

SYMPOSIA

S1- THE SPRING STUDY: CHARACTERIZING RESILIENCE AND FRAILTY TO PHYSICAL STRESSORS USING A DYNAMICAL PHYSIOLOGICAL SYSTEMS APPROACH. Karen Bandeen-Roche (*Johns Hopkins University, Baltimore, USA*)

Communication 1: *The Measurement of Physical Resiliencies: Conceptualization and Study Design*, Karen Bandeen-Roche (Johns Hopkins University, Baltimore, USA)

We aim to develop signatures of physical resilience in older adults who will undergo clinical stressors; validate the signatures' ability to distinguish those who will, or not, respond resiliently, and characterize underlying physiological determinants. This presentation describes the study conceptualization and design. The underlying physiology is conceptualized as a dynamical system, and resilience, as a property thereof. A pilot/confirmatory study has been initiated with branches addressing three clinical stressors. Resilience signatures will be grounded in dynamical data from multiple stress-response assessments; many other markers are being collected. We propose a data analytic strategy to build signatures, and evaluate their success predicting both short- and long-term responses to stressors, with both data- and theory-driven elements. If successful, our study will generate new means to identify individuals with impaired resiliency to stressors, deepen knowledge of age-related biological changes that impair stress-response, and open the way for novel interventions to bolster resiliency.

Communication 2: *Physical Resiliencies in Three Major Clinical Stressors*, Jeremy Walston (Geriatric Medicine and Gerontology, Johns Hopkins University, Baltimore, USA)

To study resiliencies among older adults, we designed and are implementing pilot projects in three clinical stressors: total knee replacement surgery (TKR); initiation of hemodialysis; and bone marrow transplantation (BMT) in hematologic malignancies. Each study aims to characterize signatures of resiliency in older adults by gathering extensive measurements before, during and after a stressor. For each stressor, we present rationale for stressor selection, considerations for conceptualizing resilience, study design and progress, and challenges encountered in the research. Re-attainment of baseline physical function or improvement over baseline function (as in TKR) is a shared resiliency response whereas resolution of pain, post-dialysis recovery time, and immune recovery exemplify responses specific to the respective stressors. Challenges include uncertainty in hemodialysis initiation timing and BMT eligibility. Each stressor is increasingly prevalent in older adults and elicits heterogeneous responses. The development of resiliency signatures may allow targeted interventions before stressor onset.

Communication 3: *Do Dynamical System Measures at Baseline Predict Responses to Clinical Stressors? Findings from Pilot Studies of Physical Resilience and Aging*, Ravi Varadhan (Oncology Biostatistics, Johns Hopkins University, Baltimore, USA)

Resilience of an organism is essentially a dynamic property. Hence, in order to characterize the resilience of an organism, it is essential to perturb it and study its response. In the Study of Physical Resilience and Aging (SPRING), we are assessing a number of dynamical responses at baseline. These include response of cardiac autonomic nervous system using Holter monitoring, oral glucose tolerance test, 24-hour diurnal cortisol response, fatigability to treadmill test, and ACTH stimulation test. We have collected pilot data in 58 subjects undergoing 3 clinical stressors. The data will be analyzed using a dynamical systems modeling framework that we have developed. Our preliminary results show that the stimulus-response data from multiple dynamic systems can be parsimoniously characterized using two principal components, which reflect overall and adaptive homeostatic regulation. We will evaluate how these two measures of resiliency predict the recovery of physical, cognitive, and clinical trajectories. We will present the preliminary findings from these dynamic responses in three different clinical stressors: bone-marrow transplantation in hematologic malignancies, hemodialysis initiation in end-stage renal disease, and total knee replacement.

S2- SARCOPENIA AND NEUROSCIENCE: A FAILURE TO COMMUNICATE. Stephen B. Kritchevsky (*Sticht Center for Healthy Aging and Alzheimer's Prevention, Wake Forest School of Medicine, Winston Salem, USA*)

Communication 1: *Welcome and Introductory Comments*, Stephen B. Kritchevsky (Sticht Center for Healthy Aging and Alzheimer's Prevention, Wake Forest School of Medicine, Winston Salem, USA)

Professor Kritchevsky will introduce the symposium. His introductory comments will focus on the clinical significance of both muscle strength and gait speed having predictive power in relation to a range of health conditions — even when these are assessed decades later — has motivated claims that they can serve as a «vital signs» for middle-aged and older adults.

Communication 2: *Sarcopenia - Dynapenia: Reflecting back on the last decade*, Brian C. Clark (Ohio Musculoskeletal and Neurological Institute (OMNI), Ohio University, Athens, USA)

Professor Clark will introduce the premise that strength is a simple measure of physical performance that provides a marker of skeletal muscle status in general, and sarcopenia in particular. He will then present recent data and analyses arguing that central neural mechanisms are a, if not the, critical determinant of the age-related loss of muscle strength as

well as mobility. Here, he will provide an overview of the concept of dynapenia (age-related loss of muscle strength) highlighting key findings suggesting that dynapenia and the age-related loss of muscle mass, which was originally defined as sarcopenia, are not as mechanistically linked as originally believed. In this context, he will discuss the evolution of the definition of sarcopenia over the past decade, and present new data illustrating that older adults with clinically-meaningful leg extensor muscle weakness exhibit impairments in their central neural activation capacity of muscle and corticospinal hypoexcitability. He will also present neuroimaging data examining the neural correlates of weakness and mobility.

Communication 3: *Get a grip: individual variations in grip strength are a marker of brain health*, Richard G. Carson (Trinity College Institute of Neuroscience & School of Psychology, Trinity College Dublin, Dublin, Ireland)

Professor Carson will argue that the application of grip force is a complex coordinated behavior that is mediated by integrated activity across distributed brain networks, with individual variations in the capacity to generate grip force being closely associated with a broad spectrum of markers that reflect brain health. Collectively, this symposium will highlight the convergent functional and structural mediation of cognitive and motor processes by the brain. Accordingly, the origins of the close and pervasive relationships between age-related declines in maximum grip strength and expressions of cognitive dysfunction will be readily appreciated. The overriding conclusion arising from the analyses that will be presented is that maximum strength testing provides a discriminating measure of neurological function. The ramifications are clear. To the extent that changes in maximum strength can be registered over relatively short periods, they have the potential to serve as early markers of incipient changes in brain health. In presaging the accumulation of deficits that will ultimately impact negatively not only on cognitive status but also give rise to manifestations of frailty, loss of functional independence, and reduced quality of life, the monitoring of strength may assist in prognosis and facilitate early intervention. With respect to various conditions of aging, including those to which the designations sarcopenia or frailty have been applied, the implications of this symposium will extend beyond our understanding of etiology. They also bear prominently upon the design and deployment of therapeutic interventions geared to combat these conditions. It is not unusual to read statements along the lines of “sarcopenia is the major cause of frailty”. Although the basis for such conclusions is typically evidence (e.g., statistical associations with expressions of frailty) derived using consensus classifications of “sarcopenia” that include indices of “muscle function” (maximum grip strength and/or walking speed), the associated discussion of causal relations is often restricted entirely to the molecular and cellular physiology of skeletal muscle. While in any domain of research there will be a range of emphases that emerge in the interpretation of empirical findings, there is presently a wide spread and striking disconnect between the multifactorial measures that are used

to assess “sarcopenia” and the rather uniform prescriptions that issue forth. The latter are in many instances predicated upon an interpretation of the “muscle function” dimension of “sarcopenia” determinations that excludes entirely the contributory role of the central nervous system. This uniformity of emphasis is reflected in the pharmacological approaches being developed, or currently available, with the goal of treating “sarcopenia”. These include vitamin D, protein (essential amino acids), testosterone, selective androgen receptor modulators, growth hormone, ghrelin agonists, myostatin inhibitors, activin 11R antagonists, angiotensin-converting enzyme inhibitor (perindopril), espidolol (B1/B2 adrenergic receptor antagonist), and fast skeletal muscle troponin activators. Although the respective efficacy of these treatments is a matter for empirical enquiry, it is clear that the assumed nature of the underlying pathophysiology does not in most cases extend to the brain. Why is this of practical concern? The achievement of a useful endpoint in phase II trials of such treatments may be defined in terms of some measure of muscle mass or muscle quality (i.e., consistent with the presumed mechanism of action of most of the pharmacological agents listed previously). This may however prove to be entirely irrelevant if a consensus definition of “sarcopenia” is used to judge efficacy in phase III clinical trials. The data and analyses to be presented in this symposium will illustrate that tests of maximum strength (as well as gait sufficiency) — the elements of the current consensus definitions of “sarcopenia” that have the greatest predictive power in relation to functional status — reflect primarily the integrity of the brain. Stated directly, a case will be made that the steps that are being taken presently to address a perceived deficiency in muscle mass or muscle quality are quite distinct from those actually mandated by what are evidently deficits in neuromuscular control.

S3- PRIMARY CARE APPROACH TO GERIATRIC ASSESSMENT, FRAILTY AND SARCOPENIA. John Morley (*Division of Geriatric Medicine, Saint Louis University School of Medicine, Saint Louis, USA*)

Communication 1: *Primary Care approach to frailty and sarcopenia*, Jean Woo (The Chinese University of Hong Kong, Hong Kong)

There exists unmet needs in ageing populations that require to be addressed using integrated health and social care systems in the primary care setting. Problems commonly encountered include poor oral health, problems with hearing and vision, physical and cognitive frailty, poor psychological wellbeing, dependency in instrumental activities of daily living, problems with medication and polypharmacy, problems with finance and care, all of which promote increase use of hospital services. This presentation describes a step care model involving community centres in all 18 districts of Hong Kong, using automated means to carry out geriatric screening as well as blood pressure measurements, followed by protocols for dealing with identified problems. Data are transferred to cloud for analysis and generation of individual reports. Subsequent action

may include one on one consultation with a nurse or social worker, or group activities. Only if necessary will the older person be directed to a medical clinic for further management. The commonest unmet needs were memory complaints (>70%); frailty and pre-frailty (>60%), chewing difficulties (38%); Problems with IADL; polypharmacy (24%); and a feeling of life having no meaning (22%). Exercise programs for sarcopenia improve strength, physical function and activities of daily living that lasted 12 weeks beyond the cessation of exercise program, while addition of a nutrition supplement containing HMB has incremental effect on muscle mass but not function, only during the period of supplementation. A multi-component frailty prevention program also reverses frailty and improves physical and cognitive functions as well as self-rated health among those who were pre-frail. Opportunities exist in the primary care setting to address unmet needs of older people by detection of geriatric syndromes followed by community-based intervention programs. A medico social model could represent the first step in a step care approach that can be linked to healthcare facilities with multidisciplinary health care professionals.

Communication 2: *The Rapid Geriatric Assessment: a Tool for Primary Care Physicians*, John Morley (Division of Geriatric Medicine, Saint Louis University School of Medicine, Saint Louis, USA)

The Rapid Geriatric Assessment screens for frailty (FRAIL), sarcopenia (SARC-F), anorexia of aging (SNAQ) and cognition (Rapid Cognitive Screen (RCS)). All are validated in multiple continents. We will give an overview of its validation and on the results of its use in over 14,000 older persons in multiple clinical sites in Missouri. We will also show the results for components of FRAIL and its treatment algorithm.

Communication 3: *The Utility of Rapid Geriatric Assessment App to Identify Unmet Needs of Older Adults in Primary Care*, Reshma A Merchant (National University Health System of Singapore, Singapore)

With rapid increase in ageing population, especially in Asian countries and limited number of geriatricians, there is an immediate need to enhance ability of primary care physicians, coordinators and nurses to screen and manage geriatric syndromes. There is increasing emphasis on primary care in the 21st century to provide comprehensive, preventive and person-centered care plan, and are well positioned to succeed in population health. Frailty, Sarcopenia, cognitive impairment, falls, nutrition and loneliness are well known precursors of functional decline and disability. Rapid Geriatric Assessment (RGA) developed by Saint Louis University measures frailty, sarcopenia, anorexia and cognition. In addition to screening, the RGA also includes additional questions should a person screen positive eg for fatigue, to exclude depression, sleep apnoea and additional investigations to exclude hypothyroidism, B12 deficiency and management plans eg recommendations on exercise and vitamin D. RGA application

(eRGA) is practical, fast and efficient app which can be used by coordinator and nurse in primary care. Frailty is measured using the FRAIL scale, sarcopenia using Sarc-F, nutrition using SNAQ (Simplified Nutritional Assessment Questionnaire) and cognition using the rapid cognitive screen. For those with fatigue, depression was measured using PHQ-9. More than 1/3 were either pre-frail or frail but 1/6 had difficulties with climbing 1 flight of stairs or walking 1 bus stop. More than 2/3 of those who complained of fatigue had underlying depression. Similarly, 1 in 6 were significantly at risk of having at least 5% of weight lost in 6 months. Using Sarc-F, 1 in 5 had underlying sarcopenia. eRGA app is a practical and feasible way to identify seniors at risk in primary care even before they develop disability. The RGA app identified relevant geriatric syndromes and with appropriate implementation pathway could lead to improved outcomes.

S4- NOVEL BIOMARKERS AT THE INTERSECTION OF FRAILTY AND ALZHEIMER'S DISEASE. Jeremy D. Walston (Johns Hopkins University, Baltimore, USA)

Communication 1: *Nuclear factor-kappa B-mediated (NFκB) related inflammatory markers and cognitive impairment*, Esther Oh (Johns Hopkins University, Baltimore, USA)

Inflammatory markers are well known to be associated with frailty and other comorbidities including cognitive impairment. Among inflammatory markers, nuclear factor-kappa B-mediated (NFκB) related markers have been known to be associated with aging and its associated adverse outcomes including mortality. Elevated levels of NFκB related inflammatory markers may also be associated with cognitive impairment. Inflammatory markers CRP, IL6, TNFR1, and TNFα were measured in the sera of the study participants from the Religious Orders Study and Rush Memory and Aging Project (N=659). All assays were performed on the Meso Scale Discovery (MSD) electrochemiluminescence platform. The most significant association was found with TNFR1 and composite global cognitive score with a 7.7 standard unit lower score per 1 log unit of higher TNFR1 (-7.7; 95% CI -10.55 to -4.84). TNFR1 was also associated with different domains of cognition including working memory (-0.31; 95% CI -0.47 to -0.15), episodic memory (-0.38; 95% CI -0.55 to -0.22), semantic memory (-0.41; 95% CI -0.56 to -0.25), perceptual speed (-0.50; 95% CI -0.68 to -0.32), and perceptual orientation (-0.23; 95% CI -0.39 to -0.08). CRP and IL-6 were both associated with perceptual speed, but TNFα was not associated with cognition. Higher levels of TNFR1, CRP, and IL6 are associated with cognitive function. Of these, only TNFR1 was associated with all five cognitive domains examined. We will also present data on the association of NFκB related markers and longitudinal cognitive changes as well as the association of inflammatory markers with circulating cell-free (ccf) DNA fragments that were measured in the same population.

Communication 2: *Circulating cell-free DNA is associated with faster rates of cognitive decline and worsening physical measures over time*, L. Nidadavolu (Johns Hopkins University, Baltimore, USA)

In tissue homeostasis, damaged and dysfunctional cells die, releasing DNA fragments into circulation. Circulating cell-free (ccf) DNA fragments come from two sources: nucleus (ccf-nDNA) and mitochondria (ccf-mtDNA). The quantity of ccf-nDNA serves as a marker of total cell death, while the size and relative abundance of ccf-mtDNA fragments can be utilized to distinguish mechanism of cell death. The utility of ccf-DNA fragments in identifying and predicting progression of patients at high risk for frailty and Alzheimer's disease is currently unknown. Profiling of genomic and mitochondrial (short, intermediate and long) ccf-DNA was performed in sera of older individuals from Rush University Alzheimer Disease Center's Religious Orders Study/Memory and Aging Project (median age 80.4 years, N=670). Ccf-DNA levels were correlated with physical and cognitive performance scores including walking speed, grip strength, frailty score as well as composite cognitive testing scores. Associations with trajectories of physical and cognitive decline as well as other molecular measures including serum cytokines were also determined. Ccf-nDNA was negatively correlated with minimal status exam (MMSE) score ($r = -0.112$, $p = 0.005$), overall global cognition ($r = -0.102$, $p = 0.01$) and gait speed ($r = -0.116$, $p = 0.01$). Longitudinal analysis showed baseline increases in ccf-nDNA resulted in decreased global cognition score of 0.11 per year and a decrease in grip strength of 0.2 units per year. Higher levels of short ccf-mtDNA fragments normalized per cell was also associated with increased mortality (hazard ratio for death = 1.11). Mitochondrial dysfunction and cellular senescence constitute primary theories of aging and are common age-related changes seen in patients with physical and cognitive decline. Our data highlights the utility of ccf-DNA fragments in identifying and risk stratifying older patients at high risk for frailty and AD.

