals and Faculty of Medicine, Geneva, Switzerland; (11) Department of Health Services Research, CAPHRI Care and Public Health Research Institute, Maastricht University, Maastricht, The Netherlands)

Background: While Sarcopenia, defined by a progressive loss of muscle mass and function, has been shown to be associated with several individual and public health outcomes. Identifying hard clinical outcomes of patients with sarcopenia is an important step in designing valid and useful clinical trials and outcome studies. **Objectives:** This study aims first to identify which outcomes are important for patients with sarcopenia and second to assess the most importance ones. **Methods:** The identification and prioritization of outcomes for patients with sarcopenia was conducted following a 4-step procedure: 1) a literature review to generate an initial list of outcomes of sarcopenia; 2) an expert consultation (n=11) to restructure initial outcomes and validate them; 3) three focus groups with participants suffering from sarcopenia (2 in Belgium, 1 in Spain) to validate these outcomes, to generate additional ones and to rank the most important outcomes; 4) an expert meeting (n=11) to identify the 5 most important outcomes of sarcopenia based on the results of the focus groups. **Results:** In the first step, the initial list of outcomes comprised 6 different outcomes: mortality, functional decline, hospitalisation, falls, fracture and length of hospitalisation. With the second step, the list was extended to 9 outcomes including mortality, hospitalisation, falls, fractures, institutionalisation, quality of life, difficulties in self-care, difficulties in moving and difficulties in domestic duties. In the third step, the focus groups with sarcopenic subjects (n=19, 6 men and 13 women, mean age 78 years) identified a large number of additional outcomes such as fatigue, affected mood, physical and mental slowness, loss of balance, fear of walking, etc; and each patient ranked the five most important ones. Based on the ranking of all the outcomes during the focus groups, experts agreed on the 5 most important outcomes: "quality of life", "mobility", "domestic activities", "fatigue" and "falls". **Conclusion:** This study identified and prioritized important outcomes for sarcopenia. The five important outcomes were used, during a next step, in a discrete-choice experiment to further elicit the relative importance of these outcomes in a larger group of patients and experts.

Communication 2: *A cross-European discrete choice experiment to assess patients' preferences for sarcopenia outcomes,* Mickael Hiligsmann[1], Charlotte Beaudart[2,3], Olivier Bruyère[2,3], Emmanuel Biver[4], Jürgen Bauer, MD[5], Alfonso J. Cruz-Jentoft[6], Antonella Gesmundo[7], Sabine Goisser[5], Francesco Landi[8], Medea Locquet[2,3], Stefania Maggi[9], Rene Rizzoli[4], Yves Rolland[10], N. Vaquero[6], Jean-Yves Reginster[2,3] ((1) Department of Health Services Research, CAPHRI Care and Public Health Research Institute, Maastricht University, Maastricht, the Netherlands; (2) Department of Public Health, Epidemiology and Health Economics, University of Liège, Liège, Belgium; (3) WHO Collaborating Centre for Public Health Aspects of Musculo-Skeletal Health and Aging; (4) Service of Bone Diseases, Geneva University Hospitals and Faculty of Medicine, Geneva, Switzerland; (5) Center for Geriatric Medicine, University of Heidelberg, Heidelberg, Germany; (6) Servicio de Geriatría, Hospital Universitario Ramón y Cajal (IRYCIS), Madrid, Spain; (7) Department of Medicine, University of Padua, Padova, Italy; (8) Department of Geriatrics,Neurosciences and Orthopedics, Catholic University of the Sacred Heart Rome, Milano, Italy; (9) National Research Council, Neuroscience Institute, Aging Branch, Padua, Italy;(10) Gérontopôle of Toulouse, University of Toulouse III, CHU Purpan, Toulouse, France)

Background: It is important to assess how patients trade-offs between the five most important sarcopenia outcomes previously identified. Discrete-choice experiment (DCE), a stated-preference method, is nowadays increasingly used to detect preferences in healthcare and represents a useful method for quantifying the relative importance of attributes and the trade-offs that respondents make between them. **Objectives:** This study aims to evaluate the preferences of patients for sarcopenia outcomes by establishing how they trade between the five previously identified outcomes using a DCE. **Methods:** In the DCE survey, patients were repetitively asked to choose which one of two patients (Patient A and Patient B) suffering from sarcopenia who were eligible to receive a drug treatment to improve their muscle mass and muscle function and then to reduce their sarcopenia, deserves the most a treatment. The two patients presented different levels of risk for the five outcomes previously identified, i.e. quality of life, mobility, domestic activities, fatigue and falls. An efficient experimental design was used to construct the 12 choice sets and a dominance choice set was added for detecting validity of responses. The questionnaire was pilot tested with 10 experts of sarcopenia and 20 sarcopenic subjects to check interpretation problems and face validity. The DCE was thereafter conducted in subjects of 65 years and older suffering from sarcopenia recruited in Belgium, France, Switzerland, Germany, Spain and Italy. Sarcopenia was diagnosed according to valid published definitions (EWGSOP, FNIH, Baumgartner criteria, IWGS). A mixed logit panel data model was used to estimate patients' preferences and a latent class model was conducted to identify profiles of responses. **Results:** A total of 228 patients completed the survey of which 26 were excluded because they failed the dominance test. 202 sarcopenic subjects were thus included for the analysis (68% of women; mean age of 78 years). All five sarcopenia outcomes were shown to be significant and thus important for patients. Overall, the most important sarcopenia outcome was mobility (29%) followed by the ability to manage domestic activity (23%), the risk of falls (18%), fatigue (17%) and quality of life (12%). Significance variations in preferences between patients were observed for mobility and domestic activity. The latent class model identified two classes of respondents with class

probabilities of 56% and 44%, respectively. In the first class, patients valued the most the mobility (42%) followed by ability to manage domestic activity (24%) and risk of falls (17%). In the second class, fatigue was the most important outcome (27%) followed by mobility (19%), domestic activity (19%), risk of falls (18%) and quality of life (17%). **Conclusion:** This study suggests that all five sarcopenia outcomes were important for patients. Overall, the most important outcomes were mobility and ability to manage domestic activity although variations in preferences were observed between respondents.

SPRINTT SYMPOSIUM: SARCOPENIA & PHYSICAL FRAILTY IN OLDER PEOPLE: MULTI-COMPONENT TREATMENT STRATEGIES. Roberto Bernabei *(Università Cattolica del Sacro Cuore, Roma, Italy)*

CONFERENCE

C1- RACE DEPENDENT CHANGES TO GENE EXPRESSION IN FRAIL, MIDDLE AGED ADULTS. Calais S. Prince[1], Nicole Noren Hooten[1], Nicolle Mode[1], Yongqing Zhang[2], Ngozi Ejiogu[1], Kevin Becker[2], Alan B. Zonderman[1], Michele K. Evans[1] *((1) Laboratory of Epidemiology and Population Sciences, National Institute on Aging, National Institutes of Health, Baltimore, MD, USA; (2) Laboratory of Genetics and Genomics, National Institute on Aging, National Institutes of Health, Baltimore, MD, USA)*

Backgrounds: Frailty prevalence is 8.6% in adults between 65-69 years old in the United States and increases with age. Most clinical and molecular studies focus on older, largely white cohorts even though the prevalence of frailty among older adults is higher among minorities. However, our work in the Baltimore-based Healthy Aging in Neighborhoods of Diversity across the Life Span (HANDLS) study found that frailty prevalence is higher among whites between the ages of 45-54 years old compared with African Americans (AA). Understanding the molecular drivers of frailty in AA and whites at risk for the accelerated aging phenotype may provide important insight into aging and the biology of health disparities. **Objectives:** We hypothesize that frailty is associated with alterations in gene expression which is influenced by race and sex. **Methods:** We analyzed genome-wide transcriptional changes associated with frailty in a diverse cohort (n = 16; 45-49 years old; non-frail/frail; Morley FRAIL questionnaire; AA/white, women/men). Total RNA was isolated from peripheral blood mononuclear cells and subjected to total RNA sequencing. We analyzed differential gene expression patterns, parametric analysis of gene set enrichment (PAGE) analysis. To visualize the functional interactions between differentially expressed genes, we constructed interaction networks. Differential gene expression was validated in an expanded cohort (n = 52) using RT-qPCR. **Results:** We identified 5,082 genes differentially expressed with frailty. The PAGE and network analyses identified race, not sex, dependent, significantly altered gene sets and interactions associated with hypoxia, gene transcription, innate immune response, and inflammation. The expanded, gene expression validation study showed a significant two-way interaction between frailty status and race for IL1B and EGR1 expression, a cytokine associated with fever induction and a transcription factor associated with replicative senescence. The expression of SLC2A6 (a glucose transporter), FCGR3B (membrane bound receptor associated with calcium mobilization and neutrophil degranulation), and C17orf56 (accessory protein) are decreased with frailty. **Conclusion:** Differential molecular markers for frailty depend upon race in middle aged adults, which could explain the differences in frailty prevalence. Our novel approach and diverse, community-based cohort provide some evidence for demographic dependent, divergent biological pathways underlying frailty diagnosis, which warrants further investigation.

C2- TRANSLATING UROLITHIN A BENEFITS ON MUSCLE MITOCHONDRIA INTO HUMANS. A. Singh[1], P. A. Andreux[1], W. Blanco-Bose[1], P. Aebischer[2], J. Auwerx[3], C. Rinsch[1] *((1) Amazentis SA, Switzerland; (2) Brain Mind Institute, Ecole Polytechnique Fédérale de Lausanne, Switzerland); (3) School of Life Sciences, Ecole Polytechnique Fédérale de Lausanne, Switzerland)*

Backgrounds: Urolithin A (UA) is a natural metabolite produced by the gut microflora upon ingestion of ellagitannins, a class of molecules that is abundant in pomegranates, nuts and berries. We have published a study demonstrating that UA induces mitophagy in vivo following oral consumption in worms and in rodents (Ryu et al., Nature Medicine 2016). In worms, UA extends lifespan, prolongs normal activity, including mobility and pharyngeal pumping, and maintains mitochondrial respiratory capacity during aging. These effects translate to rodents, where UA improves exercise capacity in two different models of age-related decline of muscle function. **Objectives:** We will discuss clinical results clearly demonstrating the safety of UA in humans as well as the ability of UA to positively impact mitochondrial biomarkers following 28 days oral UA administration. Ongoing efforts continue to build on these findings and UA is being investigated in long term Phase 2 studies and in other experimental pre-clinical models where mitochondrial dysfunction is a hallmark feature. **Methods:** Recently, in a first-in-human randomized, double blind, placebo controlled study (NCT02655393), we have characterized the safety profile of UA in elderly, sedentary human subjects (n=60). **Results:** UA was found to be safe across all oral dosing regimens and no serious or any product related non-serious adverse effects were recorded during the single and multiple ascending studies. UA was bioavailable in human plasma and detected in the skeletal muscle. In addition to safety and bioavailability endpoints, we have measured biomarkers linked to mitochondrial function in the skeletal muscle, including mitochondrial gene expression profiles in skeletal muscle biopsies and plasma metabolomics. Results from another recently published non-interventional clinical study (Andreux et al., Scientific Reports; 2018) in pre-frail elderly showing how mitochondrial dysfunction is impaired in the muscle during age related muscle decline will also be discussed and compared at the transcriptomic level between the two studies. **Conclusion:** UA could be a promising approach to both manage and treat muscle and mitochondrial functional decline in humans

C8- DEVELOPMENTS IN THE PATHOPHYSIOLOGIC BASIS OF FRAILTY IN TYPE 2 DIABETES AND EMERGING ROLES OF APELIN IN FUTURE CLINICAL TRIALS Cedric Dray *(Unité Inserm 1048, France)*

C4- COMPENSATORY ADJUSTMENTS IN MOTOR UNIT BEHAVIOR DURING FATIGUE DIFFER FOR YOUNGER VERSUS OLDER MEN. Matt S. Stock[1], Jacob A. Mota[2], Dennis P. Kwon[1], Mark Kennedy[1], Eric J. Sobolewski[3], Youngdeok Kim[4], Joaquin Gonzales[4] *((1) University of Central Florida, Orlando, FL, USA; (2) University of North Carolina at Chapel Hill, Chapel Hill, NC, USA; (3) Furman University, Greenville, SC, USA; (4) Texas Tech University, Lubbock, TX, USA)*

Backgrounds: The ability to maintain force as a muscle fatigues is supplemented by compensatory adjustments in the nervous system's

control of motor units. While some studies have reported that older adults demonstrate less fatigue than their younger counterparts, it is unclear if changes in motor unit control differ for these two age groups. **Objectives:** We sought to compare vastus lateralis motor unit recruitment and firing rate data for younger versus older men during an isometric fatigue protocol. We specifically assessed three attributes of motor unit control: 1) the recruitment of additional high threshold motor units, 2) firing rates, and 3) recruitment thresholds. **Methods:** Twelve younger (mean ± SD [range] age = 25 ± 3 [21-30] years) and 12 older (75 ± 8 [65-91] years) men with a BMI ≤ 30 kg/m2 performed contractions of the knee extensors at 50% of maximal voluntary contraction (MVC) force until exhaustion. Participants increased isometric force from 0-50% MVC in five seconds, held 50% MVC for 15 seconds, and decreased force from 50-0% MVC in five seconds. Throughout testing, bipolar surface electromyographic (EMG) signals were detected from the vastus lateralis. A surface EMG signal decomposition algorithm was used to quantify the action potential amplitude (MUAPT [mV]), mean firing rates, and recruitment threshold of each motor unit. For the latter two variables, our analyses included motor units that were active throughout the fatiguing protocol. **Results:** There was no difference for time to task failure ($p = .362$, $d = 0.381$). There were, however, differences in motor unit behavior. Both groups showed increases in MUAPT throughout the fatiguing protocol (younger and older slopes = 0.0174 ± 0.0123 and 0.0073 ± 0.0123 mV/contraction, respectively [$p = .082$, $d = .710$]), but the change was more linear for the younger adults (mean r2 values = 0.565 and 0.455). The firing rate data showed an increase over time for the younger ($p < 0.001$), but not the older ($p = 0.579$), men. Similarly, recruitment thresholds significantly decreased only for younger men ($p = 0.001$). **Conclusion:** Compared with younger men, changes in motor unit control during fatiguing contractions are much more subtle in older men.

C5- IS FRAILTY ASSOCIATED WITH WORSE OUTCOMES AFTER TOTAL JOINT REPLACEMENTS?