Communication 3: *Angiotensin system and the intersection of frailty and Alzheimer's disease*, P. Abadir (Johns Hopkins University, Baltimore, USA)

Chronic inflammation commonly accompanies frailty and increases risk of cognitive decline and the progression of AD. The Renin-Angiotensin-System (RAS) is a major hormonal system that affects every organ and mainly functions through three receptor subtypes; AT1R, AT2R and the brain-specific AT4R. The role of RAS at the intersection of frailty and Alzheimer's disease is currently controversial. Frailty status, grip strength, walking speed, falls, and mortality in community-dwelling younger (age 20-30, N=39), and older individuals (age 70-90, N=63) were correlated to serum levels of angiotensin autoantibodies (AT1RaAb) and to serum cytokines. Brain frontal cortex AT1R, AT2R and AT4R gene expression, protein synthesis, and signaling pathways were also examined in a separate group of age- and sex-matched control and angiotensin

receptor blocker treated (80-90Y) non-AD and AD subjects (The Rush Alzheimer's Disease Center) (N=30 each group). Our data suggests that in older adults with normal cognition, higher serum levels of AT1RaAb were strongly associated with higher inflammation and frailty; the risk of all-cause mortality was 4 times higher than in those with lower AT1RaAb levels. This excess risk of death did not diminish after multiple adjustments. Angiotensin receptor blocker (ARB) treatment appeared to be most protective in these older adults with higher AT1RaAb serum levels. Similarly, at brain tissue level, in older subjects with AD there is an increase in the proinflammatory brain AT1 expression ($P < 0.01$) and signaling (pERK) ($p < 0.008$). The anti-inflammatory AT2R expression was also increased ($P < 0.003$). However, AT2R signaling pathways (eNOS, nNOS) were not up-regulated, suggesting discordance between receptor expression and activity. Our findings highlight dysregulation of circulating and Brain RAS in patients with frailty and AD. Dissecting and understanding circulating and tissue specific RAS changes in frailty and AD is therefore critical for accurately targeting the impaired parts of the system.

S5- SCREENING AND ASSESSMENT FOR FRAILTY IN PRIMARY CARE. Solomon Yu (*National Health and Medical Research Council Centre of Research Excellence in Frailty and Healthy Ageing, Adelaide, Australia*)

Communication 1: *Utilisation Of General Practice Health Assessments Around An Aged Care Assessment Is Associated With Lower Mortality Risk In Older Australians*, R. Visvanathan (National Health and Medical Research Council Centre of Research Excellence in Frailty and Healthy Ageing, Adelaide, Australia)

The Medicare Benefits Schedule (MBS) supports an annual comprehensive assessment of older (75+) people by general practitioners through MBS item number 705/707 (45 minutes+). The aims of this study were to: 1) describe the utilisation of comprehensive assessments within 6 months of the national Aged Care Assessment Program (ACAP) assessment for home care packages (HCPs); and 2) investigate the impact of the comprehensive assessment item numbers on the risk of mortality and entry into permanent residential aged care (PRAC). Retrospective cohort study utilising the Historical Cohort of the Registry of Senior Australians (ROSA). 75,172 individuals ≥ 75 years old having an eligibility assessment between 2011 and 2015 were investigated. The use of comprehensive assessments MBS items 705/707 in the six months before and after the eligibility assessment for HCP and impact on time to death and entry into PRAC were investigated. Of the 75,172 individuals, 28.2% (95% confidence interval (CI): 27.8– 8.5%) had comprehensive assessments. Individuals with a comprehensive assessment had a 5% lower risk of mortality (adjusted hazard ratio (aHR, 95%CI=0.95,0.92–0.98), but 5% higher risk of transition to PRAC (aHR, 95%CI=1.05, 1.02–1.08) compared to those who did not have these services. The utilisation of comprehensive assessments was associated with a lower risk of mortality.

Communication 2: FRAIL Scale and SARC-F: Predictive Validity and Diagnostic Test Accuracy, M.Q. Thompson (National Health and Medical Research Council Centre of Research Excellence in Frailty and Healthy Ageing, Adelaide, Australia)

This study examined the predictive validity of the FRAIL scale and SARC-F to predict mortality, and their diagnostic test accuracy (DTA) against the respective reference standards of the frailty phenotype (FP) and sarcopenia. A total of 668 participants aged ≥ 65 years (mean age 74.0 [SD 6.2] years, 56.1% female) were included. Frailty was measured using the FRAIL scale and FP, and Sarcopenia using SARC-F and clinical measurement. Mortality was matched to official death records with a minimum 10 years follow-up. DTA estimates considered as acceptable: Sensitivity $\geq 80\%$, \geq Specificity 60%, Youden index $\geq 50\%$. Both instruments demonstrated significant predictive validity for mortality up to 10 years in an analysis adjusted for sex, age, education, and income (FRAIL scale. HR: 2.08, $p < .001$; and SARC-F. HR: 2.04, $p < .001$). The FRAIL scale demonstrated acceptable DTA findings against the FP for both Sensitivity (86.3%), Specificity (63.6%) and Youden index (49.9%), while the SARC-F did not produce acceptable estimates (Sensitivity: 78.2%, Specificity: 36.5, Youden: 14.7%). The FRAIL scale is a suitable frailty screening instrument. While the SARC-F did not produce acceptable DTA estimates, it did demonstrate predictive validity for mortality.

Communication 3: The Pictorial Fit-Frail Scale (PFFS) Malay Version: Validity and Reliability Testing in Malaysia, S.S. Ahip (National Health and Medical Research Council Centre of Research Excellence in Frailty and Healthy Ageing, Adelaide, Australia)

The aim was to investigate test-retest and inter-rater reliability as well as validity of the PFFS- Malay version (PFFS-M). 240 patients and their caregivers from 4 public primary healthcare clinic completed the PFFS-M version. All patients were systematically assigned to either a nurse (nurse 1) or a healthcare assistant (HCA 1) for their first PFFS-M assessment and a second assessment was done by a second staff member from the same professional category (nurse 2 and HCA 2) on the same day. All patients also had the PFFS-M completed by the clinic doctor. The research assistant completed the Adelaide Frailty Index. All patients returned after one week for a reassessment by the same health care professionals who had assessed them at recruitment stage and they were also required to complete the PFFS-M for a second time. The test-retest reliability was strong for patients ($r=0.81$), caregivers ($r=0.90$), HCA 1 and 2 ($r=0.91$ and 0.92), nurses' 1 and 2 ($r=0.91$ and 0.92) and doctors ($r=0.87$). Inter-rater reliability assessments calculated for total PFFS-M scores by various combinations of participant type, and across all participants were good (ICC=0.81-0.95). The association between PFFS-M total score and the AFI was statistically significant (P value <0.0001). The PFFS-Malay version was

found to have good reliability and validity within the Malaysian context.

S6- TRYPTOPHAN METABOLISM LINKS CHRONIC INFLAMMATION TO FUNCTIONAL DECLINE & PHYSICAL FRAILITY. Jeremy Walston (*Division of Geriatric Medicine and Gerontology, Johns Hopkins University School of Medicine, Baltimore, USA*)

Communication 1: Altered Tryptophan Metabolism Links Chronic Inflammation to Functional Decline & Physical Frailty in Mice and Humans, Reyhan Westbrook (*Division of Geriatric Medicine and Gerontology, Johns Hopkins University School of Medicine, Baltimore, USA*)

Chronic inflammation is associated with frailty and functional decline in older adults but the molecular mechanisms of this linkage are not well understood. The interleukin 10tm1Cgn (IL10tm) mouse develops chronic inflammation, a frailty-like phenotype with age, and has increased mortality making it an ideal model to study the biological mechanisms of frailty and functional decline. In order to pinpoint specific biological pathways that change with age as well as connect chronic inflammation to functional decline and physical frailty, we utilized a targeted metabolomic platform to agnostically identify differences in metabolite levels in chronically inflamed IL10tm mice. Our initial profiling identified several metabolite alterations in the plasma of the IL10tm mouse compared to controls, with the most prominent and consistent alterations being in metabolites of the tryptophan degradation pathway (TDP), including decreased tryptophan and concomitantly increased kynurenine in middle-aged IL-10tm mice, and an intensification of these changes in old aged IL-10tm mice relative to controls. To translate these findings into human subjects, we then analyzed the composition of metabolites in the blood of a population of young, non-frail and frail older adults ($n=166$). Analysis of metabolites revealed significant alterations in the TDP with aging and frailty. Among the top metabolites to correlate with age and frailty status were kynurenine and the kynurenine/tryptophan ratio. The kynurenine/tryptophan ratio also tightly correlated with serum inflammatory cytokines TNF α R1 and IL-6. Higher kynurenine/tryptophan levels were associated with weaker grip strength and slower walking speed, even after adjusting for age, gender, BMI and blood pressure. Profiling of downstream metabolites of the TDP revealed the accumulation of 3-hydroxykynurenine, a cytotoxic and neurotoxic intermediate metabolite, with frailty. The increased levels of cytotoxic and neurotoxic molecules in the TDP may in part explain the link between inflammation and cognitive and physical decline in frailty.

Communication 2: *Neurotoxic Kynurenines are Linked to Reduced Neuromuscular Connectivity in a Mouse Model of Chronic Inflammation and Frailty*, Tae Chung (Department of Physical Medicine and Rehabilitation, Johns Hopkins University School of Medicine, Baltimore, USA)

Chronic inflammation is known to be associated with frailty and sarcopenia, but the underlying mechanisms are not well understood. In order to pinpoint specific biological pathways that connect chronic inflammation to functional decline and physical frailty, we recently utilized a targeted metabolomic platform to identify categories or signatures of differences in metabolite levels and saw increased tryptophan degradation and production of kynurenines in the IL-10tm mouse model of chronic inflammation. Interestingly, some of kynurenine metabolites are neurotoxic and known to play a role in the pathogenesis of various neurodegenerative diseases, such as Alzheimer and Parkinson diseases. Therefore, we hypothesized that chronic inflammation is related to age-associated muscle weakness via neurotoxic kynurenines. We compared force vs frequency relationship between IL-10tm (n=8) and control (n=7) mice, and found that total isometric force is reduced in IL-10tm mice. The kinetics of contraction were also measured at 80Hz tetanic stimulation, and we saw that the maximal rate of contraction (+dF/dt) was significantly lower in IL-10tm mice. We then harvested EDL muscles and performed immunofluorescent staining of neuromuscular junction (NMJ) for morphological study. Using laser confocal microscope, we compared presynaptic to postsynaptic areas in a semi-quantitative way, and found that reduced presynaptic to postsynaptic coverage is significantly reduced in IL-10tm mice, suggesting increased partial denervation in their muscles. Finally, we tested the neurotoxicity of 3-hydroxykynurenine (3-HK) or quinolinic acid (QA) on a model of peripheral spinal motor neuron, MN1 cells. Both 3-HK and QA showed neurotoxicity at a higher concentration in a dose-dependent manner. However, these concentrations are much higher than physiological concentrations found in human. Interestingly, when MN1 cells are incubated with both 3-HK and QA, neurotoxicity is potentiated, and occurred at a concentration that can be found during inflammation and other conditions. In conclusion, our findings suggest that neurotoxic kynurenines may explain reduced neuromuscular connectivity and frailty phenotype in the IL-10tm mouse model of chronic inflammation.

Communication 3: *Effects of tryptophan degradation pathway blockade on age-related decline in physical performance and life span of Drosophila melanogaster*, Mariann M. Gabrawy (Division of Geriatric Medicine and Gerontology, Johns Hopkins University School of Medicine, Baltimore, USA)

The tryptophan degradation pathway (TDP) has been implicated as a contributor to frailty and life span. In humans, the TDP is activated by inflammation and produces kynurenines, some of which are neurotoxic or cytotoxic and,

in frail older adults, are at elevated levels. Various components of the pathway are well-characterized and serve as therapeutic targets. However, the etiological role of altered kynurenine levels in reduced physical performance is not known. As the TDP is conserved across species and has homologues in *Drosophila melanogaster*, we used a previously characterized DGRP_229 line from the *Drosophila* Genetic Reference Panel and an established physical performance battery to elucidate the role of altered levels of kynurenines in age-related decline in climbing speed and endurance. To test whether increased levels of cytotoxic kynurenines will accelerate age-related decline in physical performance, flies were chronically fed 3-hydroxyanthranilic acid (3-HAA) and assayed at young, middle, and old age. We also tested whether blocking the production of kynurenines, via chronic treatment with alpha-methyl-tryptophan (alpha-MT) supplemented with nicotinamide (NAM), will improve physical performance. Further, we measured the effects of the aforementioned metabolites on survivorship. Our results show that flies treated with 3-HAA have accelerated age-related decline in climbing speed and endurance. Flies treated with a combination of alpha-MT and NAM have significantly improved speed and endurance than those treated with each metabolite alone. Treatment with 3-HAA significantly decreased life span while treatment with a combination of alpha-MT and NAM significantly increased life span. We conclude that treatment with alpha-MT and NAM attenuated the effects of age on the decline of physical performance in an age-specific manner while increasing survivorship.

S7- PROTEIN + EXERCISE INTERVENTIONS IN DIFFERENT POPULATIONS OF OLDER ADULTS.

Lisette de Groot (*Nutrition and Ageing, Wageningen University, Wageningen, The Netherlands*)

Communication 1: *Effectiveness of a combined diet and resistance exercise intervention on muscle health for community-dwelling older adults: ProMuscle in Practice study*, Berber Dorhout (Wageningen University, Wageningen, The Netherlands)

The combination of resistance exercise (RE) and a protein-rich diet is effective in improving muscle mass and physical performance of older adults in a clinical setting. However, not much is known about the effectiveness of this strategy in practice. We aimed to evaluate effectiveness of a RE and dietary protein intervention for older adults implemented in practice. This multicentre RCT included 168 Dutch community-dwelling older adults (75±6 years). The intervention group received a 12-week intensive support intervention, consisting of supervised RE and a protein-rich diet. After that, they received a 12-week moderate support intervention, to continue the adapted lifestyle pattern. The control group received no intervention. Physical functioning (Short Physical Performance Battery; SPPB), leg strength (MicroFET), lean body mass (DXA), and quality of life (EQ-5D-5L) were measured at baseline, after 12 and 24 weeks. After 12 and 24 weeks,

the intervention group significantly increased their protein intake compared to control group ($P < 0.001$). Also SPPB score increased in intervention participants (from 10.1 ± 0.2 to 10.4 ± 0.2 at week 12 and 10.6 ± 0.2 at week 24), whereas control participants decreased (time*treatment interactions $P < 0.05$). Additionally, leg strength and lean body mass improved in the intervention group compared to control group ($P < 0.05$), whereas no difference between groups was found for quality of life. This study shows that ProMuscle in Practice leads to improvements on muscle health-related outcomes in community-dwelling older adults. Further research should focus on feasibility of implementation in a real-life setting and improving long-term behaviour maintenance.

Communication 2: *A combined nutrition and exercise intervention improves nutritional status and bone health of healthy Chinese middle-aged and older adults*, Inge Groenendijk (Wageningen University, Wageningen, The Netherlands)

Hong Kong faces several public health problems including malnutrition, osteoporosis and its consequences. Considering the typical Chinese diet and the overall low physical activity levels of Chinese adults, there is a need for timely interventions to improve nutritional status and bone health. This study investigated the effects of a combined nutrition and exercise intervention on serum vitamin B-12 and 25(OH)D levels, bone turnover markers, and parathyroid hormone (PTH) levels in apparently healthy community-dwelling Chinese middle-aged and older adults. In this 24-week randomized controlled trial, 180 Chinese adults (85 women, mean age 61 y) were randomly assigned to receive two glasses of a fortified milk supplement and an exercise program or no intervention. Blood samples were collected at baseline, 12 and 24 weeks to assess vitamin B-12 and 25(OH)D levels, bone turnover markers, and PTH levels. A significant time x group interaction ($p < 0.001$) was found for serum vitamin B-12 and 25(OH)D levels and the bone turnover markers, but not for PTH levels ($p = 0.09$). The intervention increased vitamin B-12 levels from baseline (345 ± 119 pmol/L) to 24 weeks (484 ± 136 pmol/L), while levels remained stable within the control group. For 25(OH)D levels, the intervention group had a greater increase from baseline (54.7 ± 14.2 nmol/L) to 24 weeks (80.1 ± 19.2 nmol/L) compared to the control group (60.6 ± 15.2 vs 65.6 ± 14.6 nmol/L). The ratio of the net effect of bone formation and resorption was greater for the intervention group (median=0.70) than the control group (median=-0.11, $p < 0.001$), suggesting less bone loss in the intervention group, irrespective of gender. This study showed that nutritional supplementation combined with exercise is effective in improving vitamin B-12 and 25(OH)D levels as well as the balance of bone turnover markers of apparently healthy community-dwelling Chinese middle-aged and older adults.