Lisa A. Mandl[1,2], Charles N. Cornell[1,2]; Michael B. Cross[1,2], Alejandro Gonzalez Della Valle[1,2], Mark P. Figgie[1,2], Seth A. Jerabek[1,2], Justin T. Do[1], Mayu Sasaki[1], Nathaniel Hupert[2], Jackie Finik[1], Steven K. Magid[1,2] ((1)Hospital for Special Surgery, New York, NY, USA; (2) Weill Cornell Medicine, New York, NY, USA)

Backgrounds: Frailty, "a clinically recognizable state of increased vulnerability resulting from aging-associated decline in reserve and function across multiple physiologic systems", is a potential modifiable risk factor for poor outcomes after total joint arthroplasty (TJA, i.e., total hip or knee replacement, THR/TKR). **Objectives:** To determine whether frailty is associated with clinical outcomes 1-year after TJA. **Methods:** Patients >=65yo scheduled for elective TJA were recruited from a musculoskeletal specialty hospital. Frailty was measured using validated criteria. A variety of instruments, including Hip/Knee Injury and Osteoarthritis Outcome Score (HOOS/KOOS) and Katz ADL were administered pre-operatively and at 1-year. Postoperative adverse events were evaluated by chart review and self-report. All variables significant at the 0.05 level in univariate analysis were assessed by backwards selection for inclusion in a multivariable regression model; age and gender were forced in to all models, and other variables were retained if their significance remained <= 0.05. **Results:** 797 subjects were enrolled for 325 THR/474 TKR, with mean age 72 years (range 65-94), 98% Caucasian, 63% female, and 7.5% frail. 94% follow-up of eligible cases yielded 524 cases with 1-year data. Regression models showed that (1) preoperative number of frailty elements predicted being an OMERACT-OARSI responder at 1-year in TJA, (OR 1.64 in THA and 1.43 in TKA, p<0.05); (2) pre-operative Katz ADLs predicted 1-year HOOS Function in Daily Living (β -10.9 +/- 2.6 SD, p<0.001) and 1-year HOOS Sports and Recreation (β -17.0 +/- 5.1 SD, p<0.001); and (3) pre-operative number of frailty elements also predicted HOOS Sports and Recreation at 1-year (β -6.13 +/- 1.6 SD, p<0.001). Frailty was not a significant predictor of severe AEs. **Conclusion:** The number of frailty elements, and especially having poor Katz ADL disability score, significantly increased the risk of poor functional outcomes after TJA. Monitoring the development of frailty or ADL disability may help inform optimal timing of TJA in patients contemplating this elective procedure. Prospective studies of OA patients contemplating TJA are needed.

C6- THE ASSOCIATION BETWEEN MUSCLE MASS ASSESSED BY D3CR DILUTION WITH INCIDENT ADL AND IADL DISABILITY IN COMMUNITY DWELLING OLDER MEN.

Peggy M. Cawthon, Terri Blackwell, Steven R. Cummings, Eric S. Orwoll, Kate A. Duchowny, Deborah Kado, Katie L. Stone, Kristine E. Ensrud, Jane A. Cauley, William J. Evans (California Pacific Medical Center, Alameda CA, USA)

Backgrounds: Low muscle mass has been postulated to be a risk factor for disability. Previous studies have reported inconsistent associations of muscle mass with disability. Limitations of this previous work include use of dual energy x-ray absorptiometry (DXA) to measure lean mass (which includes water, muscle, and all other non-bone non-fat tissue), not muscle mass per se. We have previously shown that men with low muscle mass assessed by D3Cr (deuterated creatine) dilution are more likely to have incident injurious falls and worse physical performance. However, the relation between D3Cr muscle mass and incident ADL (activities of daily living) and IADL (instrumental ADL) disability is unknown. **Objectives:** Among men free of disability at the Year 14 Visit of the MrOS study (mean age 84.2 yrs) we tested the hypothesis that men with lower D3Cr muscle mass (standardized to body mass) were more likely to develop disability (unable to complete IADLs or ADLs) over 2.2 years. We also hypothesized that similar associations would not be seen with DXA-based appendicular lean mass/height2 (ALM/ht2). **Methods:** Logistic models determined the OR for ADL and IADL disability separately. Models were adjusted for age, clinical center, alcohol use, smoking status, comorbidities, physical activity, percent fat, exhaustion, and cognitive function. **Results:** Men in the lowest quartile of D3Cr muscle mass/wgt were much more likely develop ADL disability (OR, Q1 vs Q4 for ADL disability: 3.5, 95% CI: 1.4, 8.8; p for trend across quartiles <.001); or IADL disability (OR, Q1 vs Q4 for IADL disability 2.9, 95% CI: 1.4, 6.3; p for trend across quartiles <.001). DXA ALM/ht2 was not associated disability (p>0.05 for all models). **Conclusion:** These results suggest that low D3Cr muscle mass is a strong risk factor disability in older men, while DXA ALM/ht2 is not useful for prediction of disability. Our results also provide evidence that the role of low muscle mass in adverse health outcomes may be underappreciated. These preliminary results should be further evaluated in other populations including women and younger men and populations with acute muscle wasting.

C7- DIFFERENCES IN AMINO ACID COMPOSITION BETWEEN VARIOUS TYPES OF PROTEIN SUPPLEMENTS.

Nathaniel Johnson, Kara Trautman, Christopher Kotarsky, Nathan Dicks, Kyle Hackney, Sherri Stastny (Department of Health, Nutrition, and Exercise Sciences, North Dakota State University, Fargo, ND, USA)

Backgrounds: Adequate protein intake is important for maintaining muscle mass. Animal-based foods typically provide better

quality protein than plant-based foods. However, this disparity may not exist within the context of protein supplements where manufacturing and processing can affect protein quality. Analysis of the composition and cost of protein supplements may help consumers make prudent decisions when purchasing protein supplements. **Objectives:** The goal of this preliminary work was to determine if there are differences in protein quality and cost between animal and plant-based protein supplements. **Methods:** Ten different protein supplements, two bars and eight powders, were analyzed for their amino acid and protein composition using cation-exchange chromatography and post-column ninhydrin derivatization and quantitation. Only one sample was analyzed for each product. Total percentages of protein and leucine by weight (%) were used to measure protein quality. Costs were estimated from a national online retailer. Six protein supplements, including both bars, contained protein sources that were entirely-animal based, two powders used entirely plant-based protein sources, one powder contained both animal and plant-based protein sources, and one powder was a branched-chain amino acid supplement. **Results:** Total protein and leucine were highest in the branched-chain amino acid supplement (74.02%, 14.22% respectively). The two protein bars were lowest in total protein (19.30%, 28.83% respectively) and leucine (1.74%, 2.77% respectively). Animal based protein powders had total protein contents ranging from 60.81 to 68.90%, whereas plant-based powders had lower total protein contents of 52.38, and 43.63%. Similarly, animal-based powders had greater leucine contents with amounts between 5.44% and 7.04%; the two plant-based powders had leucine contents of 4.18% and 3.45%. On a per gram of total protein basis, animal-based powders have the lowest cost, ranging from $0.037/g to $0.157/g, plant-based powders are slightly more expensive costing $0.088/g and $0.111/g, and bars are the most expensive costing $0.118/g and $0.236/g. **Conclusion:** Animal-based protein powders have better protein quality than plant-based powders and can be less expensive than plant-based powders on a per gram protein basis. Bars provide less total protein and leucine and are on a per gram of protein basis more expensive.

C8- ALLOGENEIC BONE MARROW-DERIVED MESENCHYMAL STEM CELLS AS A TREATMENT FOR AGING-RELATED INDICATIONS. J Hare, LLC Longeveron *(Miami, FL, USA))*

Backgrounds: A chronic proinflammatory state is a prominent feature of many aging-related conditions, such as Alzheimer's disease, the metabolic syndrome, and Aging Frailty. In particular, the cytokine TNF-alpha has been correlated with increased mortality in elderly adults. Stem cell depletion is also a key mechanism postulated to contribute to aging Frailty. Allogeneic human Mesenchymal Stem Cells (MSCs) are potent immuno-modulatory cells that can modulate cytokine production from lymphocytes and myeloid-derived immune cells without producing immunosuppressive toxicity. Importantly, allogeneic MSCs are immune-privileged and have exhibited a high safety profile in numerous clinical studies. Together these properties render allogeneic MSCs an attractive therapeutic candidate for treating Alzheimer's disease, the metabolic syndrome, and Aging Frailty. **Objectives:** To establish the safety and efficacy of Longeveron Mesenchymal Stem Cells (LMSCs), a proprietary formulation of allogeneic MSCs, in reducing markers of inflammation and improving measures of physical and mental functioning, and quality of life. These endpoints are being evaluated in clinical trials for Alzheimer's disease (ClinicalTrials.gov NCT02600130), the metabolic syndrome (NCT02587572), and Aging Frailty (NCT03169231 and NCT02982915). **Methods:** Sample size was determined as appropriate for each study. Primary endpoints include safety of LMSCs as assessed by treatment related-serious adverse events. Secondary endpoints include efficacy measures resulting from therapeutic intervention. Post-treatment changes in biomarkers are compared against baseline and placebo controls, and include immune biomarkers and cytokines, e.g., TNF-alpha, IL-2, IL-6, and VEGF. **Results:** We have currently treated n=114 patients with LMSCs administered intravenously. In our published studies to date, there have been no treatment-related serious adverse events or significant donor specific immune reactions. TNF-alpha levels decreased at 6 months. Treated groups had significant improvements in physical performance measures and decreased inflammatory makers. **Conclusion:** LMSCs are safe and immunologically tolerated in individuals with aging Frailty and Alzheimer's disease. Improvements in functional and immunologic status support the ongoing conduct of larger clinical trials with the potential to expand health span in the aging population. This work was supported by the Alzheimer's Association (grant PTC C-16-422443), the National Institutes of Health/National Institute of Aging (grant 1R44AG062015-01 and 1R42AG054322-01A1), and the Maryland Stem Cell Research Foundation (MSCRF) TEDCO (2018-MSCRFCL-4346).

C9- DISTINGUISHING AMONG DYNAPENIA WITHOUT FRAILTY, FRAILTY WITHOUT DYNAPENIA, AND FRAILTY WITH DYNAPENIA: IS IT CLINICALLY RELEVANT?

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Backgrounds: Sarcopenia is a key potentially modifiable physiologic substrate for the development of frailty and disability. Albeit inter-related, sarcopenia may occur without frailty, and vice-versa. Dynapenia is a key criterion for determination of sarcopenia, as well as frailty. Research seeking to characterize the extent to which it may be clinically relevant to distinguish among dynapenia without frailty, and frailty with and without dynapenia is warranted, as it may help guide implementation of sarcopenia/frailty-related assessments in the clinical setting, and elucidate more targeted intervention for disability prevention. **Objectives**: To compare incident disability risk according to the conjoint and separate presence of frailty and dynapenia. **Methods:** Prospective study using data pooled from 784 community-dwelling women 70-80 years old participating in the Women's Health and Aging Studies I and II (Baltimore, USA). Median follow-up was 3 years. Self-reported difficulty performing >=3 basic (ADLs) and instrumental activities of daily living (IADLs) were disability outcomes. Frailty phenotype (Fried et al.) and dynapenia (grip strength<20th percentile for body-mass-index) were prognostic measures. Discrete-time survival modeling compared ADL and IADL incidence risk separately as a function of combined frailty and/or dynapenia status with adjustment for demographics and comorbidities. **Results:** Incident ADL disability risk was increased for those who met criteria for both frail and dynapenia (HR: 6.05; 95%CI: 3.20-11.43), but not for those with frailty without dynapenia (HR: 1.39; 95%CI: 0.32-6.06), or with dynapenia alone (HR: 1.43; 95%CI: 0.67-3.02), as compared to those with neither. Frail subjects with dynapenia had 4 times the risk of ADL disability than frail subjects without dynapenia (HR=4.34; 95% CI = 0.99 -19.01; p=.052). A stepwise IADL disability risk gradient was observed: none (reference), dynapenia alone (HR:

0.87; 95%CI: 0.28-2.72), frailty without dynapenia (HR: 3.77; 95%CI: 1.06-13.36), and both frailty and dynapenia (HR: 7.85; 95%CI: 3.89-15.84). **Conclusion:** Disability risk varied meaningfully among frail older women depending on whether they had dynapenia or not, as well as among those with dynapenia depending on frailty status. Results provide preliminary support for further evaluation on the prognostic importance of distinguishing among varying combinations of dynapenia – and, speculatively, sarcopenia – and frailty status in the clinical setting.

C10- IMPROVING MUSCLE, BONE AND MOBILITY IN OLD AGE. Prof. Gustavo Duque *(Australian Institute for Musculoskeletal Science (AIMSS), Australian and New Zealand Society for Sarcopenia and Frailty Research (ANZSSFR), St Albans VIC, Australia)*

C11- ROLE OF MALNUTRITION IN THE DEVELOPMENT OF FRAILTY AND COST IMPLICATIONS AMONG COMMUNITY-DWELLERS. Leocadio Rodríguez-Mañas[1], Suzette Pereira[2] *((1) Geriatric Department Fundación de Investigación Biomédica, Hospital Universitario de Getafe, Getafe, Spain; (2) Abbott Nutrition, Columbus, OH, USA))*

C12- FRAILTY AND SARCOPENIA IN LATIN AMERICA. PRESENT AND FUTURE. Clemente Zuniga-Gil *(Head of the geriatric department at Tijuana's general hospital. universidad autonoma de Baja California. Mexico)*

C13- PREDICTING FIRST TIME INJURIOUS FALLS IN OLDER MEN AND WOMEN LIVING IN THE COMMUNITY – THE FIF SCREENING TOOL. Stina Ek[1], Debora Rizzuto[1], Amaia Calderon Larrañaga[1], Erika Franzén[2,3], Weili Xu[1], Anna-Karin Welmer[1,2, 3,4] *((1) Aging Research Center (ARC), Department of Neurobiology, Care Sciences and Society, Karolinska Institutet and Stockholm University, Stockholm, Sweden; (2) Division of Physiotherapy, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet, Stockholm, Sweden; (3) Allied Health Professionals, Function Area Occupational Therapy & Physiotherapy, Karolinska University Hospital, Stockholm, Sweden; (4) Stockholm Gerontology Research Center, Stockholm, Sweden)*

Backgrounds: Falls among older people are of urgent public health concern due to their medical and economic consequences, especially in light of an increasing older population. Current approaches to fall prevention typically relies on secondary prevention, which aims at reducing the risk for falls among people who have previously fallen and were identified after a fall. An even more effective approach is early prevention, which implies identifying older adults at high risk of falls who have not fallen previously, and who may benefit from being referred to a further fall risk assessment and primary preventive interventions. **Objectives:** We aimed to create a screening tool to predict first time injurious falls in community-living older men and women. **Methods: Design:** Longitudinal cohort study between 2001 and 2011. **Setting:** The Swedish National Study on Aging and Care in Kungsholmen (SNAC-K), Sweden. **Participants:** Community-living older adults (n=2808, >=60 years). **Measurements:** Injurious falls were defined as hospitalization or receipt of outpatient care because of a fall within five years of baseline. Data on the risk factors for falls were collected through interviews, clinical examinations, and tests at baseline. Several previously established fall risk factors were identified for the development of the screening tool. The tool was formulated based on the β coefficients from sex-specific multivariate Cox proportional hazards models The discriminative power was assessed using Harrell's C statistic. **Results:** Old age, living alone, being dependent in instrumental activities of daily living (IADL) and impaired balance were the factors included in the final score of the First Injurious Fall (FIF) screening tool. The predictive values (Harrell's C statistic) for the scores were 0.75 for women and 0.77 for men. The sensitivity and specificity at the Youden cut-off points were 0.69 and 0.70 for women, and 0.72 and 0.71 for men. **Conclusion:** The FIF screening tool can be quickly and easily administered. Thus, it is ideal for use in primary care or in public health interventions to identify older men and women at high risk of first-time injurious falls who may benefit from primary preventive interventions.