Communication 3: *A 4-week exercise and protein prehabilitation program improves muscle mass and physical functioning in Dutch older adults*, Pol Grootswagers (Wageningen University, Wageningen, The Netherlands)

Prehabilitation might attenuate common hospitalization-related losses in muscle mass and physical performance. Beneficial effects of physical exercise with protein supplementation have been reported in older adults multiple times before, but typically after an intervention of at least 12 weeks. The time-window for pre-surgery training is often limited, and it is not known if it is possible to achieve comparable results in such a short time window. The aim of this study was to pilot-test the effectiveness of a 4-week combined exercise and protein supplementation program on skeletal muscle related outcomes in a Dutch older adult population. Seventeen older sedentary men and women, aged 55-75y, were included in this one-armed pilot study. Participants followed a 4-week intervention program consisting of a twice-weekly supervised resistance and high-intensity aerobic exercise training of 75 min, combined with daily protein supplementation (30g). After two and four weeks, quadriceps cross-sectional area (CSA) was assessed via magnetic resonance imaging and isometric quadriceps maximal voluntary contraction (MVC) via Biodex. Other outcome measures were handgrip strength, chair rise time and maximal aerobic capacity (VO₂-max). The 4-week exercise and protein program improved quadriceps CSA with 5% ($\Delta 3.2 \pm 3.2$ cm², $P = 0.001$), quadriceps MVC with 12% ($\Delta 17.1 \pm 24.1$ Nm, $P = 0.004$), VO₂-max with 8% ($\Delta 2.4 \pm 5.5$ ml/min/kg, $P = 0.016$) and chair rise test with 19% ($\Delta -2.7$ (IQR -5.5, -2.3) sec, $P < 0.001$). We observed no changes in body weight and handgrip strength. A 4-week exercise and protein intervention led to clinically relevant improvements in muscle-related outcomes in healthy older adults.

S8- ADDRESSING THE DRIVERS OF FRAILTY: ACTIVE NUTRIENTS FOR MITOCHONDRIAL HEALTH, BIOENERGETICS AND FUNCTIONALITY.
Roger Fielding (Tufts University, Boston, USA)

Communication 1: *The impact of Age Associated Cellular Decline on bioenergetics and functional impairment*, Bret H Goodpaster (AdventHealth Translational Research Institute, Orlando, USA)

Communication 2: *Correcting glutathione deficiency in aging: Impact on mitochondrial and metabolic health*, Rajagopal V Sekhar (Baylor College of Medicine, Houston, USA)

S9- COMMUNITY-BASED PRIMARY FRAILTY PREVENTION AND ITS IMPLEMENTATION AND DISSEMINATION. Hidenori Arai (*National Center for Geriatrics and Gerontology, Minoru Yamada, Tsukuba University, Japan*)

Communication 1: *Community-based Prevention of Frailty: Japanese experience*, Hidenori Arai (National Center for Geriatrics and Gerontology, Minoru Yamada, Tsukuba University, Japan)

Japan has a stunning percentage of older people in the population and preventing frailty and its adverse health outcomes is crucial for the healthy life expectancy. Since the long-term care insurance (LTCI) system was launched, the number of certified older adults with LTCI service requirement has continued to increase. This is a serious problem, because the LTCI service requirement certification is equivalent to disability and leads to long-term care cost. Therefore, the Japanese government has been focusing on the population approach to mitigate the increase of disabled older adults. The aim of this study was to evaluate the effect of a self-management group intervention on new LTCI service requirement certifications in community-dwelling older adults in Japan. In this prospective cohort study, we recruited community-dwelling adults aged 65 years and older who were independent in a city in Kyoto prefecture in 2012. The subjects in the participation group (n = 1620) attended 60-min group training sessions once or twice every two weeks from December 2012 to December 2016. The exercise sessions consisted of mild-intensity aerobic exercise, mild strength training, flexibility and balance exercises, and cool-down activities. These exercise classes were facilitated by well-trained volunteer staff. The outcome measure was the number of new LTCI requirement certifications during a four-year follow-up period. During the four-year follow-up period, 247 subjects (15.2%) in the participation group and 334 (20.6%) in the control group were newly certified for LTCI service requirements. The hazard ratio for new LTCI service requirements in the participation group compared with the control group was 0.73 (95% CI =0.62–0.86) in the four-year follow-up period. These results indicate the usefulness of self-management group exercise to reduce the incidence of disability in older adults. We will show other interventions to prevent frailty and disability which can be applied to other communities.

Communication 2: *SAYGo: Community-based Peer-led Classes to Improve Falls Risk, Frailty, and Social Connection*, Debra L Waters (Director of Gerontology Research, University of Otago, New Zealand)

New Zealand has a long history of developing and delivering innovative programmes for older adults. These include the Otago Exercise Programme (OEP), Steady as You Go (SYGo), Senior Chef, and an adaptation of Australia's Men's Sheds. These interventions improve physical function and

social connection through group settings and a peer-led class model. New Zealand has been successful in achieving long-term and scalability with the Steady as You Go (SAYGo) programme which has been running since 2003 and has more than 1500 participants and > 150 peer leaders in the Otago and Southland region alone. This programme was adapted from the OEP exercises to a group setting and has been shown to significantly improve strength and balance, to reduce falls by ~27%. Long-term participation (>3 years) has demonstrated significantly lower falls incidence (IRR0.90, 95%CI: 0.84 to 0.98, p=0.02) and also fewer injurious falls (p=0.03, β -.155, 95%CI -.115-0.005). More recently, there has been coordinated effort between Age Concern (charitable organizes across NZ), ACC- the New Zealand Crown entity responsible for administering the country's universal no-fault accidental injury scheme, Health Quality Safety Commission, regional Public Health Organizations and Falls and Fracture Liaison Services in coordinating primary care falls screening, population-based falls incidence tracking and enrollment in regional strength and balance classes across New Zealand. It has resulted in a significant increase in older people attending strength and balance classes across the county. This model has worked well, but it has not been without its' challenges. Developing and sustaining peer-led strength and balance classes requires specific features and support. This talk will present the development and evolution of SAYGo over the past 17 years in New Zealand.

Communication 3: *A Peer-Led Multi-Domain Community Program to Reverse Frailty and Improve Cognition: HAPPY Outcomes*, Reshma A Merchant (National University Health System, Singapore)

With rapid increase in ageing population, especially in Asian countries, the prevalence of frailty, dementia and associated consequence including falls and disability will increase putting a strain on finite healthcare resources and shrinking workforce. Multidomain interventions including physical exercise and cognitive training, conducted in group settings have shown to postpone and / or reverse cognitive impairment and frailty. Many countries have tried different approaches to sustain and scale up community interventions to prevent frailty and dementia, and to improve overall population health and psychosocial wellbeing. Healthy Ageing Promotion Program For You (HAPPY) is an all in one successful community based peer-led multidomain intervention conducted island wide in Singapore in more than 70 different locations in partnership with Agency of Integrated Care. HAPPY is adapted from cognitive in Nagoya Japan, and comprises of more than 200 dual task exercises and self empowerment. The program is led by trained peer-leaders which makes it sustainable and easily scalable. More than 50% improved in frailty scores, and almost half of those initially classified as pre-frail became robust at the end of 6 months. More than 2/3 improved in cognitive scores with 1/3 self-reported improvement in memory. Almost half had improvement in depression scores. A peer-led group intervention program with incorporates physical activity,

cognition training and at the same time empowering the seniors is effective in reversing frailty and improving cognition. This talk will share the implementation tips and challenges.

S10- “WHY” RATHER THAN “HOW”: A TRANS-PARADIGMATIC DISCUSSION ON THE URGENCY OF THE FRAILTY CONCEPT FOR OPTIMIZING OUTCOMES FOR OLDER ADULTS. Susan E Howlett^{1,2}, Karen Bandeen-Roche³, Brian Buta⁴, Ravi Varadhan⁵, Qian-Li Xue², Matteo Cesari^{6,7}, Emanuele Marzetti⁸ ((1) Department of Pharmacology, Dalhousie University, Halifax, Nova Scotia, Canada; (2) Department of Medicine / Geriatrics, Dalhousie University, Halifax, Nova Scotia, Canada; (3) Department of Biostatistics, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA; (4) Department of Medicine, Johns Hopkins School of Medicine, Baltimore, MD, USA; (5) Department of Oncology, Johns Hopkins School of Medicine, Baltimore, MD, USA; (6) Department of Clinical Science and Community Health, University of Milan, Milan, Italy; (7) Geriatric Unit, Fondazione IRCCS Ca’ Granda Ospedale Maggiore Policlinico, Milan, Italy; (8) IRCCS Fondazione Policlinico Universitario Agostino Gemelli, Rome, Italy)

As the world’s population ages, there is urgent need for strategies by which to extend health, function and independence for older adults. Frailty holds high promise as a focus by which to advance this goal, because this concept characterizes individuals who become vulnerable to stressors and so are at risk for adverse health and functioning outcomes. Frailty assessment therefore stands to accelerate efforts to extend healthy aging in older populations and to optimally manage older adults’ care in clinical settings. Yet, theories as to the nature of frailty, as well as methods for its measurement, are highly diverse. This sometimes confuses practitioners seeking to implement frailty in health care settings and hampers development and dissemination of best practices into public health and clinical domains. This symposium features speakers representing three of the leading paradigms framing frailty research, practice and implementation efforts: Deficit Accumulation, the Physical Frailty Phenotype, and the Physical Frailty & Sarcopenia (PF&S). It aims to communicate their paradigms’ goals in frailty assessment, rather than to debate methodology. Speakers specifically are charged with addressing, for each paradigm: 1) How is frailty conceptualized? 2) What is the importance of frailty for older individuals, for public health policy and practice aimed at older adults, and for clinical care of older adults? How can frailty assessment and/or management be of benefit in these areas? 3) What are the highest research imperatives / gaps to address in order for the envisioned benefits to be realized?

S11- MUSCLE MASS WITH THE D3-CREATINE DILUTION METHOD: PRACTICAL ASPECTS OF IMPLEMENTATION AND DATA ON THE RELATIONSHIP OF MUSCLE MASS WITH HEALTH-RELATED OUTCOMES IN OLD MEN. Luigi Ferrucci (National Institute on Aging, National Institutes of Health, Baltimore, MD, USA)

Communication 1: Methodology - Description of pre-clinical and clinical validation studies. How to employ the method into clinical trials including large cohort studies and randomized, controlled trials, William J. Evans (University of California, Berkeley, USA)

The assessment of total body skeletal muscle mass has, until recently, been problematic. Skeletal muscle is a significant but not the only component of lean body mass (LBM). In a large number of clinical trials LBM is incorrectly referred to as muscle mass and, as a result use of LBM as a surrogate for muscle mass has resulted in erroneous conclusions on the importance of skeletal muscle in development of late-life dysfunction and risk of chronic disease. The D3-Creatine (D3Cr) dilution method allows a direct and accurate measurement of skeletal muscle mass that is undiluted by hydration status or accumulation of intramyocellular fibrosis or lipid. The method provides a measurement of creatine pool size and, because ~98% of the body creatine pool is located in the sarcomere, muscle mass. Because the method is non-invasive and only requires a single fast ingested urine sample, the method is ideal to measure muscle mass in large cohort studies. The method has been incorporated into a large prospective longitudinal trial in more than 1,300 older men (MrOS cohort, > 80 yr). This method employs an enteral dose of a specific amount of deuterated creatine (D3Cr). The tracer is absorbed and transported into the sarcomere. The D3Cr is irreversibly converted to D3-creatinine (D3Crn) and excreted, thus allowing the measurement of D3Crn enrichment from a single, fasting urine sample. Details of dosing, sampling, and measuring muscle mass in longitudinal studies will be discussed.

Communication 2: D3Cr muscle mass and assessment skeletal muscle quality. Is Sarcopenic Obesity an anachronistic term? Eric Orwoll (Oregon Health Science University, USA)

The combination of sarcopenia and obesity has been associated with physical dysfunction in older people. However, because accurate assessments of muscle are challenging, previous research has relied on assessments of lean mass as a surrogate for muscle mass. We postulate that inaccurate measures of muscle mass may have led to a misunderstanding of the role of obesity in sarcopenia and related outcomes. We compared a direct measurement of muscle mass (D3 creatine dilution; D3Cr) with a commonly-used approximation of muscle mass (appendicular lean mass (ALM) by dual energy x-ray absorptiometry (DXA)) and their associations with measures of physical performance (gait speed, chair stand time) and adverse outcomes (incident injurious falls and mobility problems).

Data on the relationship of body fatness and muscle mass on walking speed suggests that sarcopenic obesity and risk of disability may not be a risk factor when muscle mass is accurately measured.

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

The use of inaccurate measurements of muscle has resulted in an assumption that muscle mass is not associated with late-life disability and health related outcomes. Sarcopenia definitions are controversial and none, so far, have used muscle mass. We review the current evidence, and highlight what additional steps are needed to support the use of d3-creatine to define sarcopenia.

S12- ASSESSMENT OF QUALITY OF LIFE IN SARCOPENIA: FROM CLINICAL TRIALS TO DAILY PRACTICE. Charlotte Beudart (*WHO Collaborating Centre for Public Health Aspects of Musculoskeletal Health and Aging, Division of Public Health, Epidemiology and Health Economics, University of Liège, Liège, Belgium*)

Communication 1: *Importance of patients related outcomes measures (PROM) as primary endpoints for the development of medications aimed at the treatment of diseases related to musculoskeletal outcomes*, Francesca Cerreta (Human Medicines Research and Development Support Division, Scientific Advice, London, UK)

The association between sarcopenia and quality of life became a topic of high interest in the past 10 last years. The prospective and generalized loss of muscle mass, muscle strength, physical performance and muscle quality resulting from sarcopenia could contribute to a lower QoL in sarcopenia. HR-QoL assessments are important for healthcare providers and regulatory agencies to understand the needs and preoccupation of important segments of the population, such as elderly subjects suffering from sarcopenia. Moreover, with the future expected development of interventions targeting sarcopenia, Patients Reported Outcomes (PROMs) such as quality of life questionnaires will also be useful to measure the effectiveness and relevance of these new therapeutic strategies. Indeed, complete assessment of the benefits of a therapeutic intervention should provide evidence of an impact on patients' HR-QoL.

Communication 2: *Assessment of quality of life in sarcopenia with the SarQoL questionnaire : where do we stand ?* Charlotte Beudart (*WHO Collaborating Centre for Public Health Aspects of Musculoskeletal Health and Aging, Division of Public Health, Epidemiology and Health Economics, University of Liège, Liège, Belgium*)

For sarcopenic patients, literature and patient surveys indicates that the QoL impact is felt on physical and functional

domains, and that the use of generic measures could lack the specificity and sensitivity needed to capture a detailed and accurate picture of the quality of life of these patients. The SarQoL questionnaire, a specific HR-QoL questionnaire for sarcopenia developed in 2015, has demonstrated in several studies that it is a valid and reliable instrument for measuring quality of life in sarcopenic older people. As it is relevant both in observational and interventional studies, the smallest detectable change of the SarQoL has also recently been measured. On individual subjects, a change in overall quality of life of at least 7.35 points (on a scale from 0 to 100) would have to be observed to confirm that a true change, beyond measurement error, has occurred. This questionnaire is recommended both in research and clinical practice but also in clinical trials, since its responsiveness has recently been demonstrated.

Communication 3: *Discussion - conclusion*, Olivier Bruyère (Belgium)

S13- EVIDENCE AND POSITION STATEMENTS FROM THE SARCOPENIA DEFINITIONS AND OUTCOME CONSORTIUM (SDOC). Roger Fielding (*Tufts University, Boston, USA*)

Communication 1: *Evidence for deriving cutpoints for defining sarcopenia*, Todd Manini (USA)

Communication 2: *Evidence for performance of potential sarcopenia variables predicting outcomes*, Peggy Cawthon (USA)

Communication 3: *SDOC Position Statements: process and conclusions*, Shalender Bhasin (USA)

S14- INNOVATIONS IN NON-PHARMACOLOGICAL INTERVENTIONS TO KEEP AGEING MUSCLES STRONG AND AGILE AND THE MIND SHARP. Robin M. Daly (*Institute for Physical Activity and Nutrition, Deakin University, Melbourne, Victoria, Australia*)

Communication 1: *Novel nutritional approaches to enhance the effects of exercise on muscle, mobility and the mind in older people*, Robin M. Daly (Institute for Physical Activity and Nutrition, Deakin University, Melbourne, Victoria, Australia)

Sarcopenia and cognitive impairment can occur simultaneously in older adults, and collectively have been linked to an increased risk for frailty, falls, disability and dementia. While it has been suggested that this association is bidirectional (eg. factors causing sarcopenia can contribute to cognitive impairment or vice versa), there are many similarities in the pathophysiological pathways to both these conditions. Both are multifactorial in origin, and their onset and progression share many of the same risk factors, including inadequate nutrition and physical inactivity. It is likely that the multi-faceted nature of both these conditions has contributed

to the mixed findings reported from various trials with regard to the efficacy of single-domain interventions (eg. exercise, nutrition, cognitive training) on both cognitive function and muscle loss. As a result, it has been suggested that an integrated approach incorporating multi-factorial interventions that simultaneously target muscle and cognitive function and their underlying risk factors may provide the greatest benefits. This presentation will provide an update of the evidence from recent large-scale intervention trials which have evaluated the efficacy and effectiveness of multi-factorial approaches incorporating both exercise and various nutritional factors (beyond dietary protein alone), including vitamin D, omega-3 fatty acids, creatine, phospholipids, multi-nutrient supplements and various diets (Mediterranean diet) or foods (dairy products), on cognition, dementia risk, muscle health and functional performance in older people. This will include several of our recent trials in which we evaluated whether multi-modal resistance-based exercise programs combined with either a protein enriched diet achieved through lean red meat or multi-nutrient supplemental drinks enriched with vitamin D, whey protein, omega-3 fatty acids and/or phospholipids, can improve cognitive function as well as muscle mass, strength and function in older adults, those with memory complaints and type 2 diabetes.