ORAL COMMUNICATIONS

OC1- MEMBRANE LIPID REPLACEMENT WITH ORAL NTFACTOR LIPIDS® TO RESTORE MITOCHONDRIAL FUNCTION, REDUCE FATIGUE, PAIN AND OTHER SYMPTOMS AND IMPROVE QOL INDICATORS IN AGED SUBJECTS. Garth L. Nicolson[1], Paul Breeding[2] *((1) Dept. of Molecular Pathology, The Institute for Molecular Medicine, Huntington Beach, CA, USA; (2) Blue Hole Wellness, San Antonio, TX, USA)*

Backgrounds: Aging is associated with decreased mitochondrial function, which is directly related to muscle function, fatigue, pain and other symptoms. We have found a principal defect in aged individuals is loss of inner mitochondrial membrane (IMM) trans-membrane potential due to membrane lipid damage by age-related excess ROS that damages membrane lipids and directly translates to loss of IMM trans-membrane potential and lower total cellular ATP production. **Objectives:** We have found that replacement of damaged IMM glycerolphospholipids restores IMM trans-membrane potential and reduces fatigue, pain and other symptoms. In aged patients who have lost IMM function, Membrane Lipid Replacement with oral glycerolphospholids can restore IMM function and reduce symptoms. We have used a placebo-controlled cross-over trial to confirm this in aged patients. We have also found that fatigue, pain and other symptoms as well as QOL indicators can be significantly improved in aged patients taking 4 g/day of oral NTFactor Lipids®. **Methods:** Mitochondrial function was measured by using redox dyes and FACS to measure IMM trans-membrane potential. Fatigue, pain, and other symptoms and QOL indicators were measured by patient severity scores in validated survey forms. **Results:** A placebo-controlled cross-over trial confirmed that oral NTFactor Lipids® can improve IMM trans-membrane potential and mitochondrial function while significantly reducing fatigue (p<0.001) in aged subjects. Using aged patients with chronic fatigue, CFS, fibromyalgia and other dx oral NTFactor Lipids® significantly reduced pain (p<0.001), fatigue (p<0.001) and GI symptoms (p<0.001) while improving mitochondrial function and QOL indicators (p<0.001). There was no evidence of any adverse reactions or toxicity, and other studies have shown that 20X higher daily doses of oral membrane glycerolphospholipids are completely non-toxic. **Conclusion:** Aging-related loss of mitochondrial function and severity of symptoms (fatigue, pain, and other symptoms) and reductions in QOL can be significantly improved in aging subjects using Membrane Lipid Replacement with oral NTFactor Lipids® with no adverse events or evidence of any toxicity.

OC2- OLDER ADULTS WITH BOTH COGNITIVE AND PHYSICAL IMPAIRMENTS ARE AT HIGHEST RISK TO DEVELOP DEMENTIA: A 12-YEAR LONG POPULATION-BASED STUDY.

Giulia Grande[1], Debora Rizzuto[1], Davide L Vetrano[1,2], Anna Marseglia[1], Nicola Vanacore[3], Erika Laukka[1], Anna-Karin Welmer[1]; Laura Fratiglioni[1,4] *((1) Aging Research Center, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet and Stockholm University, Stockholm, Sweden; (2) Department of Geriatrics, Catholic University of Rome, Italy; (3) National Centre of Epidemiology, National Institute of Health, Rome, Italy; (4) Stockholm Gerontology Research Center, Stockholm, Sweden)*

Background: The simultaneous presence of impairments in cognitive and physical function is deemed a distinctive at-risk condition. However, which is the impact of their co-occurrence on cognitive decline and dementia remains unclear. **Objectives:** We investigate the impact of cognitive impairment and slow walking speed on cognitive decline and dementia among older adults. **Methods:** Study participants included 2550 dementia-free people aged 60+ years enrolled in the Swedish National study on Aging and Care in Kungsholmen, Stockholm. Physical impairment was defined as walking speed (WS) <0.8 m/s; cognitive impairment–no dementia (CIND) as -1.5 SD below age- and educational group-specific means on at least one of five cognitive domains of an extensive neuropsychological battery. Trajectories of cognitive decline (as assessed with the Mini Mental State Examination) were derived from mixed-effect linear regression models. Piecewise proportional hazard models were used to estimate the risk of dementia over short (<6 years) and long (12+ years) term follow up. **Results:** Participants with both CIND and slow WS had the worst prognosis, especially in the short term (<6 years). Those people had the steepest cognitive decline over the follow-up period (-0.85 [95%CI -0.99, -0.71], p-value<.001) and, within the first six years of follow-up, four -times higher risk of dementia (HR: 4.5; 95%CI: 3.4-6.2) as compared to people free from these conditions. Attenuated results have been obtained when we considered isolated CIND (HR: 2.6; 95% CI: 1.8-3.4); no statistically significant association arose for those people with isolated slow WS (HR: 1.4; 95% CI: 0.9-2.0). These findings resulted attenuated for longer follow-ups. **Conclusion:** The simultaneous presence of CIND and sWS is a clinical marker of impending dementia, and identifies a special share of the population that might deserve ad hoc assessments and care.

OC3- LONG TERM RATES OF CHANGE IN MUSCULOSKELETAL AGING: FINDINGS FROM THE HEALTH, AGING AND BODY COMPOSITION STUDY.

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Background: Aging is associated with declines in muscle mass, strength, function and bone density, increasing the risk of sarcopenia and osteoporosis. **Objectives:** To describe change in grip strength, walking speed, lean mass and hip BMD over 9 years among 3075 men and women (aged 70-79 years at baseline) who participated in the Health, Aging and Body Composition Study. **Methods:** Total hip BMD and whole body lean mass were ascertained using DXA; muscle strength by grip dynamometry; and customary walking speed was measured for muscle function. Each characteristic was assessed at least 5 times from baseline to follow-up. For each characteristic, mean and variability in annual percentage change were compared and measures of conditional change (independent of baseline levels) were derived. Pearson correlations between conditional change measures were calculated. The mean trajectory of each characteristic in relation to age was estimated using linear mixed models. **Results:** Mean annual percentage declines for walking speed and grip strength were 2.1% and 1.5% respectively; declines were smaller for hip BMD (0.6%) and lean mass (0.5%). Variation in percentage decline in grip strength and walking speed was greater compared with the other characteristics (p<0.001). Mean trajectories for grip strength, walking speed and hip BMD were quadratic in relation to age such that declines accelerated with advancing age; decline in lean mass was linear. Significant (p<0.05) and positive correlations between all conditional change measures were observed. Conditional changes in hip BMD and lean mass were most strongly correlated (r=0.42, p<0.001); 0.08<r<0.24 for correlations between other conditional change measures. **Conclusion:** These analyses provide unique insights into the lifecourse trajectory of body composition, muscle strength and physical performance. The indices of body composition (BMD and lean mass) clearly cluster together; furthermore, baseline values explain around 80% of the variance in these markers some 9 years later. In marked contrast, grip strength and walking speed are much more susceptible to alterations in their loss rate, with only around 50% of the variance in later measurement explained by baseline values. Finally, declines in grip strength and walking speed accelerate with advancing age and are considerably greater than those observed for lean mass and BMD.

OC4- INTERVENTIONS TO TREAT FRAILTY: A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS.

Ahmed Negm[1,2], Courtney C Kennedy[1,3], Ian D Cameron[4], Lehana Thabane[5], Areti-Angeliki Veroniki[6,7], Jonathan D. Adachi[3], Julie Richardson[2], Maria Petropoulou[6], Saad Alsaad8, Papaioannou[1,3] *((1) Geriatric Education and Research for the Aging Sciences (GERAS), St Peter's Hospital, Hamilton ON, Canada; (2) School of Rehabilitation Science, McMaster University, Hamilton, ON, Canada; (3) Department of Medicine, McMaster University, Hamilton ON, Canada; (4) John Walsh Centre for Rehabilitation Research, Sydney Medical School Northern, University of Sydney, Kolling Institute Royal North Shore Hospital, St Leonards, NSW, Australia; (5) Department of Health Research Methods, Evidence, and Impact, McMaster University, Hamilton ON, Canada; (6) Department of Primary Education, School of Education, University of Ioannina, Ioannina, Greece; (7) Li Ka Shing Knowledge Institute, St. Michael's Hospital, East Building, Toronto, Ontario, Canada; (8) Department of Family and Community Medicine, College of Medicine, King Saud University, Riyadh, Saudi Arabia)*

Background: Frailty and age-related declines in physical performance are reversible. To guide clinical management, a systematic review and network meta-analysis (NMA) were performed. The latter methodology enables the simultaneous assessment of the effects of multiple interventions for the same condition. **Objectives:** To determine the comparative effectiveness of interventions targeting the prevention, treatment, or management of frailty. Secondary outcomes included: quality of life; short physical performance battery (SPPB); cognition; depression, and adverse events. **Methods:**

Randomized controlled trials (RCTs) were identified by systematic search of several databases (MEDLINE, EMBASE, CINAHL, AMED). Duplicate title/abstract and full-text screening, data extraction and risk of bias assessment were performed. Inclusion criteria were singular or multi-faceted interventions targeting frailty and/or improvement in physical performance. Comparators were standard care, placebo or another intervention. We performed both standard pairwise meta-analysis and Bayesian NMA under a random-effects model. Pooled estimates of treatment effects were odds ratios for dichotomous outcomes and standardized mean difference (SMD) for continuous outcomes. Interventions of each outcome were ranked using the surface under the cumulative ranking curve (SUCRA) and presented in a rank-heat plot. The GRADE approach specific to NMA was used to assess the quality of the evidence. **Results:** A total of 89 RCTs were included after screening of 7090 citations and 749 full-text articles. The mean age of included studies ranged between 75 and 85 years, body mass index between 25 and 30; 62.5% of participants were female. Of the included RCTs, 77.7% had overall high risk of bias. The NMA for frailty (including 20 RCTs, n=4838, 8 interventions) suggested that physical activity interventions, when compared to placebo/standard care, were associated with the greatest reduction in frailty (SMD, -0.93 (95% CI, -1.57 to -0.27) followed by physical activity with nutritional supplementation (SMD, -0.62 (95% CI, -1.47 to 0.21). According to SUCRA, physical activity interventions and physical activity plus nutritional supplementation were the most effective interventions (100% and 71% likelihood, respectively). **Conclusion:** Physical activity and physical activity with nutritional supplementation were most effective in reducing frailty. Given the low quality of evidence available, more intervention studies that rigorously examine treatments to reduce frailty are required.

OC5- INHIBITION OF KYNURENINE PRODUCTION PROTECTS SKELETAL MUSCLE FROM THE AGE-RELATED LOSS OF MASS AND STRENGTH.

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Background: The cellular and molecular mechanisms underlying loss of muscle mass and strength with age (sarcopenia) are not well-understood; however, heterochronic parabiosis experiments show that circulating factors are likely to play a role. Kynurenine (KYN) is a circulating tryptophan metabolite that is generated by the enzyme Indoleamine, 2, 3 dioxygenase (IDO), is known to increase with age, and is implicated in several age-related pathologies. We have previously shown that an increase in KYN in young male and female mice increased oxidative stress, and decreased skeletal muscle mass. **Objectives:** Here we tested the hypothesis that inhibition of KYN using a small-molecule inhibitor of IDO, 1-methyl-D-tryptophan (1MT) protects against the loss of muscle mass and strength with age. **Methods:** We tested this in male and female C57BL/6 mice by treating young (6-8 month) mice with KYN (10mg/kg), and aged (22-24 month) mice with 1MT (10mg/kg). We then measured In vivo peak muscle strength in young and aged mice, then sacrificed and measured oxidative stress and skeletal muscle fiber size in aged mice, and protein from all groups. **Results:** Results indicated that both male and female aged mice treated with 1MT showed an increase in muscle fiber size (P<.05), peak muscle strength (P<.05), and oxidative stress (P<.05), Young mice treated with KYN had a decrease in peak muscle strength (P<.05). Protein analysis identified mitochondrial very long chain acyl-coa dehydrogenase as a downstream candidate that increases hydrogen peroxide through lipid peroxidation that is increased with KYN treatment, (P<.01) in young mice, and in human myoblasts treated with KYN (10uM) (P<.01). **Conclusion:** Our data suggest that IDO inhibition may represent a novel therapeutic approach for the prevention of sarcopenia and possibly other age-associated conditions associated with KYN accumulation such as bone loss and neurodegeneration.

OC6- EARLY KIDNEY DYSFUNCTION IS ASSOCIATED WITH LONGITUDINAL DECLINE IN PHYSICAL PERFORMANCE IN THE ELDERLY.

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Background: Appendicular bone and muscle share common blood supplies, function, and risk factors for impaired function. We have previously shown that mildly reduced renal function and elevated urine protein levels are each prospectively associated with hip fracture risk in older adults. **Objectives:** We determine whether these markers are also associated with impaired muscle performance. **Methods:** Using data from the Cardiovascular Health Study, we prospectively examined the associations of mild impairments of urine albumin creatinine ratio (ACR) and estimated glomerular filtration rate (eGFR) levels with longitudinal changes in grip strength and gait speed over 2 years in 2888 community-dwelling men and women (median age 77 years). Median ACR was 9.8 [IQR, 5.40-21.50] mg/gram creatinine and median eGFR was 71.6 [IQR, 59.1-83.56] ml/minute/1.73m2. Models were adjusted for demographic factors, clinical history, and biochemical measures in three candidate pathways: oxidative stress, inflammation, and fibrosis. **Results:** In demographic and covariate adjusted models, a two-fold greater urine ACR was associated with longitudinal changes of -0.17 (95% confidence interval [CI], -0.29, -0.06) kilogram in grip strength over 2 years and -1.10 (-1.67, -0.53) cm/second gait speed per year. Corresponding estimates for a 10 ml/minute/1.73m2/ year lower baseline eGFR were -0.13 (-0.23, -0.04) kg and -0.89 (-1.37, -0.40) cm/second, respectively. The associations of a doubling of ACR with grip and gait were approximately equivalent as an additional 2-3 years of age; the corresponding associations of 10 ml/min/1.73m2/year decrement in eGFRcys approximated 1.25-1.5 additional years of age. Adjustment for covariates in candidate pathways did not materially attenuate these estimates. **Conclusion:** In older adults, higher urine ACR and lower eGFR are independently and prospectively associated with declines in grip strength and gait speed. Even in late life, modest decrements in kidney function are longitudinally associated with more rapid functional decline.

OC7- EVALUATING THE PHYSIOTYPE OF FRAILTY: VALIDATION OF A MEASURE OF PHYSIOLOGICAL MULTISYSTEM DYSREGULATION IN TWO DATASETS.

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Background: Physical frailty is thought to be a manifestation of multisystem physiological dysregulation, which results from a loss of complexity of interactions among individual physiological systems in addition to their own deterioration. **Objectives:** The objective of this study was to evaluate criterion validity of a theory-driven measure of multisystem physiological dysregulation using biomarkers from multiple systems, using clinical frailty and time to incident mobility difficulty. **Methods:** We used data from the Women's Health and Aging Studies (WHAS) I and II (N=649), and replicated findings in the Health ABC study (N=1,514). We derived a factor for physiological dysregulation based on bifactor analysis of 12 biomarkers representing multiple systems including stress response and energy regulation. We evaluated convergent criterion validity against clinical frailty, and predictive criterion validity with incidence of mobility difficulty. **Results:** Using WHAS data, a half-standard deviation elevated level of general factor score representing multisystem dysregulation was associated with a 2.2-fold increased odds of frailty (95% confidence interval, CI: 1.4, 3.7). Adjusting for age and race, greater levels of physiological dysregulation were associated with onset of mobility difficulty in WHAS I (HR=2.11, 95% confidence interval, CI: 1.39, 3.19), WHAS II (HR=1.50, 95% CI: 1.12, 2.02), and Health ABC (HR=1.63, 95% CI: 1.42, 1.87). **Conclusion:** Biomarker data from two epidemiologic studies lend support for the construct of multisystem physiological dysregulation, which is associated with clinical frailty and onset of walking difficulty and mortality.

OC8- CT-DERIVED MUSCLE MASS AND MYOSTEATOSIS IN PATIENTS WITH SOFT-TISSUE SARCOMA: RESULTS FROM A PHASE-3 TRIAL AT 81 SITES IN 13 COUNTRIES.

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Background: Soft-tissue sarcomas are twice as common as primary bone malignancies, usually occur in older adults (age > 50 years), and require intensive management, including diagnostic evaluation using computed tomography (CT). Sarcoma treatment and prognosis are determined at the time of diagnosis by tumor stage, tumor histology, and patient functional status. There is an unmet need for identifying imaging biomarkers that distinguish among patient subgroups that experience differential treatment responses. CT measurement of muscle mass and myosteatosis has been shown to be a useful prognostic biomarker in many cancer cohorts. **Objectives:** To assess the association of CT muscle mass and myosteatosis with all cause mortality in patients with soft-tissue sarcomas. **Methods:** This international, open-label, randomized, phase-3 study was performed in 640 participants over 24 months at 81 sites through the Sarcoma Alliance for Research through Collaboration (SARC). All patients had locally advanced unresectable or metastatic soft-tissue sarcomas and were in one of two chemotherapy treatment arms (either single-drug doxorubicin or the combination of doxorubicin plus evofosfamide). Secondary analysis of pre-treatment CT scans was performed for skeletal muscle density (SMD, in HU, a marker of muscle quality) and skeletal muscle index (SMI, muscle area in cm2/patient height in m2, a marker of muscle mass) at the L3 level. Cox regression analysis was performed to determine the associations between muscle metrics and all-cause mortality, adjusting for age, sex, race, and treatment arm. **Results:** CT scans at the L3 level were available in 445 of 521 (85%) participants (234 M, 287 F; mean age, 60 years [range, 18-89]). Higher SMD was associated with lower mortality. A one-unit standard deviation increase was associated with a hazard ratio of 0.86 (95% CI = 0.75-0.99; p = 0.029). The association of SMI with mortality did not reach significance (hazard ratio = 0.88; 95% CI = 0.75-1.03; p = 0.105). **Conclusion:** CT obtained for routine clinical purposes can be used opportunistically to quantify muscle metrics. Muscle density at L3 is associated with all-cause mortality. CT-derived muscle phenotypes warrant further investigation as potential biomarkers in sarcoma patients.

OC9- EFFECT OF RESISTANCE EXERCISE TRAINING AND FISH OIL SUPPLEMENTATION ON THE ADAPTIVE RESPONSE OF MUSCLE IN SARCOPENIC OLDER WOMEN.

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Backgrounds: Previous studies have shown a benefit of fish oil supplementation on muscle mass and function. However, there is no consensus on the effect of the duration of the intervention on the results obtained, some studies showing that training programs with shorter duration were not effective in increasing muscle mass or strength in healthy older people. Also, the populations studied have varied, some studies including healthy older adults only, others including sarcopenic older adults. **Objectives:** To investigate the effect of fish oil supplementation on the adaptive muscle response in sarcopenic older women undergoing resistance exercise training during a short period. **Methods:** This was a randomized, double-blind, placebo controlled trial. Thirty-two women aged 65 years or older, classified as sarcopenic according to the criteria of the 2010 EWGSOP consensus participated. The participants were allocated into two groups: (1) Exercise and placebo (EP) and (2) Exercise and fish oil (EFO). The two groups undertook a resistance exercise program over 14 weeks, with three supervised sessions per week. All participants were instructed to ingest two capsules of 1g supplement at lunch and

dinner (4g/day in total); the EP group received sunflower oil capsules (placebo) and the EFO group, fish oil capsules (EPA 440mg and DHA 220mg). Pre and post-intervention measurements of lower limb strength were performed using a Biodex dynamometer. Muscle volume of the quadriceps was calculated from magnetic resonance imaging and the skeletal muscle mass index (SMMI) was calculated from total muscle mass assessed by bioelectrical impedance. Paired t-tests were used for comparison within groups and the Independent Samples Student's t-test for comparison between groups. **Results:** Muscle volume and strength increased in both groups after the intervention. However, the EFO group showed significantly greater changes as compared with the EP group, with respect to both muscle volume (47.4cm3 (13.5%) versus 15.4cm3 (5.09%), respectively, p<0.001) and muscle strength (14.52NM (22.1%) versus 4.46NM (7.12%), p=0.016). SMMI changed by 2.2kg.m-2 (36.1%) and 1kg.m-2 (16, 4%), respectively, p=0.01. **Conclusion:** Supplementation with fish oil improves the effects of resistance exercise training, even with a short duration training program, on the adaptive response of muscle in sarcopenic older women, improving the sarcopenic status.

OC10- SARCONEOS (API BIO101) TARGETS MAS RECEPTOR WITHIN THE PROTECTIVE ARM OF THE RENIN ANGIOTENSIN SYSTEM AND PROVES EFFICACY IN VARIOUS MODELS OF MUSCLE WASTING.

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Background: Muscle wasting affections such as sarcopenia and disuse atrophy lead to a progressive or temporary decrease in mobility and reduced quality of life. The drug candidate BIO101, a first-in-class drug targeting Mas receptor, has been developed pre-clinically and clinically for its potential on muscle quality and function. BIO101 is the API of Sarconeos currently tested in clinical IIb trial in patients with sarcopenia. **Objectives:** The aim of this work was to demonstrate and characterize the impact of BIO101 on models of sarcopenia and disuse atrophy. **Methods:** Adult (12-month-old) and aged (22-month-old) C57BL6/J mice were assessed for running performance after 14 weeks of oral treatment with BIO101 at 50mg/kg*day. Young (8-week-old) mice continuously administered orally at the same dose were assessed for muscle mass and specific maximal force at completion of the 14-day hindlimb immobilization. The impact of BIO101 on mouse and human myoblasts differentiation was determined by q-PCR, western blot and fluorescence microscopy. Mitochondrial respiration and biogenesis were evaluated using a Seahorse XF Analyzer and the Mitotracker Deep red dye, respectively. **Results:** Old BIO101-treated animals ran significantly faster than old control animals (+17%) which demonstrated that BIO101 compensated for the significant aging-related loss of maximal running velocity. In young animals, BIO101 treatment prevented the loss of muscle functionality and improved muscle strength by 17,5% after 14 days of immobilization compared to vehicle-treated muscles. Improvement of muscle function demonstrated in young and old treated-animals, immobilized or not, was consistent with in vitro findings in terms of mitochondrial function and anabolism. BIO101 increased mitochondrial mass (+75%) and oxygen consumption rate in myotubes (+23% in spare respiratory capacity). The percentage of myogenin-positive cells was significantly increased after continuous BIO101 exposure (+ 80%) consistently with increased fusion index and number of nuclei/myotube, suggesting an acceleration of differentiation process by the drug candidate. **Conclusion:** These studies demonstrate the overall beneficial properties of BIO101 on muscle cell function in two distinct physiopathological contexts and brings together evidences for improved anabolism and mitochondrial function. These results support the clinical development of Sarconeos in sarcopenic patients and warrant further studies in other muscle wasting indications.

OC11- SURMOUNTING THE AGED NICHE TO IMPROVE SKELETAL MUSCLE REGENERATION.

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Background: Muscle repair after injury entails an immune response that promotes efficacious regeneration. As we age, infiltration of inflammatory cells, fibroadipogenic progenitors and senescent cells leads to a deleterious microenvironment that impedes skeletal muscle regeneration. Muscle stem cells are key for regeneration, but their function and numbers decrease as we age, to great extent due to these extrinsic niche changes. **Objectives:** Previously, we have shown Prostaglandin E2 (PGE2) is essential for skeletal muscle stem cell function in regeneration in young mice, but it remained undetermined the status of PGE2 signaling in aged skeletal muscle. **Results:** Here we identify PGE2 signaling is dysregulated in aged skeletal muscle. By treatment with a small molecule, this aberrant signaling is surmounted, and muscle strength and regenerative capacity of aged mice are increased. **Conclusion:** Our data show a new role for PGE2 signaling in aging, and the importance of restoration of EP4 signaling to improve skeletal muscle regeneration in the aged.

OC12- DIETARY SUPPLEMENTATION WITH FISH OIL AND CURCUMIN IMPROVES GAIT SPEED AND MITOCHONDRIAL FUNCTION DURING AGING.

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Background: Sarcopenia is a progressive and generalized skeletal muscle disorder associated with adverse outcomes including falls, fractures, physical disability and mortality. Sarcopenia has multi-factorial causes going from life style changes to metabolic and cellular perturbations. **Objectives:** The objective of this study was to determine the functional benefits of a nutritional intervention with curcumin and fish oil alone or in combination on Sarcopenia and to characterize the underlying mechanisms of action. The concept of this study was to provide combination of ingredients targeting different patho-physiological mechanisms. **Methods:** Twenty month-old rats received a control diet supplemented with cellulose (CON), or a diet supplemented with either curcumin (CUR), fish oil (OM3) or a combination of both (CUR+OM3). Muscle functionality and metabolism was evaluated after chronic treatment during 3 months and molecular mechanisms were evaluated after short-term treatment over 4 weeks. **Results:** Walking speed measured with the catwalk gait analyzer significantly improved in the CUR and CUR+OM3 vs CON groups, and also tended to improve with OM3 alone. These functional benefits involved an activation of the muscle antioxidant capacity by OM3 through SOD and catalase induction. This was associated with synergistic enhancement of mitochondrial bioenergetics by CUR+OM3 through increased activity of citrate synthase and respiratory complexes. **Conclusion:** Curcumin and

fish oil supplementation prevent the functional decline of muscle health during aging by directly targeting gait speed independently of muscle mass. The physiological benefits of these two ingredients are associated with the enhancement of muscle antioxidant capacity and the synergistic activation of mitochondrial energy production in aged muscle.

OC13- PREDICTING ONSET, PREVALENCE AND MORTALITY IN MALE AND FEMALE MICE USING THE MOUSE FRAILTY PHENOTYPE.

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Background: Preclinical studies are important in the identification of the underlying mechanisms contributing to frailty. However, little is known whether frailty assessments in mice are capable of distinguishing important characteristics of the frailty syndrome. **Objectives:** The goals of this study were to identify the onset and the prevalence of frailty across the lifespan and to determine whether a frail phenotype predicts mortality in male and female mice. **Methods:** Body weight, walking speed, strength, endurance and physical activity were assessed in male and female C57BL/6 mice every three months starting at 14 months of age for the male cohort and 17 months of age for the female cohort. Mice that fell in the bottom 20% for walking speed, strength, endurance and physical activity, and in the top 20% for body weight were considered to have a positive frailty marker, from the data analyzed at 20 and 23 months of age for female and male mice, respectively. Mice with three or more frailty markers were identified as frail, with two markers as pre-frail, and one or no markers as non-frail. **Results:** The onset of frailty occurred at 17 months for both genders, and represented only 3.5% of the male mouse cohort and 3.7% of the female mouse cohort. The percentage of frail mice steadily increased until basically every mouse was identified as frail or pre-frail in both genders at 32 months of age. Frail, pre-frail, and non-frail male mice had mean survival ages of 27, 29 and 34 months, respectively. For the female mouse cohort, frail/pre-frail and non-frail mice had mean survival ages of 27 and 30 months. Frailty status predicted mortality with the non-frail mice living longer than the frail/pre-frail in both male and female mice. **Conclusion:** In closing, frail mice lack resilience to the aging process, in that multiple tissue/organs system deteriorate at an accelerated rate compared to non-frail mice, which ultimately leads to early mortality. Identifying the onset and prevalence of frailty, in addition to predicting mortality, has potential to yield information about several aging processes.