Communication 2: *Importance of initial protein intake on muscle function during aging and following an exercise intervention*, Mylene Aubertin-Leheudre^{1,2} ((1) Department of Exercise Sciences, Groupe de recherche en activité physique adapté (GRAPA), Université du Québec à Montréal, Montreal (Qc), Canada; (2) Centre de Recherche de l'Institut Universitaire de Gériatrie de Montréal, Montreal (Qc), Canada)

Aging is associated with losses of muscle mass, strength and quality which are strong risk factors of functional impairment. One potential mechanism that could explain this age-related muscle loss, in addition to age or physical inactivity, is protein intake. It has been shown that the amount and the distribution of protein intake could influence physical performance changes occurring during the aging process, even in community living older adults. In addition, it seems that loss of muscle strength (dynapenia) is a better predictor of physical limitations than loss of muscle mass (sarcopenia) or gain of fat-mass (obesity). Nevertheless, these body composition modifications can be combined and lead to worsening health effects in older adults. Thus, determining their specific impact, and if it is dependent of body composition profiles, is important. The first part of this presentation will address these questions. In addition, physical activity is one of the most promising non-pharmacological avenues to counteract functional incapacities. More precisely, it has been proposed that aerobic training (such as High Intensity Interval Training (HIIT)) or resistance (power) training are both efficient to maintain muscle quality in older adults aged over 65 years. Nevertheless, lifestyle habits (such as protein intake) seem able to influence muscle adaptations following exercise intervention to improve body composition and functional capacities in older people. Thus, the second aim of this

presentation will be to evaluate if the initial amount of protein intake could influence body composition, muscle strength and functional capacity improvements following an exercise training (power or interval training) intervention combined or not with nutritional supplementation (citrulline) in older adults.

Communication 3: *Assistive technologies for supporting healthy nutrition behaviours in community-dwelling older adults now and in the (not too distant) future*, Dr David Scott^{1,2} ((1) School of Clinical Sciences at Monash Health, Monash University, Australia; (2) Australian Institute for Musculoskeletal Science, Department of Medicine - Western Health, The University of Melbourne, Australia)

Assistive technologies are devices or systems used to maintain or improve physical functioning in populations with disability. Community-dwelling older adults represent an important population who commonly experience limitations in activities of daily living, and these disabilities can potentially contribute to unhealthy nutrition behaviours which may exacerbate functional declines. Thus, poor nutrition is likely to be an important contributor to the anticipated unsustainable demand for aged care services in the coming decades. Commonly used assistive technologies to support nutrition behaviours in older adults with functional limitations currently include simple devices which aid in preparation and consumption of food. Emerging assistive technologies may in future support older adults with disability to better maintain their independence and age in place. Smart homes of the future will include numerous connected appliances and sensors that can assist older adults to maintain adequate nutrition through monitoring dietary intake, providing meal reminders and individualised eating plans, and ordering food through online delivery services. Robotics and exoskeleton devices may also play a role in supporting food preparation. Furthermore, three-dimensional food printers may in coming years allow meals to be printed in the home. These customisable meals can provide specific nutrient contents which support individuals in meeting recommended dietary intakes, and also ensure safe consumption for those with age-related oral health issues. Nonetheless, emerging assistive technologies need to be developed while taking into consideration individual privacy concerns, common issues of patient abandonment of devices, and in particular, the need to prioritise movement over sedentary behaviour in older individuals. This presentation will summarise strategies by which emerging assistive technologies may support nutrition behaviours in the home for older adults, thereby reducing demand on aged care. It will also propose several research questions which need to be addressed in order to confirm feasibility, safety and effectiveness of these technologies.

CONFERENCE

C1- THE SENESCENCE-ASSOCIATED SECRETOME AS A BIOMARKER OF AGE AND MEDICAL RISK.

Marissa J. Schafer, Xu Zhang, Amanika Kumar, Thomas A. White, Sarah K. Jachim, Elizabeth J. Atkinson, Nathan K. LeBrasseur (*Mayo Clinic, Rochester, MN, USA*)

Backgrounds: Senescent cells accumulate with advancing age and, in part, drive tissue degeneration and compromise tissue rejuvenation through their robust secretome, the senescence-associated secretory phenotype (SASP).

Objectives: The objectives of this study were to develop a candidate panel of senescence biomarkers, determine the extent to which components of the SASP can be reliably detected in human blood, and examine whether circulating concentrations associate with parameters of biological age in humans.

Methods: We first assessed whether predefined SASP proteins were abundantly secreted by senescent compared to non-senescent human cells of the same origin. Next, we determined whether candidate SASP factors could be reliably measured in human plasma and tested their associations with chronological age (280 men and women 20 to 90 years of age). We then assessed the associations between plasma biomarkers and biological age, as quantified by the frailty index, in relatively healthy older adults, and older adults undergoing surgery for either aortic stenosis or ovarian cancer. In the surgical groups, we also tested associations of plasma biomarkers with adverse outcomes, including complications (e.g., pneumonia, stroke, infection), ICU admission, and/or hospital readmission.

Results: High levels of both distinct and overlapping SASP factors were identified in all senescent cells assayed, relative to non-senescent cells, with the largest increase in SASP produced by senescent endothelial cells and preadipocytes. Circulating concentrations of 19 out of 24 SASP proteins were associated with chronological age. GDF15 and activin A were the strongest biomarkers of chronological age. Eleven SASP factors were associated with the frailty index in any one of the three participant groups, with CCL4, GDF15, OPN, and TNFR1 significantly associated in all three, even after adjustment for effect modifiers. Gradient boosting machine modeling identified a single panel of seven biomarkers that was consistently able to predict adverse events in both surgical populations better than chronological age + sex, a single biomarker, or frailty index. **Conclusion:** These results support the hypothesis that circulating SASP factors are informative biomarkers of biological age that may be leveraged to predict risk for adverse health outcomes in a disease-agnostic manner. The biomarkers may have considerable relevance for clinical practice and clinical research

C2- FRAILTY AND CARDIOVASCULAR DISEASE (CVD): A COMPLEX RELATIONSHIP. Nicola Veronese, (*Consiglio Nazionale delle Ricerche, Padova, Italy*)

Dr Veronese will talk about the association between frailty and CVD in terms of epidemiological evidence. This association is relatively new in geriatric medicine particularly for the studies assessing the impact of frailty in predicting the onset of CVD. Some parts will be spent for explaining the newer studies reporting data on this important issue that probably suggests a bi-univocal relationship between frailty and CVD.

C3- FRAILTY AND ITS ASSOCIATION WITH POTENTIAL BIOMARKERS AT BASELINE - FIRST RESULTS FROM DO-HEALTH.

Michael Gagesch^{1,2}, Patricia Chocano-Bedoya^{1,2}, Reto W. Kressig³, Bruno Vellas⁴, René Rizzoli⁵, Heike A. Bischoff-Ferrari^{1,2} for the DO-HEALTH investigators ((1) *Department of Geriatrics and Aging Research, University Hospital Zurich and University of Zurich, Zurich, Switzerland*; (2) *Centre on Aging and Mobility, University of Zurich, Zurich, Switzerland*; (3) *University of Basel, Switzerland*; (4) *Felix Platter Hospital, Basel, Switzerland*; (5) *Gerontopôle, University of Toulouse, France*; (6) *University of Geneva, Switzerland*)

Backgrounds: Chronic low-grade inflammation (CI) is a risk factor for adverse outcomes in older adults and has been linked to frailty. Further, CI and frailty are associated with cardiovascular disease (CVD). Finally, insulin resistance (IR) is a pathophysiologic state connected to CI, CVD and frailty. **Objectives:** To investigate the association between two inflammatory biomarkers (CRP, IL-6) and two heart health biomarkers (NT-pro BNP and HOMA-IR) with frailty among DO-HEALTH participants at baseline. **Methods:** Cross-sectional analysis of baseline findings in the DO-HEALTH trial including all 2157 community-dwelling participants age 70+ from five European countries. We used the Fried phenotype to identify frail, pre-frail and robust adults. Because of the skewed distributions of all biomarkers, we used logarithmic transformations and report geometric means. Mean biomarker levels by frailty status were compared with ANOVA. We investigated the association between CRP, IL-6, NT-pro BNP and HOMA-IR and frailty using multinomial regression with the 'robust' group as the reference, adjusting for age, gender, BMI, center, and priorfalls. For NT-proBNP we additionally adjusted for reported cardiovascular disease and tropon in levels for NT-proBNP and reported diabetes for HOMA-IR levels. **Results:** 3.1% of participants were frail and 44% were pre-frail. Mean IL-6 level (pg/L) was 2.54 in robust, 2.84 in pre-frail and 3.89 in frail participants (P Value <0.0001). Mean NT-pro BNP level (ng/L) was 108.7 in robust, 126.9 in pre-frail and 155.1 in frail participants (P Value <0.0001). There were no significant differences in the mean CRP and mean HOMA-IR levels by frailty status. Cross-sectionally, participants with IL-6 levels in the highest tertile (median 4.6 pg/L, range 3.3-188.8) were 1.3-fold more likely pre-frail (OR=1.34, 95% CI=1.06-1.67)

and more than 2-fold more likely frail (OR=2.18, 95% CI=1.03-4.59) after adjustment for age, gender, center, BMI and prior falls. There were no significant differences for CRP, HOMA-IR and NT-proBNP regarding frailty status. **Conclusion:** In this cross-sectional analysis, higher levels of IL-6 and higher levels of NT-proBNP were found in frail participants in DO-HEALTH at baseline. No significant associations were found between CRP or HOMA-IR and frailty status

C4- EFFECTS OF FORTETROPIN® ON THE RATE OF MUSCLE PROTEIN SYNTHESIS IN OLDER MEN AND WOMEN: A RANDOMIZED, DOUBLE-BLINDED CONTROL STUDY. William Evans¹, Mahalakshmi Shankaran¹, Edna Nyangau¹, Tyler Field¹, Hussein Mohammed¹, Robert Wolfe², Scott Schutzler², Marc Hellerstein ((1) University of California Berkeley, USA; (2) University of Arkansas for Medical Sciences, USA)

Backgrounds: Fortetropin is an all-natural proteo-lipid complex made from fertilized egg yolk and has been demonstrated to lower circulating myostatin levels. In young men, Fortetropin supplementation has been shown to increase lean body mass compared to placebo. **Objectives:** The purpose of this study was to examine the effects of Fortetropin supplementation on the fractional rate of muscle protein synthesis (FSR) in healthy, older men and women. **Methods:** We used 2H₂O labeling to measure the rate of synthesis of multiple muscle protein ontologies in 10 men and 10 women (66.4 ±4.5 yr). All subjects received 30 mg of D3-creatine prior to submitting a fasting urine sample to determine muscle mass at baseline. On days 1, 2, 3, and 4, subjects ingested 50 ml of 70% 2H₂O TID, and BID for 17 days. Saliva samples were collected to determine body 2H₂O enrichment on study days 4, 7, 14, and 21. A muscle micro biopsy (~10 mg) was taken from the m.vastus lateralis on day 21. Subjects were randomly assigned to Fortetropin (19.8 g/d) or placebo (cheese powder 19.8 g/d). In-solution digestion with trypsin was performed on SDS-soluble proteins prior to LC/MS-MS analysis using 27-min gradient runs. FSR was calculated with average body water used as the precursor enrichment. **Results:** Body water enrichments reached an average plateau of ~1.5% during labeling period. MS/MS analysis identified 210 proteins with >= 2 peptides/protein. Kinetic data comprised 117 proteins meeting analytic criteria including >= 2 peptides measured in at least 4 subjects per group. The average FSR for a majority of proteins in several muscle gene ontologies was higher in the Fortetropin group compared to placebo (33/38 myofibril, 36/44 cytoplasmic and 15/19 mitochondrial proteins) and this proportion was significant using a Binomial Test. The effects of Fortetropin were independent of sex or baseline muscle mass. **Conclusion:** The overall magnitude of increase was 15%, demonstrating a stimulatory effect of Fortetropin on muscle protein FSR, with multiple gene ontologies affected. While these results should be confirmed in larger cohorts, they suggest that oral Fortetropin supplementation is safe and effective for promoting muscle growth in older men and women.

C5- NIH MOLECULAR TRANSDUCERS OF PHYSICAL ACTIVITY CONSORTIUM (MOTRAC) PROGRESS. Lyndon Joseph (National Institute on Aging, Bethesda Maryland, USA)

Backgrounds: Physical activity is beneficial to human health and well being across the lifespan. The numerous benefits of regular physical activity have long been recognized. Despite this, most exercise studies are associational and the molecular mechanisms that are the bases for the beneficial effects remain obscure as are the mechanisms of multi-organ communications and benefits. **Objectives:** The NIH Common Fund initiated the Molecular Transducers of Physical Activity Consortium (MoTrPAC) in December 2016 by issuing 19 grants to 37 Principal Investigators from 23 institutions. Fundamentally, MoTrPAC is a large discovery project the goals of which are to: Aim 1: Assemble a comprehensive map of the molecular changes that occur in response to exercise and provide insights into how they are altered by age, sex, body composition and fitness level. Aim 2: Develop a user-friendly database to facilitate investigator-initiated studies and catalyze the field of physical activity research whereby researchers can develop hypotheses exploring novel mechanisms by which physical activity improves or preserves health. **Methods:** This project will explore and document changes in molecules mobilized in blood, muscle and fat in humans as well as 15 additional tissues for rats in response to different exercise regimes (Resistance and Aerobic exercise intervention). The human studies are a multi-center clinical trial cohort of people of both sexes from 10-80 years of age. Preclinical animal Studies (PASS) have been conducted in 6 and 18-month old F344 rats and tissues harvested from control inactive rats and rats at seven time-points following a single 30 minute acute bout of treadmill running. A separate group of rats were subjected to an intensive (70% VO₂max) and progressive run training program of 5 day/week for 1,2, 4, or 8 weeks with 18 tissues collected per rat. Multiple state of art and omics platforms including genomic, transcriptomic, epigenomic, proteomic and metabolomics are being employed to define and discover the molecules mobilized in response to exercise that will serve as a valuable resource for the research community and support future investigator-initiated studies to understand the molecular mechanisms of exercises effects. **Results:** This presentation will highlight data from the initial public data release (November 15th, 2019). Data will be available to the extramural community to collaborate with the MoTrPAC investigators to explore innovative mechanisms to expand the impact of the initial studies. PASS tissues not analyzed are stored in the MoTrPAC BioRepository and will be available for ancillary studies. **Conclusion:** The product from this consortium will begin to characterize the molecular mechanisms of molecules identified in the 'molecular map' that underlie the beneficial effects of physical activity. In addition, the publicly available data resource will help to enhance and accelerate subsequent mechanistic research on overall physiology and diseases and/or conditions affected by physical activity.

C6- ADAPTATION AND VALIDATION OF A SCALE TO ASSESS INTRINSIC CAPACITY IN MEXICAN COMMUNITY-DWELLING ELDERLY ADULTS. Luis Miguel Gutiérrez-Robledo, Rosa Estela García-Chanes, Oscar Rosas-Carrasco (*Instituto Nacional de Geriátria, México*)

Backgrounds: Intrinsic capacity (IC) is a composite of all the physical and mental attributes on which an individual can draw, not only in older age, but across their lives. Following the construct proposed by the WHO clinical consortium, we have developed and validated an Intrinsic Capacity (IC) scale suitable for use in clinical practice, consisting of 5 domains: cognition, psychological, sensory, vitality and locomotion. **Objectives:** To develop and validate a clinically useful IC measurement scale in a sample of community-dwelling Mexican older adults. **Methods:** Data for this analysis come from Frailty Dynapenia and Sarcopenia in Mexican Adults, a cohort of community-dwelling adults, from 2 municipalities in Mexico City. Each domain is measured either with 0 1, Or 2 points for a total score from 0-10 (0 low IC to 10 Optimal IC). To evaluate cognition we used the MMSE. The 7-item CES-D to analysis the psychological domain. The Snellen Eye Test to measure visual acuity and the self-report of hearing to assess the sensory domain. For the evaluation of vitality, the phase angle derived from bioimpedance measurement was used. For locomotion, gait speed and grip strength were assessed. For validation we tested internal consistency, known-group validity based on age and validity by construct with factor analysis. **Results:** The IC score showed reliability (Cronbach alfa=0.49). All item in the scale correlated to the scale 's total score, rho= .36 to .68). The IC score decreases with age (p<0.05). The scale was also positively correlated to other related measurements (Quality of life), short physical performance (SPPB) and negatively correlated with SARC-F, Frailty phenotype and Gerontopôle Frailty scale. The factor analysis demonstrated substantial, clustering of each domain to a single factor. **Conclusion:** We propose a new, clinically useful intrinsic capacity scale awaiting prospective validation.

C7- EFFECTS OF A BLENDED HOME-BASED EXERCISE PROGRAM AND DIETARY PROTEIN INTERVENTION ON PHYSICAL PERFORMANCE IN COMMUNITY-DWELLING OLDER ADULTS: RESULTS FROM THE VITAMIN CRCT. Jantine van den Helder^{1,2}, Sumit Mehra^{3,4}, Carliene van Dronkelaar¹, Gerben ter Riet¹, Michael Tieland¹, Bart Visser¹, Ben J.A. Kröse^{3,5}, Raoul H.H. Engelbert^{1,6}, Peter J.M. Weijs^{1,7,8} ((1) *Center of Expertise Urban Vitality, Amsterdam University of Applied Sciences*; (2) *Amsterdam University Medical Centers, VU University, Amsterdam Movement Sciences*; (3) *CREATE-IT Applied Research, Amsterdam University of Applied Sciences*; (4) *Faculty of Applied Social Sciences and Law, Amsterdam University of Applied Sciences*; (5) *Informatics Institute, University of Amsterdam*; (6) *Department of Rehabilitation, Amsterdam University Medical Centers, University of Amsterdam*; (7) *Department of Nutrition and Dietetics, Amsterdam University Medical Centers, VU University*; (8) *Amsterdam Public Health research institute, Amsterdam University Medical Centers, VU University; Amsterdam, The Netherlands*)

Backgrounds: With the aging population, there is an increasing demand for strategies to optimize muscle mass, strength and physical performance in community dwelling older adults. We designed a new innovative e-health intervention "VITAMIN", including behavior change techniques in exercise and nutrition, and targeting on improvement of physical performance in older adults. The blended home-based exercise intervention contains an exercise application with personalized coaching. Additionally, a dietary protein counseling intervention was designed to complement the exercise intervention. **Objectives:** To determine the 6-months effectiveness and 12-months sustainability of blended home-based exercise and dietary protein counseling interventions on physical performance in community-dwelling older adults. **Methods:** This cluster randomized controlled trial randomized community-dwelling older adults with a regular weekly exercise program into three research groups; 1) no intervention (Control), 2) blended home-based exercise intervention (HBex) or 3) blended home-based exercise intervention with dietary protein counseling (HBex-Pro). The entire study included a 6-month intervention period and a 6-month follow-up. The primary outcome was physical performance assessed by the modified physical performance test (m-PPT). Secondary outcomes included the categories physical functioning, nutritional status, health status, executive functioning and adherence to interventions. An intent-to-treat analytic strategy with Linear Mixed Models of repeated measures was applied to analyze changes over time. **Results:** In total 245 older adults were randomized, mean[SD] age 72.0[6.5] years, 71% was female, 44% low education and 54% had comorbidities. For m-PPT no significant intervention effects (HBex,p=.933; HBex-Pro,p=.730) or follow-up effects (HBex,p=.396;HBex-Pro,p=.362) were found. Gait speed, physical activity level, protein intake, appendicular muscle mass, and muscle strength improved significantly in HBex-Pro compared to Control

after 6-month intervention. The protein intake, as well as muscle mass and strength remained significantly improved after 12-months as compared to Control. **Conclusion:** Although the interventions showed no effect on physical performance, clinically relevant changes were observed in protein intake, muscle mass and physical functioning after 6-months and remained improved after 12-months. Blended home-based exercise training and dietary protein counseling are promising and sustainable strategies to counteract the decline in muscle mass and physical functioning in an aging population. **Key words:** Aging, Behavioral interventions, E-health, Exercise, Sarcopenia.

C8- DEVELOPMENT OF A NEW DEVICE FOR ASSESSMENT OF WIDE CROSS-SECTIONAL AREAS OF THE THIGH MUSCLE. Yasumoto Matsui¹, Yasuo Suzuki^{1,2}, Tsuyoshi Watanabe¹, Hiroki Iida¹, Kazumasa Yamada¹, Satoshi Nakamura³, Tatsuo Arai³, Hidenori Arai¹ ((1) National Center for Geriatrics and Gerontology, Japan; (2) Nihon Fukushi University, Faculty of Health Sciences, Department of Human Care Engineering, Japan; (3) Furuno Electric Co, Ltd, Japan)

Backgrounds: According to EWGSOP2, computed tomography (CT) can be used in addition to dual X-ray absorptiometry (DXA) and bioelectrical impedance analysis (BIA) for measuring muscle mass to diagnose sarcopenia. However, CT has some limitations in its clinical application. We developed a new diagnostic device that produces a wide cross-sectional area (CSA) of the muscle using ultrasonography (US). **Objective:** The aim of this presentation was to present the images, evaluation methods, and reliability of our newly developed device and to compare them with CT images taken at the same site. **Methods:** The reliability was assessed by three examiners by measuring the mid-thigh area of three volunteers, and the intra-rater and inter-rater reliability were calculated. In addition, the correlation between the CSA of the CT and US images, and between the CT value (CTV) and echo intensity were investigated using the Pearson correlation coefficient. The subjects were 58 participants (23 men and 35 women) whose mean age was 71.1 years and who visited the Integrated Healthy Aging Clinic of our hospital. CT images were analyzed using the Slice Omatic software. **Results:** It took approximately 15 seconds to obtain the whole image of the quadriceps, which displayed an image similar to that of CT. The reproducibility study demonstrated that both the intra-rater and inter-rater reliability were high, with ICC (1,1) of 0.968 and ICC (3,1) of 0.934, respectively. Furthermore, a correlation was found between the CSA on CT and that on US (Pearson correlation, 0.996; $p < 0.000$). and a correlation was found between CTV and echo intensity (Pearson correlation, 0.785; $p < 0.000$). **Discussion and Conclusion:** The new ultrasonography diagnostic device for muscle assessment can produce a wide range of images similar to CT. As the echo intensity of the muscle image is considered to represent the intra-muscle adipose tissue and our new device demonstrated high reproducibility and correlated with CT in terms of CSA

and CTV, our new device is expected to be a novel and effective tool for the diagnosis of sarcopenia in the future.

C9- THE GERIATRIC FRAILTY CLINIC IN TOULOUSE: PRESENTATION AND DESCRIPTIVE ANALYSIS OF 5000 PATIENTS. Sandrine Sourdet, Zara Steinmeyer, Anne Ghisolfi, Thomas Gemar, Bruno Chicoulaa, Bruno Vellas (*Gérontopôle, Department of Internal Medicine and Geriatrics, Toulouse University Hospital, France*)

Background: Frailty is a geriatric syndrome, defined as a state of decline in physiological reserves and increased vulnerability to stressors, and that result in greater risk of falls, disability and death. It is a potentially reversible process that can regress to a non-frail condition, with appropriate and preventive management including physical and nutritional interventions, optimization of drug prescription and management of comorbidities. Therefore, identifying and managing frailty is an opportunity to prevent or delay negative health outcome. In 2011, the geriatric “Frailty clinic” was created in Toulouse, France. This unit aims to assess frail older adults identified mainly in primary care, to look after the causes of frailty and to propose personalized preventive interventions. **Objectives:** The objective is to describe the organization of the Frailty clinic, and the main characteristics of the first 5000 patients evaluated between 2011 and 2018. **Methods:** The geriatric frailty clinic (GFC) is a geriatric day hospital dedicated to the prevention of disability in frail older patients aged 65 years and older. Patients considered frail by their physician (general practitioner (GP), geriatrist or specialist) in the Toulouse area are referred to the GFC. Each patient benefits from a comprehensive geriatric assessment performed by a multidisciplinary geriatric team (including a geriatrist or a GP trained in geriatrics, a nurse, nurse-aid, orthoptist, a dietician, neuropsychologist, and a physical activity teacher). **Results:** A total of 5000 patients were admitted between October 2011 and October 2019. We will perform a descriptive analysis of our population : 1/ socio-demographic characteristics, 2/ the frailty status (using Fried criteria); 3/ the cognitive status (MMSE score), 3/ physical status (Short Physical Performance Battery, Katz’s Activities of Daily living, Lawton’s Instrumental Activities of Daily Living), 4/ the nutritional status (Mini Mental Assessment score), 5/ sensory assessment. We will also describe the type of preventive interventions proposed to the patients, and follow-up data. **Conclusion:** The frailty clinic is the first unit dedicated to frailty management in France. Our experience demonstrates that frailty identification and management is feasible in clinical routine, with the implication of primary care professionals and the support of a multidisciplinary team.

C10- IMPLEMENTING EXERCISE THROUGHOUT HOSPITALIZATION TO COUNTERACT MUSCLE & FUNCTION DECLINE. Mylène Aubertin-Leheudre (UQAM, Montreal, Canada)

Backgrounds: Older patients experience an accentuated loss of mobility after a hospital stay increasing the risk of falls, injuries, and hospital readmissions. However there is no current recommendation for prescribing physical activity (PA) after hospitalizations. **Objectives:** 1) Develop a decisional tree to systematically prescribe an individualized, adapted and non-supervised home-based PA program for older adults after hospital discharge (Preventing loss of Autonomy by Treatment Post-Hospitalization: PATH-tool); 2) investigate its feasibility and acceptability; and 3) estimate its potential effects on physical function. **Methods:** Population: Patients admitted to Geriatric Assessment Unit (GAU; criteria: ≥ 65 , hospital length of stay > 7 days, discharge to home; no contraindications for PA; understand French/English) were recruited from March to September 2017. PATH-tool: The decisional tree includes 3 sub-tests (cognitive: MMSE/cardio-strength: 30sec-chair/SPPB balance) linked to 27 different mobility profiles and adapted PA programs based. Intervention: The PA program was performed over a 12-week period (1 session/day; 5-20 minutes each; 3-4 exercises). **Results:** Among 100 patients, 56 were eligible, 29 agreed to participate (52% prescription rate) and 17 completed the protocol. Most of the participants were satisfied (14/17) and enjoyed (13/17) the PA program prescribed. Most of the health professionals found it relevant to the patient (7/8) and reported no extra burden (6/8) associated with its implementation. Adherence to the PA program was 5 sessions/week. A medium-to-large effect size (Cohen's d) was observed for the Timed Up&Go (d=1.04) and 30-sec sit-to-stand tests (d=0.75). **Conclusion:** This study suggests that the implementation of the PATH-tool may be feasible across GAUs, safe and acceptable from the patients' and healthcare professionals' perspectives in addition to lead to some benefits.

C11- PROGRESSION OF PHYSICAL FRAILTY AND THE RISK OF ALL-CAUSE MORTALITY IN THE US NATIONAL HEALTH AND AGING TRENDS STUDY: IS THERE A POINT OF NO RETURN? Qian-Li Xue¹, Karen Bandeen-Roche^{1,2}, Jing Tian^{1,2}, Judith D. Kasper³, Linda P. Fried⁴ ((1) Center on Aging and Health, Johns Hopkins Medical Institutions, Baltimore, MD, USA; (2) Department of Biostatistics, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA; (3) Department of Health Policy and Management, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA; (4) Mailman School of Public Health, Columbia University, New York, NY, USA)

Backgrounds: While frailty appears to be reversible, with progressive severity, a complete remission becomes increasingly rare in the absence of an intervention. **Objectives:** This study investigates: (I) whether there is a point in the progression of frailty beyond which the process becomes irreversible and death becomes imminent (a.k.a. point of

no return), and (II) whether specific patterns of emergence of frailty manifestations are as relevant as the number of manifestations accumulated over time in determining the point of no return. **Methods:** The analysis included 2,161 non-frail older adults identified using the physical frailty phenotype who were living in the community or residential care setting at baseline in 2011 and had at least one annual follow-up visit between 2011 and 2018. We characterized the history of frailty dynamics in two ways. First, we modeled the number of incident frailty criteria (0-5, termed frailty score henceforth) as a time-varying covariate in a Cox model to explore a possible threshold relationship with all-cause mortality. Second, we examined the associations between mortality and a priori-defined patterns of *first* manifestations that include having: (a) weakness, slowness, and/or low activity first, (b) exhaustion and/or weight loss first, or (c) co-occurrence of ≥ 1 criteria in (a) with one or both criteria in (b). We restricted this latter analysis to 1,556 who were non-frail at baseline and developed pre-frailty or frailty during the study. **Results:** There was a step-wise association between greater number of incident frailty criteria and increasing risk of mortality, with a notable risk acceleration after having accumulated all five criteria (HR=34.6, 95% Confidence Interval (CI)=14.6-81.9). In addition, mortality risk increased by 87% when exhaustion and/or weight loss co-occurred with slowness, weakness, and/or low activity at the nascence of frailty manifestation (HR=1.87, 95% CI=1.30-2.68), compared with having slowness, weakness, and/or low activity first (reference) or having exhaustion and/or weight loss first (HR=1.14, 95% CI=0.80-1.62). The risk within pattern (b) was further elevated with co-occurrence of ≥ 3 criteria (HR=3.18, 95% CI=2.01-4.96) compared to two criteria (HR=1.13, 95% CI=0.70-1.83). **Conclusion:** Both the number and rate/pattern of accumulation of incident frailty criteria were associated with mortality risk. On going monitoring of frailty progression could aid clinical and personal decision-making regarding timing of intervention and eventual transition from curative to palliative care.

C12- HOW CAN THE MICROBIOME PLAY A ROLE IN MUSCLE FUNCTIONALITY? Anton De Spiegeleer^{1,2,3}, Dirk Elewaut³, Nele Van Den Noortgate¹, Yorick Janssens², Nathan Debunne², Selien Van Langenhove², Srinath Govindarajan³, Bart De Spiegeleer², Evelien Wynendaele² ((1) Department of Geriatrics, Faculty of Medicine and Health Sciences, Ghent University Hospital, Ghent, Belgium; (2) Drug Quality and Registration (DruQuaR) group, Faculty of Pharmaceutical Sciences, Ghent University, Ghent, Belgium; (3) Unit for Molecular Immunology and Inflammation, VIB-Center for Inflammation Research, Ghent, Belgium)

Background: Sarcopenia, the loss of muscle mass and strength associated with ageing, leads to devastating health outcomes as loss of functionality and all-cause mortality. The pathophysiological mechanisms that might lead to sarcopenia are still poorly understood. However, recent studies as well as our in vitro and in vivo data indicate the microbes in the gut, the so-called microbiome, as a possible etiologic factor.

Objectives: In this study we investigated the effects of a new class of microbial metabolites on muscle homeostasis. **Methods:** Extensive C2C12 muscle cell in vitro experiments and *C. elegans* worm in vivo experiments were conducted. **Results:** We will present our exciting results of a new class of microbial metabolites that influence C2C12 muscle cells and mobility of *C. elegans* worms. As we are currently filing a patent with our findings, these data are still confidential. **Conclusion:** Our findings are opening a new diagnostic and therapeutic dimension in the complex syndrome of muscle diseases, including sarcopenia.

C13- IL-15R α IS RESPONSIBLE FOR TRANSLOCATION OF IL-15, ANABOLIC MYOKINE, ONTO THE SKELETAL MUSCLE CELL MEMBRANE WHICH IS REQUIRED FOR IL-15 SECRETION. Taku Fujimoto¹, Ken Sugimoto¹, Toshimasa Takahashi^{1,2}, Yukiko Yasunobe¹, Keyu Xie¹, Minoru Tanaka^{1,3,4}, Yuri Onishi¹, Shino Yoshida¹, Hitomi Kurinami¹, Hiroshi Akasaka¹, Hiromi Rakugi¹ ((1) Department of Geriatric and General Medicine, Graduate School of Medicine, Osaka University, Japan; (2) Departments of Medicine and Physiology, University of Toronto, Canada; (3) Department of Rehabilitation Science, Graduate School of Health Sciences, Kobe University, Japan; (4) Department of Rehabilitation Science, Osaka Health Science University, Japan)

Background: Skeletal muscle is an organ responsible not only for motor function but also for 80% of glucose metabolism. Exercise increases glucose uptake in skeletal muscle and improves insulin resistance. On the other hand, myokine is a cytokine derived from skeletal muscle, and is considered as a carrier for skeletal muscle-organ linkage. We focused on Interleukin-15 (IL-15), anabolic myokine, and reported that skeletal muscle-specific over expression of IL-15 improves skeletal muscle glucose metabolism via the AMPK pathway. It is considered essential that IL-15 binds to IL-15 receptor alpha (IL-15R α) and moves to the cell membrane for IL-15 secretion from leukocytes. However, there is no report about IL-15 secretion in skeletal muscle cells. **Objectives:** The aim of this study is to investigate the effect of IL-15 receptor on intracellular localization of IL-15 in skeletal muscle cells. **Methods:** The vector of IL-15 tagged with GFP (IL-15-GFP) and IL-15 receptor tagged with OFP (IL-15R α / β / γ -OFP) was transfected into C2C12 (mouse-derived skeletal muscle cells), and then C2C12 was induced to differentiate into myotube. Transfected myotube was observed with a confocal microscope. **Results:** IL-15-GFP was mainly expressed in the cytoplasm, and IL-15R α -OFP was expressed on the cell membrane. When IL-15-GFP and IL-15R α -OFP were co-transfected, IL-15-GFP expression moved onto the cell membrane. IL-15E46K-GFP, which can not bind to IL-15R α , did not move to the cytoplasm even when co-expressed with IL-15R α . When IL-15-GFP and IL-15R β -OFP or IL-15R γ -OFP were co-expressed, almost all IL-15R β -OFP and IL-15R γ -OFP were localized in the cytoplasm and did not merge with IL-15-GFP. In the presence of over expressed IL-15R α , IL-15R β and IL-15R γ merged with

IL-15-GFP. **Conclusion:** IL-15 was shown to translocate to the cell membrane of skeletal muscle cells by binding to IL-15R α . This binding allows IL-15 to bind to IL-15R β / γ too. In order to secrete IL-15, it is considered that IL-15 forms a complex with IL-15R α and is fused to the cell membrane. This study showed that IL-15 translocates to the cell membrane by binding to IL-15R α even in skeletal muscle cells. IL-15R β / γ was expressed on the cell surface in leukocytes, but was expressed in the cytoplasm in skeletal muscle cells. Endocrine, autocrine, and juxtacrine are assumed as secretion modes of IL-15 in leukocytes. IL-15 signaling in skeletal muscle cells requires further investigation.