OC14- AGING-ASSOCIATED LOSS OF HYPOXIA SIGNALING LIMITS SKELETAL MUSCLE REGENERATION.

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Background: Skeletal muscle regeneration is required for the maintenance of muscle mass in aging. Hypoxia signaling, including aryl hydrocarbon nuclear translocator (ARNT), is necessary to maintain regenerative potential. **Objectives:** The present study evaluates whether loss of hypoxia signaling in aging directly limits skeletal muscle precursor (SMP) regenerative potential. **Methods:** Young (Y, 8-12 weeks) and old (O, 21-23 months) mice were utilized to determine changes in regenerative potential and muscle hypoxia signaling that occur with aging. Regeneration was quantified using cross-sectional area (CSA) of regenerating fibers following cryoinjury. Whole muscle was utilized for ELISA, PCR, FACS sorting for skeletal muscle precursors (SMPs), and immunohistochemisty. Mice containing the human skeletal a-actin (HSA) Cre recombinase promoter crossed with a homozygous ARNTfl/fl allele were created to assess regeneration in the setting of muscle specific loss of ARNT following tamoxifen activation. Experimentation regarding these mice were completed at 8-12 weeks of age. ML228, a pharmacologic ARNT mimetic, or vehicle control was injected by IP injection daily in aged mice to determine if muscle regeneration could be restored. **Results:** SMP frequency and myogenic potential decrease dramatically in aging (p<0.01). CSA in regenerating fibers decreases by 40% in O mice as compared to Y following injury at 5 (p<0.01) and 10 (p<0.01) days post-injury. In hind-limb skeletal muscle, ARNT levels are 4.7-fold lower by PCR (p<0.01) and 5-fold lower by immunoblotting in O versus Y mice (p<0.01). Using a focused PCR array, we demonstrated that the majority of hypoxia response genes were significantly down-regulated with aging. Young, tamoxifen-activated HSA-Cre ER ARNTfl/fl mice, created to mimic the loss of hypoxia signaling in old mice, exhibit an 80%, skeletal muscle specific decrease in ARNT expression (p<0.01) and a 30% decrease in regenerating muscle fiber CSA at 5 (p<0.01) and 10 (p<0.01) days post-injury, as compared to controls. ML228 administration resulted in a 30% increase in regenerating fiber CSA in O mice at day 5 (p<0.01) versus O mice treated with vehicle. **Conclusion:** Hypoxia signaling declines with aging and contributes to loss of skeletal muscle regeneration. Restoring the hypoxia pathway may promote regeneration and prevent muscle loss in aging.

OC15- DYNAPENIA IS ASSOCIATED WITH EXECUTIVE DYSFUNCTION. RESULTS FROM THE GAIT AND BRIAN STUDY.

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Background: The loss of muscle mass, sarcopenia, in older adults is an important marker of frailty due to the association with mobility decline, falls, fractures, and mortality. However, dynapenia, the loss of muscle strength, has been shown to manifest earlier than sarcopenia and is more consistently associated with disability and mortality. As highlighted in a recent systematic review1, it is unknown whether dynapenia is associated with cognitive performance in different cognitive domains. We examined the cross-sectional association between handgrip strength and cognitive domains under the hypothesis that dynapenia will be associated with executive dysfunction and related to damage in shared brain networks that control executive function (EF) and central muscle drive. **Objectives:** Determine the association between different cognitive domains and handgrip strength. We hypothesize that EF impairment is associated with dynapenia due to common damage and neural loss. **Methods:** One hundred sixty older adults from the Gait and Brain Study with varying degrees of cognitive impairment but without dementia were included in this study. Participants' cognition was assessed with MoCA and the domain sub-scorings were used to test for associations with handgrip

strength. Participants' handgrip strength was tested with a handheld dynamometer (Jamar Dynamometer). Grip strength test was performed three times and the average was used. **Results:** Using MoCA sub-scorings to assess cognitive domains (MIS-memory, EIS-EF, VIS-visuospatial, LIS-language, AIS-attention, and OIS-orientation), only high EF performance was significantly associated with high grip strength, even when adjusted for age and sex (B: 0.07, 95%CI:0.03–0.10, p<0.001). When we divided our sample in tertiles based on EF performance, we found a significant linear increase in grip strength associated with better EF (Tertile 1–low EF–: 22.61 kg-force ±9.54; Tertile 2–medium EF–: 25.25 kg-force ±8.75; Tertile 3–high EF–: 27.66 kg-force ±9.40, p=0.005). **Conclusion:** Low EF is associated with lower performance in handgrip strength, independently of important covariates. These associations suggest common mechanism potentially at brain levels and contribute to better understand cognitive frailty. Future studies using brain imaging may help to decipher whether brain networks, particularly frontal lobe EF, may also affect motor areas related to upper-limb strength.

OC16- COMPARAISON OF HIGH-INTENSITY INTERVAL TRAINING AND MODERATE-INTENSITY CONTINUOUS TRAINING ON PHYSICAL AND FUNCTIONAL CAPACITIES IN OBESE OLDER ADULTS.
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Background: Aging is associated with obesity, which is related to functional capacity decline as muscle mass and muscle strength. Even if resistance or aerobic trainings (moderate-intensity continuous trainings: MICT) are well known to be able to counteract these phenomena, the majority of older adults are sedentary. One of the main reported barriers is lack of time. High-intensity interval training (HIIT) with half of time seems to induce cardio-metabolic benefits in adults. However, its potential benefits on physical and functional parameters are unknown in older adults with or without obesity. **Objectives:** To verify if HIIT leads to higher improvements on functional capacity and body composition than MICT in obese older adults. **Methods:** Seventy-two inactive (< 2h of structured phial activity/week) obese (fat mass[FM]: Men>27%, Women>35%) older adults (>60yrs) were randomized in two groups: 1)HIIT (n=36; women(18)/men(18)) or 2) MICT (n=36; women(17)/men(19)). Participants followed a 12-week intervention (3times/week): elliptical HIIT program (30min/session; cycle:30sec>85%-Borg scale>17 and 90sec~65%-Borg scale:13-16) of maximal heart-rate; or a treadmill MICT (60min/session; ~65-75%-Borg scale:13-16) of maximal heart-rate. Body composition (FM and lean mass); fast (Timed Up-and-Go[TUG]) and self-paced (4-meter walk test[4-mWT]) walking speed, aerobic capacity (6-min walk test[6MWT]) and sit-to-stand test were measured pre and post intervention. **Results:** At baseline, groups were similar regarding age, BMI, body composition, functional capacity, lifestyle habits and adherence (HIIT=93.9±6.6% vs. MICT=94.5±9.2%). A within-group effect for functional tests (p<.001); gynoïd FM loss (DXA;p=.008) and subcutaneous FM loss (pQCT;p=.001) was observed in both group. in addition, following the 12-weeks intervention, HIIT induced greater improvements in functional capacities (sit-to-stand, p=.008; 4-mWT,p=.05; TUG,p<.001; 6MWT,p<.001) than MICT. **Conclusion:** Although of a shorter duration, our results indicate that HIIT in obese older adults is more efficient to improve functional capacities than MCIT. Our results also indicate that HIIT is as effective as MICT for FM loss.

OC17- FRAILTY AMONG PATIENTS WITH ACUTE MYOCARDIAL INFARCTION.
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Background: Frailty is an independent predictor of all-cause and cardiac mortality, non-fatal myocardial infarction, and major bleeding after acute myocardial infarction (AMI) admission. **Objectives:** The objective of this study was to estimate the prevalence of frailty among adults age 75 years or older during their first AMI admission and examine the relationship between frailty status and receipt of interventions. **Methods:** We used the Premier Healthcare Database to identify admissions for older adults with primary diagnoses of AMI (ICD-9: 410-414, 429.2; ICD 10: I20-I25). We classified individuals as frail or not using the validated Claims-based Frailty Index (CFI) algorithm, with which we generated a frailty score for each patient using 21 variables derived from inpatient and outpatient data from 6 months prior to the index AMI admission. We used a probability cutoff of 0.2 to classify individuals are as frail vs. non-frail. We compared characteristics of the frail and non-frail patients, including the frequency of receipt of coronary interventions. **Results:** From 2000 to 2016, we identified 469,390 encounters for patients >=75 years admitted with AMI. The median [IQR] age was 82 [77, 88] years, 52% were women, 75% were Caucasian, and 4% were of Hispanic ethnicity. The prevalence of frailty was 19%. Frail patients were older, more likely to be women and ethnic minority members, and have more comorbidities. Frail patients were much less likely to receive PCI than non-frail (15% vs 34%, p <0.001) and much less likely to receive CABG (frail 1% vs non-frail 9%, p <0.001). The utilization of PCI as a treatment of AMI was significantly higher in non-frail vs. frail patients at all ages, but even usage in non-frail patients decreased significantly among patients over 85 years of age. **Conclusion:** In the United States, frailty is common among older patients during AMI hospitalization and the prevalence increases with age. From a public health perspective, research efforts should focus on the evaluation of clinical outcomes for older adults after cardiovascular interventions based on their frailty status to learn whether exclusion of frail patients from interventions is appropriate or not.

OC18- CHANGE IN METABOLIC AND INFLAMMATORY BIOMARKERS AFTER A 24-WEEK MULTIMODAL INTERVENTION DESIGNED TO IMPROVE FUNCTIONAL STATUS IN HYPERTENSIVE OLDER ADULTS: A PILOT RANDOMIZED CONTROLLED TRIAL.
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Background: Systemic biomarkers including clinical metabolic profiles, inflammation, and oxidative stress are associated with hypertension and age-related functional decline and disability. First-line antihypertensive therapies may influence these biomarkers differentially when combined with physical exercise. **Objectives:** Evaluate the effects of three first-line antihypertensive medications on systemic metabolic and inflammatory biomarkers in hypertensive

older adults when combined with exercise training. **Methods:** This three-arm, double-masked, pilot randomized controlled trial (RCT) randomly assigned physically-inactive adults (>=60 years) with hypertension and physical limitations to one antihypertensive medication: i) Perindopril (A:8 mg/qd;n=10), ii) Losartan (B:100 mg/qd;n=13), or iii) Hydrochlorothiazide (C: 25 mg/qd;n=8). All participants were also assigned to a 24-week, multi-modal center and home-based exercise intervention. Outcomes included fasting blood glucose, lipids, biomarkers of inflammation [tumor necrosis factor-α (TNF-α), interleukin-6 (IL6), high-sensitivity C-reactive protein (hsCRP)] and oxidative stress [oxidized LDL and myeloperoxidase (MPO)]. Linear mixed models were applied with an intent-to-treat approach, adjusted for age, sex and baseline status. Being a pilot, data are presented as adjusted mean change with 95% confidence interval at 24 weeks post-randomization. **Results:** A total of 31 participants [70.6±6.1 yr] were randomized (A=10; B=13; C=8). Compliance was >90% to medication (A=90%; B=94%; C=97%) and >79% to exercise sessions (A=87%; B=79%; C=84%). Estimated changes in blood glucose ranged from -3.2 (B: -7.1,0.8) to 3.2 (C: -1.3,7.7) mg/dL, LDL cholesterol from -6.5 (A: -22.3,9.4) to 2.4 (B: -11.6,16.5) mg/dL, HDL cholesterol from 1.9 (B: -2.2,6.1) to 4.5 (A: -0.1, 9.1) mg/dL, and triglycerides from -12.5 (A: -39.3,14.3) to 16.1 (B: -7.8, 40.0) mg/dL. Changes in TNF-α ranged from -0.3 (B: -0.7, 0.1) to 0.2 (C; -0.2,0.6) log pg/mL, IL6 from -0.1 (B: -0.5,0.2) to 0.2 (C: -0.1,0.6) log pg/mL, and hsCRP from -0.2 (A:-0.7,0.2) to -0.1 (B: -0.5,0.3) log mg/L. Adjusted changes in oxidized LDL ranged from -0.1 (C: -0.4, 0.2) to 0.0 (A: -0.3,0.3) log mU/L and MPO from -0.3 (A: -0.5,-0.0) to 0.1 (C: -0.1,0.4) log μg/L. **Conclusion:** Antihypertensive medications may differentially influence the impact of physical exercise on metabolic and inflammatory biomarkers among hypertensive older adults. A fully-powered RCT is needed to confirm this hypothesis and to evaluate relationships with indices of physical function..

OC19- THRESHOLD DEFINITION FOR GRIP STRENGTH TO IDENTIFY RELEVANT WEAKNESS IN SWISS DO-HEALTH PARTICIPANTS.

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Backgrounds: Grip strength (GS) is a core component of the instrument library for sarcopenia and frailty. The Jamar Dynamometer is most widely used to assess GS in Kilograms (kg). Alternatively, the Martin Vigorimeter (reporting Kilopascal (kPa)) offers a dynamic GS method also suitable in older adults with hand osteoarthritis. However, reference values are missing. **Objectives:** To assess the lowest 20% GS for relatively healthy DO-HEALTH men and women age 70 and older. **Methods:** DO-HEALTH is the largest healthy aging study in Europe including 2157 community-dwelling adults age 70+ from 5 countries. For this study, we analyzed Swiss DO-HEALTH participants from Basel (n=253), Geneva (n=201) and Zurich (n=552). Baseline GS was measured following a standard protocol using the Martin Vigorimeter. The highest of 3 measurements was used. **Results:** The 1006 DO-HEALTH participants had a mean age of 75.1 (±4.5) years and 60.2% were women. Women had a lower mean GS (52.0 (±11.2) kPa) than men 78.0 (±16.5) kPa. GS of the lowest 20% for women >75 years (n=78) ranged from 4 to 46 kPa (median 42 kPa) and 12 to 39 kPa (median 33.5 kPa) for women >75 years (n=40). GS of the lowest 20% for men >75 years (n=45) ranged from 32 to 69 kPa (median 64 kPa) and from 39 to 55 kPa (median 50 kPa) in men >75 years (n=39). **Conclusion:** GS distribution in this relatively large and healthy Swiss DO-HEATH study sample may be useful to assess weakness based on the Martin Vigorimeter.

OC20- ASSOCIATION BETWEEN NUTRIENT INTAKE, PHYSICAL ACTIVITY AND SARCOPENIA-RELATED GENE-PROMOTOR DNA METHYLATION.

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Background: DNA methylation in gene-promoter regions is usually related to repressed gene expressions. DNA methylation can be affected by environmental factors such as diet and lifestyle, which are also associated with sarcopenia. This suggests a potential connection between DNA methylation and sarcopenia. However, the association between diet, physical activity and sarcopenia-related DNA methylation remains unknown. **Objectives:** To explore the relationship between nutrient intake, physical activity and sarcopenia-related methylation in promoter regions. **Methods:** 24 older Caucasian women (72.5 ± 4.2 yr) were identified as "sarcopenic" from a group of 247 (aged 65-80 yrs) by cutoff points of lower quintile hand grip strength (26 kg) and skeletal muscle index (6.75 kg/m2). A non-sarcopenic group (n=24, 70.5 ± 3.3 yr) was selected by generally age-matching with the sarcopenic one. Nutrient intake (n=20 in the sarcopenic group) and physical activity score (PASE) were assessed by questionnaires. DNA methylation of whole blood sample was assessed using Infinium MethylationEPIC BeadChip. Differentially methylated CpG sites at promoter regions were identified by comparing methylation values (β values) of sarcopenic women with non-sarcopenic ones (p-value < 0.01). Methylation scores were calculated by summing individual β values in hyper- and hypomethylated CpG sites, respectively. Participants were split into a training set (n=30) and a test set (n=14). Lasso method was applied for variable selecting and model building in the training set with methylation scores as dependent variables. Standardized values of age, BMI, nutrient intake and PASE were included as candidate independent variables. The model was further evaluated in the test set. Models with the highest R2 in the training and the test set were retained. **Results:** In the sarcopenic group, promoter regions of 1621 genes were significantly differentially methylated (420 hypomethylated, 1201 hypermethylated) compared to the non-sarcopenic group. Lasso regression showed that the hypermethylated score was negatively related to BMI, PASE and protein intake (R2 = 0.7% in the test set) and the hypomethylated score was positively related to BMI, protein and selenium intake (R2 = 9.6% in the test set). **Conclusion:** BMI, physical activity, protein and selenium intake are mildly associated with sarcopenia-related DNA methylation in promoter regions, indicating their possible influence on sarcopenia.

OC21- USING SOCIALLY ASSISTIVE ROBOTS FOR MONITORING AND PREVENTING PHYSICAL FRAILTY AMONG OLDER ADULTS: A STUDY ON USABILITY AND USER EXPERIENCE.

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Background: Physical Frailty&Sarcopenia, PF&S, (Del Signore, Roubenoff, 2017) represents an underestimated health risk among older adults leading to increased morbidity (including falls/injurious falls) and mobility disability. Socially assistive robots have the potential to play a meaningful role in assessing and monitoring the grade of physical frailty of older adults. Preliminarily, proper usability

and a positive user experience need to be ensured. **Objectives:** To test the usability and user experience toward a socially assistive robot (the NAO humanoid robot) as an innovative method 1) to administer questionnaires to frail older adults and 2) to engage them in repeating a sequence of standardised physical exercises. **Methods:** Participants after giving their informed consent were asked to complete the SARC-F questionnaire and subsequently performing physical training tasks, first administered by the NAO robot, and a second time via a Tablet PC application (as a reference technology). After using each technology, they completed the System Usability Scale for usability, and a set of rating scales for perceived usefulness, enjoyment, and control. Finally, we questioned the participants' preference for one of the technologies. All interactions were recorded on video and scrutinized for usability issues. **Results:** Twenty non-disabled, non-demented older adults (age>=70 years) accepted to participate. They awarded to both technologies 'average' usability scores. Perceived usefulness and enjoyment were rated as very positive for both modalities; control was also scored positively. Main usability issues for the robot tasks were related to speech interaction (e.g., NAO's limited speech library, NAO's difficulty to cope with some Dutch dialects) and more in general, with older adults' difficulties with taking their proper role in a human-robot interaction. Only seven participants preferred NAO: it was easier to use and more personal. **Conclusion:** Social robots have the potential to monitor and train frail older adults in adapted programs. However some key usability challenges need to be addressed, some only requiring a technical adaptation, other concerning the human expectation vis a vis of a robot, none appears critical. Next step, longitudinal studies in homogenous populations suffering from PF&S should determine if PROs administered and recorded via a social robot can be considered a suitable endpoint for clinical trials.

OC22- A GENOME-WIDE ASSOCIATION STUDY OF GRIP STRENGTH IN UK BIOBANK TO IDENTIFY GENETIC DETERMINANTS OF MUSCLE FUNCTION AND POTENTIAL THERAPEUTIC TARGETS FOR SARCOPENIA.

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Background: Sarcopenia is a progressive loss of functional capacity with age that is associated with loss of independence and quality of life in older adults. Its cause is poorly defined and potentially multifactorial, with diminished activity, chronic illness, hormonal changes, inflammatory pathway activation, fatty infiltration, and poor nutrition, potentially contributing to pathology and progression. Hand grip strength is a widely used proxy of muscular function, that is strongly predictive of sarcopenia and a range of additional morbidities. As a means to identify potential specific mechanisms contributing to muscle function, and putative targets for sarcopenia intervention, we performed large-scale genetic analyses of grip strength on all UK Biobank participants. **Objectives:** To investigate the genetic determinants of variation in human grip strength. **Methods:** We performed a GWAS of maximal grip strength adjusted for age, sex, BMI and height in UK Biobank subjects (n=448,861) to identify loci of significance effect. Effector genes at each of the significant loci were determine using a series of established and novel variant to gene (V2G) mapping methods along with manual curation. In addition, association of the loci with other traits were characterized (PheWAS in UKB/GWAS). Finally, determined genes were assessed for biological rationale and compared to aggregated (n=23) gene expression studies of human muscle atrophy and response to exercise to identify convergent pathways. **Results:** Our analysis identified 231 loci at genome-wide significance. Gene regulatory elements within muscle, connective tissue, brain and several immune cell subsets were enriched for grip strength genetic signals. Loci were most commonly associated with additional traits such as body composition and musculoskeletal phenotype. **Conclusion:** Our findings provide new biological insights into the genetic determinants of grip strength and the potential to identify novel therapeutic targets for morbidities associated with diminished functional capacity, such as sarcopenia.

OC23- EFFECT OF LOSARTAN AND FISH OIL ON SECONDARY OUTCOMES IN THE ENRGISE PILOT RANDOMIZED CLINICAL TRIAL.

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Background: Low grade chronic inflammation characterized by elevations in interleukin 6 (IL-6) is an independent risk factor of impaired mobility in older persons. Angiotensin receptor blockers and omega 3 polyunsaturated fatty acids (ω-3) may reduce IL-6 and improve mobility. The ENRGISE Pilot Study was designed to test the main effects of the angiotensin receptor blocker losartan (LO) and ω-3 on the primary outcomes of IL-6 and 400m walking speed. Results showed no effect of LO or ω-3 or their combination on either primary outcome (Pahor M et al. J Gerontol A Biol Sci Med Sci 2018). **Objectives:** To report effects of the ENRGISE interventions on secondary outcomes: Grip strength, the SF-36 physical and mental health scores and depressive symptoms. **Methods:** The ENRGISE pilot enrolled participants between April 2016 and June 2017 who participated for 12 months. Participants were aged >=70 years and had IL-6 between 2.5 and 30 pg/ml and walked <1.0 m/s at enrollment. Participants were randomized in 3 strata 2x2 factorial to LO, 50-100 mg/d or placebo (n=43); ω-3, 1400-2800 mg/dl or placebo, (n=180); or to both LO and ω-3 or placebo (n=66). Grip strength was measured every 3 months; the SF-36 and depression scale at baseline and 12 months. We report point estimates and 95% confidence intervals. All participants with baseline and at least one follow-up visit were included in the analysis. **Results:** 289 participants were randomized (mean age 78.3; 47% women, 17% black). There was no effect of LO, ω-3 or their combination as compared to placebo on grip strength, SF-36 physical health score or mental health score, or depressive symptoms, Table. Analyses of additional secondary outcomes including the short physical performance battery (SPPB), frailty, isometric knee extensor and flexor power and torque are forthcoming. **Conclusion:** Consistent with the results of the primary outcomes, the secondary endpoint results do not support these interventions to decrease IL-6 or improve grip strength, depressive symptoms or self-reported physical or mental health function.

OC24- THE BURDEN OF AUTONOMOUS LIVING AND BASIC SELF-CARE DISABILITY FOR AGING ADULTS IN THE UNITED STATES: DISABILITY-ADJUSTED LIFE YEARS.

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Background: The convergence of the rapidly growing aging population and high prevalence of aging adults that have a functional disability is an emerging public health epidemic. Understanding how longitudinal declines in functional capacity impact health is important for guiding health-related resources and informing strategies for preserving function. **Objectives:** To determine the burden of instrumental activities of daily living (IADL) and basic activities of daily living (BADL) disability for aging adults in the United States. **Methods:** A sub-sample of 31,055 adults aged at least 50 years from the 1998-2014 waves of the Health and Retirement Study were included. Ability to complete six IADLs (using a map, preparing hot meals, taking medications, managing money, using a telephone, and shopping for groceries) and six BADLs (walking across a room, bathing, eating, getting in-or-out of bed, toileting, and dressing) were self-reported at each wave. Those responding that they had difficulty or were unable to perform any IADL or BADL were considered as having an IADL or BADL disability, respectively. Participants were stratified by sex to account for differences in life expectancy. The number of years lived with a disability was summed with the years of life that were lost due to premature mortality for the calculation of disability-adjusted life years (DALY). Sampling weights were used in the analyses to make the DALY estimates nationally-representative. **Results:** There were 26,387,887 IADL disability cases for men and 27,048,201 IADL disability cases for women. Men and women with an IADL disability had 236,037,634 and 233,772,385 DALYs, respectively. Combined, there were 469,810,019 years of healthy life lost from IADL disability. Similarly, there were 19,410,703 BADL disability cases for men and 27,162,227 BADL disability cases for women. Men with a BADL disability had 178,594,974 DALYs; whereas, women with a BADL disability had 253,630,152 DALYs. Combined, there were 432,225,126 years of healthy life lost from BADL disability. **Conclusion:** Millions of healthy years of life were lost from IADL and BADL disabilities for aging adults in the United States. Prioritizing health-related resources for mitigating the burden of functional declines may help aging adults increase their quality of life and life expectancy over time.

OC25- MULTICENTER COHORT STUDY OF FRAILTY AND ACCESS TO KIDNEY TRANSPLANTATION.

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Background: Frailty, a syndrome distinct from comorbidity and disability, is clinically manifested as a decreased resistance to stressors and is present in up to 35% of end-stage renal disease (ESRD) patients. It is associated with falls, hospitalizations, poor cognitive function, and mortality. Also, frailty is associated with poor post-kidney transplant (KT) outcomes including graft loss and mortality. It is likely frailty is associated with decreased access to KT, given its association with poor outcomes on dialysis and post-KT. Yet, clinicians have difficulty identifying which patients are frail; therefore, we sought to quantify if frail KT candidates had similar access to KT as nonfrail candidates. **Objectives:** To better understand the role of frailty with access to transplantation in ESRD patients who are referred for KT evaluation, we used a multi-center prospective cohort to quantify the association of frailty with time to KT listing, waitlist mortality, and transplant rate. Additionally, to test whether frailty is a mechanism which age, sex, or race disparities can be explained, we explored interactions between frailty and each characteristic for each outcome in separate models. **Methods:** We studied 7,078 KT candidates (2009-2018) in a three-center cohort study of frailty. We estimated time to listing and transplant rate by frailty status using Cox proportional hazards and Poisson regression, adjusting for demographic and health factors. **Results:** The mean age was 54 years (SD=13; range 18-89), 40.2% were female, 33.9% were African American, and 21.1% were frail. Frail participants were almost half as likely to be listed for KT (hazard ratio:0.62, 95%CI:0.56-0.69, p<0.001) compared to nonfrail participants, independent of age and other demographic factors. Furthermore, frail candidates were transplanted 35% less frequently than nonfrail candidates (incidence rate ratio:0.65, 95%CI:0.55-0.77, p<0.001). **Conclusion:** Frailty is associated with decreased listing and decreased rate of transplant and is a potentially modifiable risk factor. Thus, assessment at kidney transplant evaluation could improve patient counseling and motivate strategies to improve pre-KT outcomes for frail candidates of all ages

OC26- FRAILTY STATUS AFFECTS T CELL RESPONSES TO CMV, BUT NOT THE LEVEL OF CMV DNA.

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Background: Chronic inflammation is believed to contribute to the pathogenesis of frailty. Frail individuals have higher serum levels of inflammatory markers such as C-reactive protein (CRP), IL-6 and TNF. Cytomegalovirus (CMV) can cause chronic inflammation, is highly prevalent in frail individuals, and elicits a very large specific

T cell response that can correlate strongly with inflammatory markers depending on host HIV and frailty status. **Objectives:** To determine the relationships among the levels of CMV DNA in peripheral blood mononuclear cells (PBMC), frailty status, and T cell responses to CMV. **Methods:** CMV DNA in PBMCs was assayed using droplet digital polymerase chain reaction (ddPCR) in 36 men from the Baltimore-Washington DC site of the Multicenter AIDS Cohort (MACS) study, using primers targeting open reading frames (ORFs) of UL123 (immediate early antigen 1), UL54 (DNA polymerase), and UL55 (glycoprotein B). Numbers of T cells responsive to overlapping peptide pools covering 19 CMV ORFs were compared between donors with and without detectable CMV DNA in 4 donor subgroups defined by HIV serostatus and frailty status (defined by the Fried frailty phenotype). **Results:** CMV DNA was detected with at least one primer in PBMC from 33/36 donors, with individual genes detected in 10-20 donors. CMV detection did not differ significantly by frailty status. However, significant differences in numbers of T cells (CD4 or CD8) responding to CMV between donors with detectable CMV DNA and those without detectable CMV DNA were observed depending on frailty status, HIV serostatus, and the specific CMV ORF assayed. For example, in HIV- frail donors, but not in HIV- nonfrail donors, 6 CMV ORFs elicited significantly greater numbers of interferon-gamma-producing CD8 T cells in donors who had detectable UL55 or UL54 DNA, than in donors who did not. **Conclusion:** The detection of CMV DNA in PBMC did not differ significantly by frailty status, but may be correlated with levels of inflammation differentially in frail vs. nonfrail people. Further studies of the immune response to CMV may improve our understanding of the role of CMV in the chronic inflammation present in frailty, and the treatment of inflammation-related conditions.