C14- INTERACTIONS BETWEEN DIETARY PROTEIN AND AUTOPHAGY IN AGED SKELETAL MUSCLE. Gabriele Civiletto¹, Claire Regard¹, Philipp Gut¹, Jerome N. Feige^{1,2} ((1) Nestle Research, EPFL Innovation Park, Lausanne, Switzerland; (2) School of Life Sciences, Ecole Polytechnique Federale de Lausanne (EPFL), Lausanne, Switzerland)

Background: The impact of muscle quality on functional capacity during sarcopenia is receiving increasing attention, yet the mechanisms and solutions to target muscle function remain poorly explored. Autophagy has emerged as a prominent cellular recycling system whose activation promotes broad health benefits in the context of aging and cellular stress. **Objectives:** In the present study, we aimed to understand how to modulate autophagy through nutrition and to study how protein intake cross-talks with the regulation of autophagy. **Methods:** Using a zebrafish LC3 reporter in skeletal muscle, we screened the effect of individual amino acids and micronutrients on skeletal muscle autophagy. The cross-talk between protein intake and autophagy was then studied using dietary interventions in mice. **Results:** We uncovered that high protein is permissive to autophagy in skeletal muscle. While Leucine represses autophagy, other amino acids stimulate autophagosome formation and cellular recycling. Importantly, the anabolic effects of dietary protein supplementation can be uncoupled from the mTOR-mediated repression of autophagy through a concomitant signaling of other amino acids to the autophagic machinery. **Conclusion:** Autophagy is a novel mechanism to target muscle functional capacity during aging, which can be induced by specific amino acids and natural bioactives. Importantly, high protein is permissive to autophagy induction in skeletal muscle, paving the way to novel nutritional concepts combining the anabolic effects of protein with natural autophagy inducers.

C15- GERAS DANCE (DANCING FOR COGNITION & EXERCISE) IMPROVES PHYSICAL PERFORMANCE IN OLDER ADULTS WITH FRAILTY. Courtney C. Kennedy¹, Patricia Hewston¹, George Ioannidis¹, Bonaventure Egbujie¹, Genevieve Hladysh², Dafna Merom³, Sharon Marr¹, Christopher Patterson¹, Ahmed Negm¹, Alexandra Papaioannou^{1,4} ((1) *Dept. Medicine, Division of Geriatrics, McMaster University, Hamilton, ON, Canada*; (2) *YMCA of Hamilton/Burlington/Brantford, ON, Canada*; (3) *University of Western Sydney, School Of Science And Health, New South Wales, Australia*; (4) *Dept. of Health Research Methods, Evidence, and Impact (HEI), McMaster University, Hamilton, ON, Canada*)

Background: Reduced physical function makes it difficult for individuals with frailty to participate in community programs and increases risk of social isolation. GERAS DANCE is a therapeutic dance program designed to reduce the cognitive and physical declines associated with frailty. **Objective:** In this pre-post, implementation study, we aimed to determine 1) the frailty profile of individuals who registered for GERAS DANCE; 2) changes in physical performance and gait-speed over 12-weeks. **Methods:** GERAS Dance was offered at 12 YMCA recreation facilities across Ontario. Individuals were recruited from community-based advertising and from geriatrics clinics. Instructors completed a training program and adhered to a standardized curriculum centred on the ABC's of movement (Agility, Balance and Coordination) and new motor learning. Over 12 weeks, dancesteps/routines were learned and practiced in both seated and standing positions (total dose=180 minutes; 2 x one-hour classes+ 10-minutes/day of homework). Pre-and post-assessments were performed by a trained assessor and included the Fit-FrailtyApp (based on a frailty index), Short Performance Physical Battery (SPPB: gait speed; repeated chair stands; balance), and a questionnaire regarding satisfaction and perceived changes in physical and social function. Changes in scores between pre-and post- assessments were examined using paired t-tests. **Results:** Overall, 215 individuals (mean age (standard deviation) 75.8 (7.5); 19% male) consented to baseline assessment and a further 113 completed post-assessments. At baseline, based on Fit-Frailty App scores, 58% of the sample was in the early-moderate frailty range and a further 11% had more severe frailty. For individuals with a post-assessment (n=113), there was improvement in gait-speed (mean difference of 0.043 m/s (0.16); p=0.009) and in SPPB total score (mean difference of 0.51 points (2.03);p=0.012) over 12-weeks. The mean attendance rate in this group was 75% (18 of 24 classes). Qualitative results indicated a positive effect of GERAS DANCE on social life (e.g. 52% connected outside of classes) and self-reported balance and strength gains. **Conclusion:** Our findings demonstrate that GERAS DANCE is an accessible program for individuals with frailty and had a beneficial effect on physical performance. Furthermore, it was an enjoyable social experience that increased opportunities for community engagement.

C16- C-REACTIVE PROTEIN AND ALBUMIN DETERMINE ACTIVITIES OF DAILY LIVING, GAIT SPEED, HANDGRIP STRENGTH AND MUSCLE MASS IN GERIATRIC REHABILITATION PATIENTS: THE RESORT STUDY. Jeanine M. Van Ancum¹, Camilla S.L. Tuttle², René Koopman³, Mirjam Pijnappels¹, Carel G.M. Meskers^{1,4}, Sanjoy K. Paul⁵, Wen Kwang Lim², Esmee M. Reijnierse², Gordon S. Lynch³, Andrea B. Maier^{1,2} on behalf of the RESORT Study group ((1) *Department of Human Movement Sciences, @AgeAmsterdam, Vrije Universiteit Amsterdam, Amsterdam Movement Sciences, The Netherlands*; (2) *Department of Medicine and Aged Care, @AgeMelbourne, The Royal Melbourne Hospital, The University of Melbourne, Melbourne, Victoria, Australia*; (3) *Centre for Muscle Research, Department of Physiology, School of Biomedical Sciences, The University of Melbourne, Melbourne, Victoria, Australia*; (4) *Amsterdam UMC, Vrije Universiteit Amsterdam, Department of Rehabilitation Medicine, Amsterdam Movement Sciences, Amsterdam, The Netherlands*; (5) *Melbourne EpiCentre, University of Melbourne and Melbourne Health, The Royal Melbourne Hospital, The University of Melbourne, Melbourne, Victoria, Australia*)

Background: Serum levels of C-reactive protein and albumin are non-specific markers of inflammation, which could affect muscle tissue during hospitalization. **Objectives:** In patients admitted to geriatric rehabilitation, we investigated the association between C-reactive protein and albumin during acute hospitalization with change in activities of daily living (ADL) score from two weeks before to immediately after acute hospitalization, and with gait speed, handgrip strength and muscle mass immediately after acute hospitalization. **Methods:** The REStORing Health of Acutely Unwell Adults (RESORT) Study was initiated in October 2017 at four geriatric rehabilitation wards of the Royal Melbourne Hospital, Victoria, Australia. Wave 1 included 693 geriatric rehabilitation patients assessed for change in Katz ADL score (maximum score 6) from two weeks before to immediately after acute hospitalization, and for ADL score, gait speed, handgrip strength and skeletal muscle mass index immediately after acute hospitalization. C-reactive protein and albumin levels were collected from serum samples and were individually as well in clusters (high or low C-reactive protein with high or low albumin) associated with ADL score, gait speed, handgrip strength and skeletal muscle mass index using multivariable linear regression analysis adjusted for age, sex and length of hospital stay. **Results:** The 638 patients included for analyses had a mean age of 82.3 years (SD 7.8), 56% were female. The ADL score declined in 88% of patients from two weeks before acute hospitalization to immediately after acute hospitalization (median -3 points, IQR -4,-2). Larger declines in ADL scores were observed for patients with lower average albumin, higher albumin variation and lower peak albumin levels during acute hospitalization. Change in ADL score was not associated with C-reactive protein levels. Higher average C-reactive protein level was associated with lower gait speed, whereas lower average, variation and peak albumin were associated with lower

ADL score, gait speed, handgrip strength and skeletal muscle mass index immediately after acute hospitalization. The least favourable cluster combining high average C-reactive protein and low peak albumin was associated with a larger decline in ADL score, and with ADL score, gait speed and handgrip strength immediately after acute hospitalization. **Conclusion:** Inflammation during acute hospitalization predisposes geriatric rehabilitation patients to lower ADL score, gait speed, handgrip strength and skeletal muscle mass index at the start of rehabilitation. Albumin was associated with ADL score, gait speed, handgrip strength and skeletal muscle mass index. C-reactive protein was associated with gait speed only.

C17- DEVELOPMENT OF AN IN VITRO PLATFORM TO PREDICT AND SCREEN COMBINATIONS OF ENDOGENOUS METABOLIC MODULATORS CAPABLE OF INFLUENCING MUSCLE PHYSIOLOGY.

William Comb¹, Murat Cokol¹, Melanie Flaender², Andrew Downey¹, Pauline Poydenot², Erwann Ventre², Tony Tramontin¹, Michael Hamill¹ ((1) *Axcella Health, Inc. Cambridge MA, USA*; (2) *CYTOO SA. Grenoble France*)

Background: Dysregulated metabolism contributes to muscle wasting which results in decreased quality of life and morbidity and mortality in aging and disease. We previously published that AXA2678, a composition of Endogenous Metabolic Modulators (EMMs) anchored by amino acids (AA), promotes maintenance of muscle mass, prevents muscle fat accumulation, decreases pro-inflammatory cytokines and promotes myogenic myokines in healthy subjects undergoing single limb immobilization (Holloway et al, 2019). To date, no culture system has existed to systematically evaluate muscle metabolism and physiology in vitro. Therefore, we developed a primary human myotube model that enables prediction and screening of EMM compositions and their impact on muscle physiology. **Objectives:** Primary human myoblasts were differentiated for 5 days using Myoscreen™ (Young et al, 2018). Established myotubes were cultured for 2-4 days in AA concentrations reflecting plasma levels of healthy humans. Metabolic dysfunction was modeled by culturing cells in high glucose, TNF α (10ng/mL), Free Fatty Acids (400uM, 2:1 oleate:palmitate), and AA concentrations reported in frail and sarcopenic individuals. Myotube area, fusion index, protein synthesis (PS), and lipid accumulation were assessed via fluorescence microscopy. Extracellular and intracellular metabolite profiling was performed via LC-MS. **Results:** We demonstrated that metabolic activity of this model system was consistent with human skeletal muscle physiology. Primary human myotube cultures consumed branched chain AAs (BCAAs, eg. Leucine, Valine, and Isoleucine) and generated non-essential AAs (NEAAs, eg. Alanine and Glutamine). Changes in extracellular and intracellular metabolite profiles were measured and informed identification of AAs important for influencing anabolism. Altering concentrations and ratios of specific AAs, alone and in combinations, differentially impacted myotube growth and PS. AA compositions that promoted PS also increased BCAA consumption and NEAA

production, highlighting the link between AA metabolism and anabolic activity. Simulating metabolic dysfunction in the culture (inflammation, glucose intolerance, and myosteatosis) inhibited myotube anabolism and altered AA metabolism. Additionally, EMM combinations were found to impact myotube physiology in these altered culture conditions. **Conclusion:** We were able to predict EMM compositions that differentially impacted myotube physiology using a primary cell platform that models human skeletal muscle metabolism. This platform is adaptable to pathophysiological conditions to model the impact of AA metabolism on disease.

C18- INCREASING FRAILTY SEVERITY IS ASSOCIATED WITH A STEP-WISE INCREASE IN RISK OF DELIRIUM IN OLDER UNSCHEDULED HOSPITAL ADMISSIONS. C Welch On behalf of the Geriatric Medicine Research Collaborative (*University of Birmingham, United Kingdom*)

Background: Delirium is common in older unscheduled hospital admissions. It is distressing and devastating. Delirium is considered to occur secondary to noxious cerebral insults, with increased risk in those with cerebral vulnerability. However, few studies have specifically evaluated the association of frailty with delirium. **Objectives:** To establish how frailty status relates to delirium risk in older unscheduled hospital admissions, and the effect upon patient outcomes. **Methods:** Clinical Frailty Scale (CFS) was recorded for older (≥ 65 years) unscheduled hospital admissions on three dates (14/3/2018, 14/9/2018, 13/3/2019) in a UK multi-centre cohort study. Delirium was diagnosed prospectively (14/3/18, 13/3/19) or retrospectively using a validated approach (14/9/2018), and we recorded if delirium was recognised by the usual care team. Outcome data to include mortality and length of stay were collected up until one month after admission. We used logistic regression analysis to assess the association of CFS with delirium status and delirium recognition, accounting for age, gender, specialty, and dementia status. **Results:** This study included 2937 unscheduled admissions from 82 hospital sites; 51.8% (1524/2937) were CFS-5 or greater and a further 17.1% (503/2937) were CFS-4. A stepwise increase in risk of delirium was demonstrated from CFS-4 to CFS-8 cf. CFS-1: CFS-4 OR 3.57 (CI 1.09 – 11.69); CFS-5 OR 5.44 (CI 1.67 – 17.72); CFS-6 OR 7.10 (CI 2.19 – 23.04); CFS-7 OR 10.41 (CI 3.18 – 34.01); CFS 8 OR 15.32 (CI 4.20 – 55.94). In addition, the odds of delirium recognition were shown to be reduced for those with CFS 7 to 9 cf. CFS 1 to 3: OR 0.34 (CI 0.14 – 0.82). Frailty and delirium status were both shown to be independently associated with increased risk of mortality and length of stay, although the increased mortality risk was only demonstrated for the most frail patients (CFS 8 or 9). **Conclusion:** We have uniquely demonstrated a stepwise increased risk of delirium prevalence with increasing frailty severity, independent of dementia status. This suggests that frailty itself is associated with cerebral vulnerability. This may relate to immunosenescence and vulnerability to inflammatory insults, or weakened blood-brain barrier protection. Unfortunately, delirium remains under-

recognised in the most frail and vulnerable patients.

C19- AN “EVOLUTIONARY ALGORITHM” TO OPTIMIZE THE CONSTRUCTION OF A FRAILTY INDEX IN A POPULATION-BASED STUDY. A. Zucchelli^{1,2}, A. Marengoni^{1,2}, D. Rizzuto¹, A. Calderon-Larranaga¹, G. Onder³, L. Fratiglioni¹, D.L. Vetrano^{1,3} ((1) *Aging Research Center, Karolinska Institutet, Stockholm, Sweden*; (2) *Università degli Studi di Brescia, Brescia, Italy*; (3) *Università Cattolica del Sacro Cuore, Roma, Italy*)

Background: The Frailty index (FI) is a reliable prognostic indicator based on the number of deficits expressed by an individual, out of those assessed. Several studies showed a strong association between the FI and poor outcomes. We hypothesize that an optimization algorithm may help to select the best candidate deficits to generate a highly-predictive FI. **Objectives:** To propose a methodology based on an evolutionary algorithm to build a highly predictive frailty index in a population of older adults. To compare the predictivity of such frailty index with that of a clinically-generated frailty index, across different age groups and sexes, and for short- and long-term mortality. **Methods:** We aimed to optimize the predictive accuracy (area under the curve; AUC) of a FI employing a “genetic algorithm” (Holland, 1975), an iterative meta-heuristic that selects and recombines the most accurate FIs among randomly-generated ones. We used data of 3363 individuals aged 60+ enrolled in the Swedish National Study on Aging and Care in Kungsholmen (SNAC-K). To avoid overfitting, the algorithm was run on a randomly-chosen subsample (70%). The best genetic algorithm-generated FI (ga-FI) was compared in terms of mortality prediction with a clinically-generated FI (c-FI) in the remaining 30% of the data. **Results:** The best GA-generated FI, including 40 deficits, showed an AUC of 0.87 for the prediction both 3- and 6-year mortality. The accuracy in the subsamples varied between 0.78 (3-year mortality within the 78+ years old participants) and 0.89 (3-year mortality within the <78 years old participants). When compared with the accuracy showed by the c-FI, the best GA-generated FI showed higher accuracy ($p < 0.05$ for all comparisons), with the exception of the prediction of 3-year mortality in the male and in the 78+ years old subsamples, although a trend was detected ($p = 0.180$ and $p = 0.274$, respectively). **Conclusion:** The genetic algorithm is feasible method to optimize the construction of a highly performant frailty index.

C20- THE ROLE OF VITAMIN D IN SKELETAL MYOCYTES. Jenny Gunton^{1,3} ((1) *Department of Diabetes and Endocrinology, Westmead Hospital, Westmead, Sydney, Australia*; (2) *Faculty of Health and Medicine, The University of Sydney, Sydney, Australia*; (3) *The Westmead Institute for Medical Research, The University of Sydney, Australia*)

Clinically, Vitamin D deficiency is associated with muscle weakness and falls. Vitamin D receptor (VDR) is present at very low levels in normal muscle so whether vitamin D

could play a direct role in muscle function is unknown. Myocyte-specific vitamin D receptor null mice (mVDR) were generated by crossing human skeletal actin (HSA)-Cre mice with floxed VDR mice. Unlike whole-body VDR knockout mice (VDRKO), mVDR mice showed a normal body size. The mVDR showed a reduced proportional lean mass (70% versus 78% of lean mass), reduced voluntary wheel-running distance (22% decrease, $p=0.009$) and running speed and lower grip strength. mVDR have increased proportional fat mass at 20% compared to 13%. Muscle fibres in mVDRs showed increased diameter and angular fibres and central nuclei suggesting ongoing remodelling. There were, however, no clear changes in fibre type. VDR is a transcription factor and gene expression studies showed decreased expression of cell cycle genes cyclin D1, D2 and D3 and cyclin dependent kinases Cdk-2 and Cdk-4. Expression of calcium handling genes sarcoplasmic/endoplasmic reticulum calcium ATPases (SERCA) Serca2b and Serca3 were decreased and Calbindin mRNA was lower in mVDR muscle. We conclude that vitamin D signalling is needed for normal myocyte function. Despite the low level of VDR protein normally found muscle, deleting myocyte VDR had important effects on muscle size and strength. Maintaining normal vitamin D may be a useful strategy to prevent loss of muscle size and function.

C21- SARCOPENIA OVER THE COURSE OF HOSPITALISATION – THE PREDICTIVE VALUE OF MUSCLE MEASURES IN THREE COHORTS INCLUDING MORE THAN 1,500 OLDER ADULTS. Esmée Reijnierse (*The University of Melbourne, Parkville Victoria, Australia*)

Background: Geriatric patients admitted to subacute rehabilitation are at high-risk of sarcopenia due to muscle atrophy arising from their acute hospital admission and extended periods of bed rest during hospitalisation, in combination with older age and multimorbidity. In this context, sarcopenia may be a key determinant of functional rehabilitation outcomes. **Methods:** The EMPOWER-GR study is an ongoing multicentre, observational, prospective longitudinal cohort of patients admitted to subacute geriatric rehabilitation wards. Our first wave of data included 693 patients. A Comprehensive Geriatric Assessment was performed assessing various health domains at admission and discharge, including muscle mass (by bioelectrical impedance analysis), handgrip strength (by dynamometry) and physical performance (by Short Physical Performance Battery; SPPB). A follow-up telephone interview was conducted three months post-discharge. **Results:** The mean age was 82.2 years (SD 7.9), 57% were female and the median length of stay was 20 days (IQR 14-30). Before hospitalization, 97% was living independently. At admission, 63% was moderately-severely frail, 52% malnourished, 96% ADL dependent and the median SPPB score was 2 points (IQR 0-4). The prevalence of sarcopenia was 40% and the in-hospital incidence 7%. Skeletal muscle mass declined by -0.1 ± 2.4 kg. Handgrip strength, gait speed and SPPB score demonstrated improvements; handgrip

strength by +0.7±4.4 kg, gait speed by +0.13±0.21 m/s and SPPB by +2±2 points. Muscle measures were significantly associated with inflammation, risk of malnutrition, functional dependency during admission, and with institutionalization and mortality at three months post-discharge. **Conclusion:** The high proportion with sarcopenia supports the importance of diagnosing sarcopenia in this setting and the need for further investigation of therapeutic strategies. Despite the minimal changes in muscle measures, there was substantive individual variation and a high incidence of sarcopenia. Collectively, these data support subacute care as an important setting for the implementation of sarcopenia diagnostics as well as preventive and therapeutic strategies.

C22- SARCOPENIA AND HEALTH-RELATED OUTCOMES: AN UMBRELLA REVIEW OF OBSERVATIONAL STUDIES. Nicola Veronese¹, Jacopo Demurtas², Pinar Soysal³, Lee Smith⁴, Gabriel Torbahn⁵, Daniel Schoene⁶, Lukas Schwingshackl⁷, Matteo Cesari⁸, Stefania Maggi¹ ((1) National Research Council, Neuroscience Institute, Aging Branch, Padova, Italy; (2) Primary Care Department Azienda USL Toscana Sud Est, 58100 Grosseto, Italy; (3) Department of Geriatric Medicine, Bezmialem Vakif University, Istanbul, Turkey; (4) The Cambridge Centre for Sport and Exercise Sciences, Anglia Ruskin University, Cambridge CB1 1PT, UK; (5) Institute for Biomedicine of Aging, Friedrich Alexander University Erlangen-Nürnberg, Nuremberg, Germany; (6) Institute of Medical Physics, Friedrich-Alexander University Erlangen-Nürnberg, Erlangen, Germany; (7) Institute for Evidence in Medicine (for Cochrane Germany Foundation), Medical Center-University of Freiburg, Freiburg, Germany; (8) Geriatric Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, University of Milan, Milan, Italy)

Background: The clinical relevance of sarcopenia has increasingly been recognized. However, whether it is associated with the development of other medical conditions is still unclear. **Objectives:** Therefore, we aimed to capture the scale of outcomes that have been associated with the presence of sarcopenia and systematically assess the quality, strength, and credibility of these associations using an umbrella review methodology. **Methods:** A systematic review in several databases was carried out, until 20th February 2019. For each association, random-effects summary effect size, 95% confidence intervals (CIs), heterogeneity (I²), evidence for small-study effect, evidence for excess significance bias, and 95%-prediction intervals were estimated. We used these metrics to categorize the evidence of significant outcomes (p<0.05) from class I (convincing) to class IV (weak), according to pre-established criteria. **Results:** From 358 abstracts, 6 meta-analyses with 14 associations were included. Sarcopenia was associated with higher risk of other comorbidities and mortality in 11 of 14 outcomes explored. However, only 3 outcomes (i.e., association between sarcopenia and increased risk of death in community-dwelling older people [odds ratio, OR=3.60; 95% CI 2.96–4.37; n=14,305], disability [OR=3.04;

95% CI 1.80–5.12; n=8569], and falls [OR=1.60; 95% CI 1.31–1.97; n=12,261]) presented a highly suggestive evidence (class II). Other association was classified as having only a weak evidence. **Conclusion:** Sarcopenia is associated with several adverse health-related outcomes in older people, and its associations with mortality, disability, and falls are supported by a highly suggestive evidence. The effect of interventions on sarcopenia to improve these outcomes needs to be investigated.

C23- IS SENSORY LOSS A RISK FACTOR FOR FRAILTY? A SYSTEMATIC REVIEW AND META-ANALYSIS. Benjamin Kye Jyn Tan¹, Ryan Eyn Kidd Man^{2,3}, Alfred Tau Liang Gan², Eva K. Fenwick^{2,3}, Preeti Gupta², Varshini Varadaraj^{4,5}, Bonnielin K. Swenor^{4,5}, Tien Yin Wong^{1,2,3}, Ecosse Luc Lamoureux^{1,2,3} ((1) Yong Loo Lin School of Medicine, National University of Singapore, Singapore; (2) Singapore Eye Research Institute, Singapore National Eye Centre, Singapore; (3) Duke-NUS Medical School, Singapore; (4) The Wilmer Eye Institute, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA; (5) Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA)

Background: Age-related sensory loss is highly prevalent among older adults and a potential modifiable risk factor for frailty. However, existing literature on this relationship has been equivocal. **Objectives:** To examine the sensory loss-frailty relationship using a systematic review and meta-analysis. **Methods:** We searched PubMed, Embase and Cochrane Library from inception until 30 April 2019, with no language restrictions, for observational studies investigating the relationship between 4 objectively-assessed and/or self-reported sensory impairments—vision (VI), hearing (HI), smell (SI), taste (TI)—and frailty. Included studies defined pre-frailty and frailty using original or modified versions of validated criteria (e.g. Fried frailty phenotype). We assessed the risk of bias using the Newcastle-Ottawa Scale. Prioritizing maximally covariate-adjusted effect estimates, we performed random-effects meta-analyses for the associations of VI and HI each with various frailty outcomes. We also examined sources of heterogeneity using random-effects meta-regression and assessed publication bias using visual inspection, Egger's test and the trim-and-fill method. **Results:** Among 666 initial non-duplicated hits, we included 14 cross-sectional and 6 longitudinal studies in our review (N=24,718), all with low to moderate risk of bias. Meta-analyses demonstrated clear associations of VI and HI with significantly higher pooled odds [OR (95% CI)] for: (i) any frailty [VI: 1.98 (1.60-2.45); HI: 1.75 (1.34-2.27)]; (ii) pre-frailty [VI: 1.80 (1.52-2.12); HI: 1.61(1.26-2.05)]; (iii) frailty (vs. robustness) [VI: 3.00 (2.17-4.16); HI: 2.49 (1.95-3.20)]; and (iv) frailty (vs. pre-frailty) [VI: 1.64(1.31-2.06); HI: 1.71 (1.25-2.35)]. The use of differing frailty criteria, Caucasian race, and high frailty prevalence were statistically significant effect modifiers of HI and frailty outcomes, although the independent association between HI and frailty persisted after accounting for these factors. Publication bias was minimally present and did not alter our conclusions. Conversely, sparse

literature and heterogeneous methods precluded meta-analyses or conclusions on the SI/TI-frailty relationships. **Conclusion:** Our findings emphasize VI and HI as important risk factors and potential intervention strategies for frailty prevention. Our review also highlights the need for longitudinal observational studies to determine the bidirectionality of these risk relationships, as well as to elucidate the effects of smell, taste and multiple sensory impairments on frailty.

C24- DIETARY INFLAMMATORY INDEX AND DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS. Kathleen Woolf¹, Mary Kiely², Yusuf Yazici² ((1) *New York University (NYU) Steinhardt, Department of Nutrition and Food Studies, USA;* (2) *NYU Langone Health, Division of Rheumatology, USA*)

Background: Rheumatoid arthritis (RA) is an autoimmune disease accompanied by pain, joint stiffness, swelling, and especially inflammation. Because nutrients can have pro- or anti-inflammatory properties, the Dietary Inflammatory Index (DII) was developed to assess the inflammatory potential of the diet. **Objectives:** Using the DII, this study examined body composition and RA disease activity among individuals with RA with a pro-inflammatory diet compared to an anti-inflammatory diet. **Methods:** 84 adults with RA (age: 52.9±14.4 years; sex: n=73 female, n=11 male; disease duration: 13.5±9.2 years) were recruited from the NYU Langone Orthopedic Center. Height, weight, waist circumference, and body composition (bioelectrical impedance assessment) were measured. Waist-to-height ratio (WHtR), body mass index, fat mass index, and fat-free mass index were calculated for each participant. Disease activity was determined using C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and the Multi-Dimensional Health Assessment Questionnaire, which includes self-reported measures of physical function, pain, & global status (summed into the RAPID3 score), fatigue, painful joint count, and duration of morning stiffness. Higher scores indicate greater disease activity. Seven-day food records were analyzed using Nutrition Data System for Research and the DII was calculated. Higher DII scores suggest a more pro- and less anti-inflammatory diet. Based upon DII score, participants were dichotomized into an anti-inflammatory diet (DII<0; n=45) or pro-inflammatory diet (PID; DII>=0; n=39) group. Independent sample t-tests examined differences in disease activity and body composition between the two diet groups using IBM SPSS Statistics. **Results:** Participants in the AID group had a lower WHtR (p=0.032), indicating greater abdominal obesity, and lower overall body fat percentage (p=0.042) compared to the PID group. Participants in the AID group had a lower ESR (p=0.017), self-reported less pain (p=0.034), and had a lower RAPID3 score (p=0.037) compared to the PID group. No significant differences were found between groups for the other measures of body composition and RA disease activity. **Conclusion:** Participants reporting a pro-inflammatory diet had a more unfavorable body composition and greater RA disease activity, both in laboratory measures and patient reported

outcomes. Additional research should examine the role of diet to disease management in RA.

C25- CLINICAL DETERMINANTS OF RESTING METABOLIC RATE IN GERIATRIC OUTPATIENTS. Suey S.Y. Yeung^{1,2}, Esmee M. Reijnierse², Marijke C. Trappenburg^{3,4}, Carel G.M. Meskers⁵, Andrea B. Maier^{1,2} ((1) *Department of Human Movement Sciences, @AgeAmsterdam, Faculty of Behavioural and Movement Sciences, Amsterdam Movement Sciences, Vrije Universiteit, Amsterdam, The Netherlands;* (2) *Department of Medicine and Aged Care, @AgeMelbourne, The Royal Melbourne Hospital, The University of Melbourne, Victoria, Australia;* (3) *Department of Internal Medicine, Section of Gerontology and Geriatrics, Amsterdam UMC, Vrije Universiteit, Amsterdam, The Netherlands;* (4) *Department of Internal Medicine, Amstell and Hospital, Amstelveen, The Netherlands;* (5) *Department of Rehabilitation Medicine, Amsterdam UMC, Vrije Universiteit, Amsterdam, The Netherlands*)

Background: Accurate estimation of the energy requirements including the resting metabolic rate (RMR) is important for optimal nutritional care, yet its clinical determinants are unknown. **Objectives:** This study examined the associations between clinical determinants of the Comprehensive Geriatric Assessment (CGA) domains with RMR among geriatric outpatients. **Methods:** This study included community-dwelling older adults (n=84, 54 females) referred to geriatric outpatient mobility clinics recruited in Amsterdam (The Netherlands) and Melbourne (Australia). Determinants within domains of the CGA included diseases (number, type and severity of diseases, polypharmacy), nutrition (body weight, body mass index (BMI), absolute and relative skeletal muscle mass (SMM), fat-free mass (FFM), fat mass (FM), risk of malnutrition), physical function (handgrip strength, Short Physical Performance Battery, Timed Up & Go), cognition (Mini-Mental State Examination), psychological wellbeing (Geriatric Depression Scale) and blood pressure (systolic, diastolic, heart rate). RMR was objectively measured using indirect calorimetry with a canopy hood. Associations between the clinical determinants with standardized RMR (country and sex-specific z-scores) were analysed with linear regression adjusted for age, sex and body weight. A Bonferroni correction (p<0.0015) was applied to account for multiple testing. **Results:** Determinants within the nutritional domain were associated with RMR. Absolute measures (i.e. body weight, BMI, SMM, FFM and FM in kg) had higher effect estimates (α) than relative measures (i.e. SMM, FFM and FM in %). Within the absolute measures, body weight showed the strongest association with RMR (α =0.58, p<0.0015). Significant associations between determinants within the nutritional domain with RMR disappeared after further adjustment for body weight. None of the other domains were associated with RMR. **Conclusion:** Body weight is the strongest clinical determinant of RMR and should be taken into account when estimating RMR in geriatric care.