OC27- NETWORK ANALYSIS OF FRAILTY AND AGING: EMPIRICAL DATA FROM THE MEXICAN HEALTH AND AGING STUDY.

Carmen García-Peña, Ricardo Ramírez-Aldana, Lorena Parra-Rodriguez, Juan Carlos Gómez-Verján, Mario Ulises Pérez-Zepeda, Luis Miguel Gutiérrez-Robledo (*Instituto Nacional de Geriatria, Mexico Mexico*)

Backgrounds: Frailty is still a challenge in the aging research area. Newer approaches to its study have been proposed, such as the complex network analysis. We tested frailty as a nonlinear phenomenon in a complex network through the use of graphical probabilistic models with empirical data to describe the interactions among specific deficits, frailty and death. **Objectives:** As the theoretical models that have been proposed do not yet identify nodes with specific physiological or functional variables; we propose testing a complex network through the use of a graphical probabilistic model based on a Bayesian methodology with empirical data to better understand the connections among deficits, using frailty and death as additional nodes. So, in the present study we applied a graphical models approach using data coming from the MHAS, Mexican Health and Aging Study, in order to contribute to a better understanding of the previously described theoretical models testing their performance with actual data. **Methods:** Data from the Mexican Health and Aging Study (main data-third wave 2012, mortality-fourth wave 2015) was used. Frailty was operationalized with a 35-deficit frailty index (FI). Analyzed nodes were the deficits, plus death and the total score of the FI. The edges, or ties, linking those nodes (set E) were obtained through structural learning, and an undirected discrete graph G (V,E) associated with a discrete graphical probabilistic model (Markov network) was derived. Structural learning was possible through hill-climbing (hc) and PC. Analyses were performed for the total population and for tertiles of the FI score. **Results:** From the total sample of 10,983 50-year or older adults, 43.8% were women and

the mean age was 64.6 years (SD=9.3). The number of connections within nodes increases according to the level of the FI score. Groups of deficits arise which are interconnected; these groups grow in number of nodes as the FI score increases. Almost all deficits related to mobility are interconnected, particularly those variables that indicate severe mobility impairment. **Conclusion:** Frailty behaves in a nonlinear way, as a complex network. Further research should aim at identifying the nature of the interactions we observed. This could eventually lead to the development of a conceptual framework

OC28- NORMATIVE DATA FOR AND PREDICTORS OF 5-YEAR CHANGE IN GAIT SPEED AMONG U.S. OLDER ADULTS IN THE NATIONAL SOCIAL LIFE, HEALTH AND AGING STUDY.

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Background: Gait speed is a marker of frailty and health among older adults, though the expected longitudinal trajectories of gait speed are not well characterized on a national level. Lack of reference data prohibits routine use of this important marker in the clinical setting. **Objectives:** The purposes of this study were to provide older adult normative data for 5-year change in gait speed by age and gender, and to identify predictors of improvement and decline in gait speed. **Methods:** We used the 2010-2011 and 2015-2016 waves of data collected from 2,142 older adults in the National Social Life, Health and Aging Project, a longitudinal, nationally-representative study of older U.S. adults. Gait speed (m/s) was calculated for each respondent using the faster of two, 8-foot timed walks performed at a usual pace. Quantile regression controlling for age and gender was used to identify the 5th, 10th, 25th, 50th, 75th, and 95th percentiles of gait speed for each age and gender category in both waves which were plotted using lowess. The difference in gait speed across waves was then calculated. A multinomial regression model identified whether age, gender, or race/ethnicity predicted 5-year change in gait speed categorized as slower, the same, or faster. **Results:** In 2010-11 and 2015-16, the mean gait speed was higher among men (0.58 m/s, 0.54 m/s) than women (0.56 m/s, 0.52 m/s). Gait speed declined with age across percentiles for both genders. The mean 5-year change in gait speed was -0.04 m/s (95% CI: -0.06 - -0.02). While 46% of the sample had slower gait speed 5 years later, 27% had faster gait speed. In a multinomial regression model, no demographic variables predicted faster gait speed 5 years later, age and African-American race predicted slower gait speed. **Conclusion:** This reference data suggests that age and gender-specific gait speed cut-points would help distinguish individuals performing above or below expected for "normal" aging in clinical practice. Furthermore, a substantial percentage of older adults do not demonstrate a decline in gait speed over time and monitoring these trajectories may offer unique information to one's position in the cross-sectional distribution of gait speed.

OC29- EFFECT OF OMEGA-3 FATTY ACID INTAKE ON RED BLOOD CELL FATTY ACID COMPOSITION AND ASSOCIATION WITH INFLAMMATION AND MOBILITY.

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Background: Observational studies suggest that chronic low-grade inflammation is related to reduced physical functioning and increased disability among older adults. No prior studies have attempted to use pharmacologic therapies to reduce inflammation to improve physical functioning among older adults with chronic low-grade inflammation. Fish-oil derived omega-3 ($\omega-3$) polyunsaturated fatty acids have been hypothesized to lower inflammation but results have been inconsistent. **Objectives:** We evaluated the response to $\omega-3$ fatty acids by measuring changes in red blood cell (RBC) $\omega-3$ concentration and related those changes to changes in inflammation using samples obtained from the ENRGISE Pilot trial. **Methods:** We randomized 289 participants (47.4% women) who were ≥70 years old with mobility impairment (0.44 m/s < gait speed < 1 m/s), IL-6 levels between 2.5 and 30 pg/ml, and completed a 400 meters walk into three strata: a) losartan 50 to 100 mg/day or placebo (n=43), b) $\omega-3$ fatty acids 1.4 to 2.8 g/day (eicosapentaenoic acid (EPA) 0.8 to 1.6 g/day plus docosahexaenoic acid (DHA) 0.4 to 0.8 g/day or placebo (corn oil) (n=180), and c) both losartan and fatty acids in a 2x2 factorial (n=66) and followed for 12 months. Data from the $\omega-3$ fatty acids alone and combined strata (n=148) were collapsed and compared to respective placebo strata (Pla strata) (n=98). RBC fatty acid concentrations were measured using gas chromatography and expressed as a percentage of total fatty acid concentration (%). Serum IL-6 was measured by ELISA. Data were analyzed using contrasts at 6 and 12-months from a mixed model using all three strata with adjustment for baseline level, visit, strata, and clinical site. **Results:** Mean age was 77.6 ± 5.4 yrs (49% female, Non-hispanic white 79%). At baseline, there were no associations between RBC EPA or DHA and IL-6. At 6 and 12 months, RBC EPA and DHA were elevated significantly with $\omega-3$ compared to Pla (6 month: EPA: $\omega-3$ arm 0.9 ± 0.4%, Pla arm 0.4 ± 0.1% (P<0.0001) DHA: $\omega-3$ arm 6.2 + 2.5%, Pla arm 5.0 ± 1.6% (P<0.0002)) (12 month: EPA: $\omega-3$ arm 1.0 + 0.6%, Pla arm 0.4 ± 0.1% (P<0.0001) DHA: $\omega-3$ arm 6.3 ± 2.7%, Pla arm 4.7 ± 1.8% (P<0.0001)). The changes in RBC EPA and DHA were not related to changes in serum IL-6 (p-value: 0.59 EPA, 0.78 EPA). **Conclusion:** $\omega-3$ fatty acid supplementation in older adults with mobility limitations and chronic low-grade inflammation can effectively increase RBC concentrations of EPA and DHA but was not related to reductions in inflammation.

OC30- NOVEL INFLAMMATORY BIOMARKERS AND THE ONSET OF FRAILTY AND MAJOR MOBILITY DISABILITY IN THE ENRGISE PILOT TRIAL.

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Background: Elevated IL6 levels are consistently linked to declining mobility. The ENRGISE study recruited persons with elevated IL6 levels to test whether omega-3 fatty acids or losartan could reduce IL6 levels and preserve mobility. It also measured CRP, sIL2Ra, TNF-alpha R1, sCD163, Lipopolysaccharide binding protein (LPSBP), and GDF-8 to provide complementary mechanistic information on inflammatory and muscle-related pathways. **Objectives:** To determine whether the baseline levels of any of these complementary measures were related to frailty or the 12-month incidence of major mobility disability (MMD). **Methods**: The study enrolled 289 mobility impaired older adults (>= 70 yrs of age; 47.4% women) with IL-6 levels between 2.5 and 30 pg/ml, and were able to walk 400 meters. Participants were randomized in three strata to: a) losartan 50 to 100 mg/day or placebo (n=43), b) fish oil 1400 to 2800 mg/day or placebo (n=180), and c) with both (n=66). Frailty was adapted from the Fried Criteria and MMD was defined as the inability to complete a 400 M walk within 15 minutes. The supplementary biomarkers were measured in a subset of 225 participants. We used logistic regression and cox proportional hazards modeling to relate the levels of each biomarker to frailty at baseline and the incidence of frailty and MMD over 12 months. Models were adjusted for: age, race, gender, randomization assignment, clinic, BMI, depression score, grip strength 4-meter walk speed and comorbidity count. **Results:** The median baseline level of IL6 was 3.7 pg/ml, and 39 (13%) participants were frail. By 12 months, 18 (7%) and 61 (21%) developed frailty or MMD, respectively. Only TNF-alpha R1 was associated with frailty at baseline (8% vs 15% comparing extreme tertiles, ORadj: 6.9, 95% CI: 1.3-38.1). Due to small numbers we do not report associations with incident frailty. For MMD, only soluble IL2 receptor α was associated with incident MMD (20% vs 28% comparing extreme tertiles, HRadj: 2.5, 95% CI: 1.1–5.5). **Conclusion:** This analysis provides tentative evidence of the contribution of additional inflammatory markers in determining the onset of frailty and MMD beyond IL6.

OC31- EFFECT OF AEROBIC OR RESISTANCE EXERCISE OR BOTH ON BODY COMPOSITION AND METABOLIC AND PHYSICAL FUNCTION IN OBESE OLDER ADULTS WHILE DIETING: RESULTS FROM THE LITOE RANDOMIZED CLINICAL TRIAL.

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Background: Obesity exacerbates the adverse effects of aging on body composition and metabolic/physical function resulting in frailty. We reported that weight loss (WL) plus combined aerobic and resistance exercise is most effective in improving functional status of obese older adults (NEJM 2017). However, it remains unclear which exercise modes are most effective in reversing age-related changes in body composition and improving metabolic and physical function in dieting obese older adults. **Objectives:** Determine the relative effectiveness of WL plus different exercise types on changes in visceral adipose tissue (VAT) and intermuscular adipose tissue (IMAT) in relation to changes in insulin sensitivity and muscle strength/physical function in obese older adults. **Methods:** One-hundred-sixty obese older adults were randomly assigned to 6-months of WL plus aerobic (AET), resistance (RET), or combined aerobic and resistance (COMB) training or control (CON). In this secondary analysis, we assessed VAT and IAT using MRI, Matsuda insulin sensitivity index (ISI) using oral glucose tolerance test, knee extension (KE) and knee flexion (KF) strength using dynamometry, and physical function using Physical Performance Test (PPT), VO2peak, and gait-speed. **Results:** Despite equal ~10% weight loss, VAT and IMAT decreased more in the COMB than in AET and RET groups (VAT: -35% vs. -19% and -18%; IMAT; -41% vs. -28% and -23%; P=.001 to .02); VAT and IMAT decreased in all 3 groups more than CON (3%) (between-group P<.001). Moreover, ISI increased more in COMB than in AET and RET groups (86% vs. 50% and 39%; P<.005 to .03). KE and KF strength improved more in COMB and RET than AET (KE: 16% and 19% vs. -6%; KF: 15% and 16% vs. -2%; all P<.05). PPT improved more in COMB than in AET and RET groups and VO2peak improved more in COMB and AET than RET group as reported. Changes in VAT and IMAT correlated with changes in ISI (r=-.56 and -.49), PPT (r= -.27 and -.29), VO2peak (r=-.52 and -.25), and gait-speed (r=-.36 and -24) (all P<.05). **Conclusion:** WL plus combined AET and RET was the most effective in improving body composition and metabolic and physical function in obese older adults.

OC32- BIOMARKERS OF SARCOPENIA IN VERY OLD PATIENTS WITH HIP FRACTURE.

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Background: Hip fracture is both a cause and a consequence of sarcopenia. Older persons with sarcopenia have an increased risk of falling, and the prevalence of sarcopenia may be increased in those who suffer a hip fracture. **Objectives:** The aim of this study was to explore potential biomarkers (neuromuscular and peripheral pro-inflammatory and oxidative stress markers) that may be associated with sarcopenia in very old persons with hip fracture. **Methods:** We recruited 150 consecutive patients >80 years old admitted to an orthogeriatric unit for a traumatic hip fracture. Muscle mass was assessed preoperatively using bioimpedance analysis; Janssen's (J) and Masanés (M) reference cutoff-points were used to define low muscle mass. Muscle strength was assessed with handgrip strength (Jamar's dynamometer). Sarcopenia was defined by having both low muscle mass and strength. Peripheral markers —pro-inflammatory and oxidative stress parameters— were determined either in the plasma or in the erythrocyte fraction obtained from peripheral whole blood of every patient preoperatively. **Results:** Mean age was 87.6±4.9 years, 79% were women. The prevalence of sarcopenia was 11.5% with Janssen's and 34.9% with Masanés cutoffs. Among the four pro-inflammatory cytokines tested in plasma, only TNF-α was different (lower) in sarcopenic than non-sarcopenic participants using both cutoffs (J 7.9±6.2 vs 8.3±5.8, M 6.8±4.7 vs 9.1±6.2). Erythrocyte glutathione system showed a non-significant tendency to lower GSH levels and GSH/GSSG ratios in sarcopenic participants compared to non-sarcopenic subjects. Catalase (CAT) activity was also lower in sarcopenic participants (J 2904±1429 vs 3329±1483, M 3037±1430 vs 3431±1498. No significant differences were found between groups in chymotrypsin-like activity of the 20S proteasome, SOD, GPx and BuChE activity, CAF, IFNγ or IL-1β. **Conclusion:** The prevalence of sarcopenia in patients with hip fracture varies according to the muscle mass reference cutoff-points used, being higher with national references. We did not find differences in most neuromuscular, pro-inflammatory or oxidative stress markers, except for lower peripheral TNF-α levels and catalase activity in sarcopenic participants, which may be markers of an early inflammatory reaction that is hampered in sarcopenic patients.

OC33- SARCOPENIC OBESITY IN ASIAN POPULATIONS: INFLUENCE OF OBESITY DEFINITIONS ON PREVALENCE AND PHYSICAL PERFORMANCE.

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Background: Sarcopenic obesity (SO) is associated with poorer physical performance in the elderly and will increase in relevance due to population ageing and the obesity epidemic. The lack of a consensus definition for SO has resulted in variability in its reported prevalence, poor agreement between different definitions, and disagreement on its impact on physical performance, impeding further development in the field. While standardized definitions for sarcopenia have been

developed, there is as yet no consensus on an obesity definition. **Objectives:** To compare between 3 widely-adopted definitions of obesity in terms of SO prevalence, agreement between definitions, and functional outcomes across body composition phenotypes. **Methods:** We studied 200 community-dwelling, cognitively-intact and functionally-independent older adults from the GERILABS study. We utilized three commonly-used definitions of obesity: body mass index (BMI), waist circumference (WC) and DXA-derived fat mass percentage (FM%). Together with the Asian Working Group for Sarcopenia criteria, we classified subjects into 4 body composition phenotypes: normal, obese, sarcopenic and SO. The outcomes were: SO prevalence; agreement between definitions; and muscle function measures of handgrip strength, gait speed and Short Physical Performance Battery (SPPB). We also performed multiple linear regression to determine the association between body composition phenotypes and SPPB. **Results:** Defining obesity as BMI>=27.5kg/m2 resulted in the lowest case detection rate of SO (0.5%) compared to FM% (10.0%) and WC (10.5%). Agreement was lowest between BMI and WC ($\varkappa$=0.364) and highest between FM% and WC ($\varkappa$=0.583). SO performed the worst amongst body composition phenotypes in handgrip strength, gait speed and SPPB (all p<0.01) only for the WC definition. In regression analyses, SO, but not sarcopenia, was associated with decreased SPPB scores (β=-0.279, p<0.001) for the WC model. **Conclusion:** There is a high degree of variation in the prevalence of SO across different definitions of obesity, with low-moderate agreement between them. Our results corroborate recent evidence that it is WC, and thus central obesity specifically, which is best associated with poor muscle function in SO. Thus, WC should be further explored as a means to define obesity for accurate and early characterization of SO among older adults in Asian populations.

OC34- UREMIC MYOPATHY: DYNAPENIA, DIABESITY-ASSOCIATED SARCOPENIA & PHYSICAL FRAILTY IN DISGUISE?

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Background: Uremic myopathy is not well-characterized. Chronic kidney disease (CKD) is a 5-stage, progressive decline in renal function with accumulating blood nitrogenous metabolites impairing skeletal muscle metabolism, mass, strength, and physical function. Though the onset of muscle impairments attributed to uremic myopathy is unknown, we contend that uremic myopathy is characterized by concurrent impairments of dynapenia, diabesity-associated sarcopenia & physical frailty that combine to underlie progressive myopathy in diabetic CKD. **Objectives:** Our objective is to determine the prevalence of dynapenia, sarcopenia and physical frailty in participants across stages of diabetes-induced CKD. **Methods:** We performed a cross-sectional cohort analysis of 55 participants (65% men) with diabetes and pre-dialysis-CKD staged by glomerular filtration rate (eGFR) from serum creatinine (Cr) levels. All participants had blood draws to assess concentration of Cr, urea nitrogen (BUN) and glycated hemoglobin (HbA1c). Each participant performed a 9-item modified Physical Performance Test (mPPT), knee extensor isometric dynamometry to determine strength, and DXA to determine appendicular limb mass (ALM) and sarcopenia by skeletal muscle index (SMI). GFR, BUN, mPPT, knee extensor peak torque, and SMI were compared across CKD stages using 1-way ANOVA. Frequency of dynapenia, sarcopenia, and physical frailty were compared across CKD stages (Stage1/2 versus Stage4/5) using Chi Square test of association. **Results:** Age of DM participants = 60 (11) years; weight = 104 (20) kg; BMI = 34 (6) kg/m2 and %BF= 35. Forty-two percent (42%) of participants were classified as uremic. BUN increased progressively from 17 (4) mg/dL in stage 1&2 to 60 (14) mg/dL in stage 4&5 (P<.01). The mPPT score decreased from 30 (3.4) in stage 1&2 to 17 (7) in stage 4/5 (P<.05). Knee extensor strength declined 45% from stage 1/2 to stage 4/5 (P<.05). Prevalence of dynapenia, diabesity-associated sarcopenia & physical frailty increased 63%, 39% and 58%, respectively from Stage 2 CKD to Stage 5 CKD (all p<0.01). **Conclusion:** As diabetic-CKD progresses from stage 1&2 to stage 4&5, the prevalence of dynapenia, diabesity-associated sarcopenia, and physical frailty increase combining to characterize the underlying impairments of uremic myopathy. Therapeutic interventions early in stage 1&2 may prevent uremic myopathy and accompanying impairments.

OC35- MUSCLE MASS IS MAINTAINED AND BODY FAT REDUCED WITH EXERCISE IN OLDER PEOPLE AGING WITH HIV.

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Background: Sarcopenia and increasing adiposity remain a concern in people aging with HIV (PAWH) despite mitigation of muscle wasting and lipodystrophy with newer antiretroviral therapies (ART). Exercise is recommended to increase muscle and reduce body fat in older adults but whether these adaptations occur in PAWH has not been investigated in response to standardized exercise. **Objectives:** To compare changes in lean mass and adiposity in previously sedentary PAWH and uninfected controls (NEG) due to exercise. **Methods:** PAWH (on ART >2 years) and NEG completed a 24-week, moderate- to high-intensity supervised cardiovascular and resistance exercise intervention. Total body lean mass (LEAN), appendicular lean mass (ALM; summed limb lean), total body fat mass (FM), and visceral fat area (VFA) were measured pre/post intervention using DXA. Participant characteristics are reported as the median {IQR} or mean (95% CI). Multivariable regression analyses were adjusted for age and exercise adherence. **Results:** Participants (27 PAWH, 28 NEG) were majority male (93%), white (80%) and non-Hispanic (86%). PAWH and NEG were of similar age [56 yr {52, 61}; 60 yr {54, 64}; P>0.05]. PAWH were diagnosed with HIV 23 years {16, 28} prior, had a CD4 count of 548 cells/μl {416, 772}, and all had plasma HIV-1 RNA <50 copies/mL. PAWH had lower FM at baseline; changes due to exercise did not differ by serostatus (Table).

Table
Baseline and Changes with Exercise [Mean (95% CI)]

	Baseline		Change	
	PAWH	NEG	PAWH	NEG
LEAN (kg)	57.7	60.0	0.6	0.8*
	(57.7, 54.2)	(56.4, 63.6)	(-0.2, 1.4)	(0.0, 1.6)
ALM (kg)	25.7	26.8	0.4	0.4
	(23.9, 27.4)	(25.2, 28.4)	(-0.6, 0.8)	(0.0, 0.9)
Fat Mass (kg)	20.6	27.2**	-2.0***	-0.9*
	(17.7, 23.6)	(24.0, 30.4)	(-2.9, -1.1)	(-1.8, 0.0)
VFA (cm2)	184	211	-17.7***	-10.3*
	(151, 217)	(184, 237)	(-27.1, -8.2)	(-19.6, 1.0)

Between Groups: **P < 0.01 Within: *P < .05, ***P < 0.001

Conclusion: Cardiovascular and resistance exercise was effective at reducing total and visceral fat in PAWH and controls. Although

greater emphasis on resistance exercise may be needed to increase muscle mass in PAWH, halting muscle loss is an important benefit of combined exercise.

OC36- A RANDOMIZED CONTROLLED PILOT AND FEASIBILITY EXERCISE AND PROTEIN EFFECTIVENESS SUPPLEMENTATION STUDY SUPPORTING AUTONOMY IN COMMUNITY-DWELLING FRAIL OLDER ADULTS.

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Background: Participation in a regular multi-component exercise program that includes progressive resistance training, aerobic activity as well as balance and flexibility, is a key strategy to improve muscle mass, strength and physical function in older adults. However, exercise combined with protein supplementation might be an even more effective strategy, especially when adherence can be maintained over the long-term. **Objectives:** The primary aim of this study was to examine the feasibility, tolerability and effects of a structured exercise program combined with twice daily protein supplements, over 6 months, on the primary outcomes of gait speed, grip strength and physical performance using the Short Performance Physical Battery (SPPB) and the Timed Up & Go test (TUG). Secondary outcomes included frailty status, muscle mass, quality of life, nutritional intake, cognitive performance and physical activity levels. **Methods:** Community living adults aged >=65 years identified as pre-frail or frail (FRAIL Screen) were recruited to participate in a center-and home-based exercise program (5x/week for 6 months) including walking, strength, balance and flexibility. In addition, participants were randomly assigned to either whey or rice based protein supplements that were consumed twice per day (90kcal, 20g protein in 150ml water). **Results:** The findings suggest that the 6-month intervention, regardless of protein source used, was feasible, tolerable and safe in pre-frail older adults living in the community. However several major challenges included difficulties with recruitment of frail participants and several gastrointestinal symptoms of mild intensity that were probably related to protein supplementation, particularly the whey protein. No differences between the two protein groups were found for any primary or secondary outcomes (p>0.05). **Conclusion:** This study provides valuable insight into the feasibility of recruiting and retaining pre-frail and frail older adults into community-based intervention programs and, on the safety and tolerability of a combined exercise and protein supplement program designed to halt or reverse the progression of frailty. Moreover, whey and rice protein supplements were found to have comparable effects on physical function parameters in pre-frail older adults inferring the quality of protein may not be critical as long as a sufficient amount is consumed.

OC37- EFFECT OF GASTRIC ACID SUPPRESSANTS ON RESPONSE TO A PHYSICAL ACTIVITY INTERVENTION AND MAJOR MOBILITY DISABILITY IN OLDER ADULTS: RESULTS FROM THE LIFESTYLE INTERVENTIONS FOR ELDERS (LIFE) STUDY.

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Background: Proton pump inhibitors (PPIs) are associated with several adverse outcomes in older adults including associated with reduced acid secretions or other pharmacologic actions including bone fractures infections, reduced mineral absorption, and renal impairment. Therapeutic alternatives, H2-receptor antagonists (H2RAs), have less potent anti-secretory effects but have additional anticholinergic side effects. The comparative effects of acid suppressants on mobility disability outcomes in older adults have not been explored. **Objectives:** This study compared PPIs versus H2RAs directly and versus non-users on mobility disability and injurious fall outcomes. **Methods:** This was a secondary analysis of the Lifestyle Interventions for Elders (LIFE) trial. Participants age 70-89 years were randomized to a physical activity (PA) or health education (HE) intervention. Confounders included baseline demographic, physical, and cognitive functioning measures as well as measures that may be related to medication use such as sleep quality and symptoms of acid reflux disease which were adjusted for utilizing propensity score weighting methods. Outcomes included incident and persistent major mobility disability (MMD) and injurious falls. Weighted Cox proportional hazard models were used to evaluate the independent effects of medications and interaction effects. **Results:** Of 1,635 participants, 89 (5.6%) used H2RA, 437 (27.4%) used PPIs. There was no interaction between medication use and the effect of the PA intervention. Drug effects were significant for H2RAs (HR=1.74) and PPIs (HR=1.32) compared to non-users for persistent MMD outcomes. Similarly, H2RAs (HR=1.65) and PPIs (HR=1.44) were associated with increased injurious falls compared to non-users. A combined H2RA and PPI exposure group showed a 26% increase of MMD (HR=1.26 [1.07-1.48]), a 44% increase in PMMD (HR=1.44 [1.16-1.77]), and a 48% increase in Falls (HR=1.48 [1.15-1.91]) compared to non-users. All direct comparisons between PPIs and H2RAs were non-significant. **Conclusion:** Compared to non-users, participants using either PPIs or H2RAs had increased risk of MMD, persistent MMD, and falls. Whether the cause of these effects is related to the individual pharmacology of each medication, reduced acid secretion, or the underlying disease state requires further evaluation.

OC38- SARCOPENIA IN OLDER ADULTS UNDERGOING TRANSCATHETER AORTIC VALVE REPLACEMENT.

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Background: Sarcopenia, defined as age-related loss of muscle mass and strength, is a biologic substrate of frailty that is relevant to the risk stratification and treatment of frail older adults referred for transcatheter aortic valve replacement (TAVR). **Objectives:** To determine the incremental prognostic value of sarcopenia as measured by a combination of psoas muscle area (PMA) and lower-extremity muscle strength in older adults undergoing TAVR. **Methods:** The FRAILTY-AVR prospective cohort study enrolled patients >=70 years of age undergoing TAVR at 14 sites in 3 countries. PMA was

measured from pre-procedural clinical CT scans using a web-based software (CoreSlicer.com). Lower-extremity strength was measured using a timed chair rise test. Patients were classified as sarcopenic if PMA was less than the sex-stratified reference value and the chair rise test was >=15 seconds. Outcomes of interest were all-cause mortality, length of stay, disposition, and disability at 1 year. **Results:** The cohort consisted of 400 patients with a mean PMA of 21.7±4.4 cm2 in males and 15.0±3.6 cm2 in females. One in five patients were found to be sarcopenic and had an observed 1-year mortality of 30%, as compared to 3% in non-sarcopenic patients (P<0.001). After adjusting for age, sex, body surface area, and predicted risk of mortality, sarcopenic patients had higher risks of 1-year mortality (OR 11.30, 95% CI 2.51 to 50.91), mortality or worsened disability (OR 2.92, 95% CI 1.40 to 6.10), discharge to skilled-care facilities (OR 3.12, 95% CI 1.21 to 8.07), and longer lengths of stay (4.42 days, 95% CI 1.51 to 7.32). **Conclusion:** Our practical assessment of sarcopenia was predictive of adverse patient-cantered outcomes in older adults undergoing TAVR and added incremental value to a clinical risk model. Further research is needed to test the hypothesis that treatment of sarcopenia will lead to improved outcomes following TAVR.