C26- BLOOD METABOLOMIC PROFILE ADAPTATION FOLLOWING 12-WEEK OF HIIT TRAINING COMBINED WITH CITRULLINE SUPPLEMENTATION IN OLDER ADULTS. Layale Youcef¹, Sylvère Durand^{2,3}, Fanny Aprahamian^{2,3}, Deborah Lefevre^{2,3}, Eva Peyrusqué^{1,4}, Guido Kroemer^{2,3}, Mylène Aubertin-Leheudre⁴, Philippe Noirez^{1,4} ((1) INSERM U1124, Université de Paris, Paris, France; (2) INSERM U1138, Centre de Recherche des Cordeliers, Sorbonne Université, Université de Paris, Paris, France; (3) Metabolomics and Cell Biology Platforms, Gustave Roussy Cancer Campus, AMMICA US23/CNRS UMS3655, Villejuif, France; (4) Department of Exercise Science, Université du Québec à Montréal, Montréal, Canada)

Background: Nowadays, ageing became a major issue in the field of public health. Physical activity as well as nutrition are recognized to play an important role in the maintenance of healthy ageing but also to prevent or counteract aging health adverse effects. It has been recently show that high-intensity interval training (HIIT) combined to citrulline (CIT) supplementation can lead to improvements of physical and functional performance. However understanding the mechanisms pathways modified through these interventions is important to prescribe it according to the specific needs of the sub-population (obese, frail, sarcopenicetc...). **Objectives:** The aim of this study is to evaluate the blood metabolomic profile adaptation following a high-intensity interval training (HIIT) combined or not to citrulline (CIT) supplementation in obese older adults. **Methods:** This study is a double-blinded randomized interventional trial. 71 sedentary obese older men and women (aged from 60 to81yrs) completed a 12-week elliptical HIIT program with a CIT (10d.day-1) or a placebo (PLA) supplementation. Metabolomic profile were obtained using blood sample analyzed through 4 mass spectrometers (1) LC/HRAM Orbitrap q-Exactive (ThermoScientific); 2) LC/QTRAP 6500+ (AB Sciex); 3) LC/QQQ 6410 (Agilent); 4) GC/7000C (Agilent)) coupled to multiple different liquid phase or gas chromatography methods. **Results:** Among the 326 metabolites and the 33 ratios obtained, 28 metabolites varied with the CIT supplementation when combined to HIIT (16 of them were decreased and 12 were increased) compared to HIIT alone. In addition, 25 metabolites varied following the intervention specifically to gender/sex (19 were more elevated only for men and 6 were more elevated only for women). **Conclusion:** The citrulline supplementation combined to HIIT has an impact on the blood metabolomic profile in older adults. These promising results need to be confirm and explore since it could allow to highlight new biomarkers related to nutrition and exercise interventions in older men and women.

C27- ADVERSE MUSCLE COMPOSITION WITHIN OBESITY IS ASSOCIATED WITH LOW FUNCTIONAL PERFORMANCE AND INCREASED COMORBIDITY – RESULTS FROM THE LARGE UK BIOBANK IMAGING STUDY. Jennifer Linge^{1,2}, Olof Dahlqvist Leinhard^{1,2,3} ((1) AMRA Medical, Linköping, Sweden; (2) Department of Medical and Health Sciences, Linköping University, Sweden; (3) Center for Medical Image Science and Visualization (CMIV), Linköping University, Sweden)

Background: Sarcopenia within obesity is not well-described. Recent results from the UK Biobank showed only 0.1% of participants with obesity had sarcopenia (EWGSOP2) while contradictory, they showed the highest prevalence of low functional performance. The main cause for under diagnosis of sarcopenia within obesity was the BMI-dependency of current sarcopenia definitions, where the correlation between body size and muscle mass was not properly adjusted through division with height², weight or BMI. **Objectives:** To investigate prevalence of low functional performance and metabolic comorbidity in individuals with obesity and adverse muscle composition identified through combined MRI-based muscle assessment. **Methods:** 9612 participants were included (N=4589 with DXA). Fat-free muscle volume (FFMV), and muscle fat infiltration (MFI) were quantified using a 6-minute MRI protocol and automated image analysis (AMRA Researcher). As a measure of deviating FFMV, the individual FFMV/height² z-score was extracted from each participant's sex and BMI-matched virtual control group(VCG)-distribution (FFMV[VCG]). Participants with obesity (BMI>=30 kg/m²) and adverse muscle composition (AMC) were stratified using sex-specific thresholds for MFI (above 75th percentile, whole cohort) and FFMV[VCG] (below 25th percentile, whole cohort). Prevalence of low functional performance (low hand grip strength, slow walking pace, no stair climbing, morethan one fall last year) and metabolic comorbidity (coronary heart disease (CHD), diabetes type 2 (DT2)) in participants with obesity and AMC were compared to those without AMC. As reference, characteristics of the sarcopenia population (EWGSOP) were included. **Results:** 311 (17.2%) out of 1808 participants with obesity had AMC. Prevalence of low functional performance was significantly higher inthis group as compared to those without AMC for all variables except falls: hand grip strength 11.3%/5.7% (factor 2.0); walkingpace 23.8%/9.2% (factor 2.6); stair climbing 16.4%/8.7% (factor 1.9); falls 8.7%/6.7% (factor 1.3) (p<0.05, age-adjusted). Corresponding values within sarcopenia (EWGSOP2) were: hand grip strength 100% (in definition); walking pace 9.8%; stair climbing 8.8%; falls 8.8%. Prevalence of CHD (15.4%) and DT2 (19.3%) in participants with obesity and AMC was 2.4 and 2.1 times higher compared to those without AMC (p<0.01, age-adjusted). **Conclusion:** MRI-identified adverse muscle composition is commonly observed within obesity and associated with high prevalence of low functional performance and increased comorbidity.

C28- BUILDING A MEASURE OF PHENOTYPIC AGE USING MULTI-DOMAIN PREDICTORS: A 18-YEAR LONGITUDINAL POPULATION BASED STUDY.

D.L. Vetrano^{1,2}, Jérôme Salignon^{3,4}, Debora Rizzuto¹, Amaia Calderón-Larrañaga¹, Alberto Zucchelli⁵, Christian G. Riedel^{3,4}, Laura Fratiglioni^{1,6} ((1) *Aging Research Center, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet, Stockholm, Sweden*; (2) *Centro di Medicina dell'Invecchiamento, IRCCS Fondazione Policlinico «A. Gemelli» and Catholic University of Rome, Italy*; (3) *Department of Biosciences and Nutrition, Karolinska Institute, Huddinge, Sweden*; (4) *Integrated Cardio Metabolic Centre (ICMC), Department of Medicine, Karolinska Institute, Huddinge, Sweden*; (5) *Department of Clinical and Experimental Sciences, University of Brescia*; (6) *Stockholm Gerontology Research Center, Stockholm, Sweden*)

Background: An inter-individual mismatch in the association between chronological age and survival emerges and becomes wider along with passing time. Observable individuals' characteristics may provide precious information to improve survival prediction. **Objectives:** To build a measure of phenotypic age using multi-domain predictors and exploring their independence of chronological age, and to compare the prognostic power of phenotypic age with chronological age, and other clinical and functional measures. **Methods:** We analyzed data from 3,095 individuals aged ≥ 60 years old participating in the Swedish National Study on Aging and Care in Kungsholmen (SNAC-K). A total of 97 variables were used to predict 18-year survival through penalized Cox regression models adjusted and unadjusted by age in a training SNAC-K subsample, including the predictors a) belonging to single domains (i.e., functional status, diseases, blood tests, socio-demographics and lifestyles), and b) all at once. The area under the receiving operating curve (AUROC) was used to test the predictivity (5- 10- and 15-years mortality) of each model in a test SNAC-K subsample. Mortality risks derived by the best fitting model were used to predict our measure of phenotypic age. AUROC was used to compare the predictive power of phenotypic age with that of other clinical and functional measures. **Results:** The inclusion of chronological age improved 10-year mortality prediction of all the considered domains apart from when functional status alone (measures of physical and cognitive function; AUROC=0.83 w/o chronological age) and all the variables together (AUROC=0.87 w/o chronological age) have been included in the model. Gait speed, female sex, hand-grip strength, chronic kidney disease and atrial fibrillation resulted the five most important predictors of survival. Phenotypic age (AUROC=0.88) resulted the best predictor of 10-year mortality when compared with chronological age (AUROC=0.84), gait speed (AUROC=0.82), number of diseases (AUROC=0.75) and other clinical and functional measures. **Conclusion:** Observable phenotypic characteristics of clinical, functional and sociodemographic nature can be used to predict survival, independently by chronological age.

C29- DYNAPENIA AND FRAILTY IN DISABLED OLDER WOMEN LIVING IN THE COMMUNITY: IMPORTANT DIFFERENCES IN RISK OF INCIDENT ADVERSE HEALTH OUTCOMES.

Paulo H. M. Chaves¹, Qian-Li Xue², Leocadio Rodríguez Mañas³, Karen Bandeen-Roche⁴ ((1) *Benjamin Leon Center for Geriatric Research and Education, Herbert Wertheim College of Medicine, Florida International University, Miami, FL, USA*; (2) *Center on Aging and Health, Division of Geriatric Medicine and Gerontology, Johns Hopkins University School of Medicine, Baltimore, MD, USA*; (3) *Department of Geriatrics, Hospital Universitario de Getafe, Getafe, Spain*; (4) *Department of Biostatistics, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA*)

Background: Sarcopenia and frailty are inter-related geriatric syndromes that contribute to the disablement process in older adults. Dynapenia i.e., low muscle strength, is a key criterion for characterization of both sarcopenia and frailty status. Whether risk of major adverse outcomes among those with dynapenia differs depending on concomitant frailty status, information useful to guide efforts aimed at implementation of sarcopenia and/or frailty assessments in the clinical setting, remains to be characterized. **Objectives:** To compare the incidence of worsening disability, hospitalization, and fall according to the conjoint and separate presence of frailty and dynapenia. **Methods:** Prospective study using data from the Women's Health and Aging Study I, which enrolled community-dwelling women 65 years and older from among the 1/3 most disabled living in Baltimore, USA. Data from the baseline and 6 follow-up visits over a median of 3 years were examined. Outcomes: new fall, new hospitalization, and incident disability (self-reported difficulty) performing ≥ 3 basic (ADLs) and instrumental activities of daily living (IADLs). Fried Frailty phenotype and dynapenia (gripstrength < 20th percentile for body-mass-index) at baseline were the main prognostic measures compared using discrete-time survival models with adjustment for demographics and comorbidities. Models included more than 3,000 observations in more than 700 subjects. **Results:** As compared to those with neither dynapenia nor frail, those with dynapenia and frailty, but not those with dynapenia without frailty, were at higher risk of incident ADL disability (HR: 2.1; 95%CI: 1.6-2.8), incident IADL disability (HR: 1.9; 95%CI: 1.3-2.6), hospitalization (HR: 1.4; 95%CI: 1.1-1.7), and fall (HR: 1.5; 95%CI: 1.2-1.8). **Conclusion:** Associations of dynapenia with adverse health risks in disabled older women in the community depended on whether frailty was also present. Findings highlight that frailty status is an independent predictor of adverse outcomes even among moderately or severely disabled older women. Results also support the hypothesis that dynapenia alone, a key clinical indicator that is enough for the classification of "probable sarcopenia", may have restricted ability in prospectively capturing risk of major incident adverse outcomes. In this context, expanded data collection for frailty status characterization may be justified for enhanced vulnerability assessment in the clinical setting.

C30- DEVELOPMENT AND VALIDATION OF A HOSPITAL ELECTRONIC RECORD FRAILTY INDEX (HERFI) USING MACHINE LEARNING TECHNIQUES.

J. Mytton¹, G.V. Gkoutos^{1,2}, C. Ferro, T.A. Jackson^{1,3} ((1) University Hospitals Birmingham NHS Trust, UK; (2) Centre for Computational Biology, University of Birmingham, UK; (3) Institute of Inflammation and Ageing, University of Birmingham, UK)

Background: Routine data can be used to identify frailty through a frailty index approach. Hospital electronic health records (HER) offer a platform towards rapid identification of frailty in older people on admission to hospital. **Objectives:** 1: To develop and validate a frailty index using routine data collected on admission to hospital. 2: To use machine learning methods to improve the model and increase replicability by reducing included parameters. **Methods:** Thirty-one routinely collected clinical measures were used to calculate an admission frailty index (FI-QEHB). A development cohort (n=6480) tested model performance to predict mortality (in-hospital and 1 year), new care home admission and readmission. Machine Learning techniques (Classification and Regression Tree Analysis) determined the most important variables that predict mortality (the HerFI), and a validation of cohort (n=19391) was used to test performance of the new model. The area under the receiving operating characteristic (ROC) curve was used to assess the performance when the frailty index was added into a multivariable logistic regression model to predict outcomes. **Results:** In the validation cohort (median age 79, 54% female, mortality 6.8% inpatient and 10.8% at 1 year) FI-QEHB predicted in-hospital mortality (OR 1.10, 95% CI 1.09–1.11, p<0.001; AUROC 0.78), care home admission (OR 1.06, 95% CI 1.05 – 1.07, p<0.001; AUROC 0.74), 30-day readmission (OR 1.02, 95% CI 1.01-1.02, p<0.001; AUROC 0.58) and 1 year mortality (HR 1.07, 95% CI 1.06 – 1.08, p<0.001; AUROC 0.72). The variables identified after six classification and regression trees to develop the HerFI were albumin, alkaline phosphatase, CRP, early warning score (SEWS), urea and the Waterlow Score (Pressure ulcer risk). The HerFI predicted in-hospital mortality (OR 1.05, 95% CI 1.05–1.05, p<0.001; AUROC 0.81), care home admission (OR 1.02, 95% CI 1.02 – 1.03, p<0.001; AUROC 0.74), re-admissions (OR 1.01, 95% CI 1.01 -1.02, p<0.001; AUROC 0.58), and 1 year mortality (HR OR 1.04, 95% CI 1.04-1.04, p<0.001; AUROC 0.75) **Conclusion:** Data routinely collected through an HER on admission can be used to predict clinically important adverse outcomes in older people. This should allow identification of those most at risk, and the signposting of interventions such as comprehensive geriatric assessment.

C31- AIR POLLUTION AND FRAILTY AMONG PATIENTS WITH END-STAGE KIDNEY DISEASE (ESKD).

Miranda R. Jones¹, Yijing Feng², Nadia Chu^{1,2}, Jeremy Walston³, Dorry Segev^{1,2}, Mara McAdams-DeMarco^{1,2} ((1) Department of Epidemiology, Johns Hopkins School of Public Health, Baltimore, MD, USA; (2) Department of Surgery, Johns Hopkins University School of Medicine, Baltimore, MD, USA; (3) Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD, USA)

Background: Frailty is triggered by inflammatory pathways and both frailty and inflammation are associated adverse outcomes among patients with end-stage kidney disease (ESKD). Exposure to air pollution is associated with increased inflammation and as such may be a determinant of frailty in patients with ESKD. **Objectives:** Therefore, we sought to estimate the impact of household-level exposure to fine particulate matter (particles <2.5 μm in diameter [PM_{2.5}]) on frailty among patients with ESKD. **Methods:** We leveraged a prospective, multicenter cohort study of 1,482 adults with ESKD undergoing evaluation for kidney transplantation (KT) (2014-2019) from 40 US states. Frailty status was assessed at KT evaluation using the physical frailty phenotype (PFP). Household-level air pollution at study enrollment was estimated as annual average PM_{2.5} concentrations at each participant's address using SEDAC national air pollution data (data available through 2016). We estimated the odds of frailty using logistic regression to compare quartiles of PM_{2.5} concentrations accounting for confounders including socioeconomic status (SES; annual household income and education). **Results:** Among the 1,482 adults with ESKD, the median age was 56, 39% were female and 47% were African-American. Compared to patients with PM_{2.5} concentrations in the lowest quartile (<9.3 $\mu\text{g}/\text{m}^3$), those with exposure to the third quartile of PM_{2.5} (10.0-11.1 $\mu\text{g}/\text{m}^3$) had 1.50-fold (95% CI: 1.04-2.17) increased odds of being frail after accounting for important confounders including age, race/ethnicity, and SES. However, exposure to PM_{2.5} concentrations in the second (9.3-10.0 $\mu\text{g}/\text{m}^3$) and fourth quartiles (>11.1 $\mu\text{g}/\text{m}^3$) were not statistically significantly associated with frailty status. PM_{2.5} was also associated with the weight loss and exhaustion components of the PFP. **Conclusion:** In this population of adults of all ages with ESKD, fine particulate matter was associated with greater and frailty, although the association may not be linear. Further study of the mechanisms by which air pollution impacts the development of frailty and the role of inflammation on this association is needed.

C32- MUSCLE MITOCHONDRIA FUNCTIONAL ADAPTATION DURING HABITUATION TO ECCENTRIC VERSUS CONCENTRIC EXERCISE TRAINING. Craig RG Willis¹, Colleen S Deane¹, Daniel J Wilkinson², Kenneth Smith², Bethan E Phillips², Philip J Atherton², Timothy Etheridge¹ ((1) *Department of Sport and Health Sciences, University of Exeter, UK*; (2) *MRC-ARUK Centre for Musculoskeletal Ageing Research and National Institute of Health Research, University of Nottingham, UK*)

Background: Lengthening eccentric (ECC) contractions typically cause acute functional decline, and chronic increases in muscle fascicle length. Conversely, shortening concentric (CON) contractions induce minimal acute functional effects and chronically increase fibre pennation angle. The mechanisms underpinning this phenotypic divergence are unknown, the delineation of which will hold therapeutic relevance to the blunted hypertrophic and aerobic training responses of ageing muscle. Since CON associates with a primarily metabolic load versus ECC, differences in mitochondrial adaptation are a logical candidate. **Objectives:** We aimed to characterise human muscle mitochondrial respiratory responses to contraction mode both acutely and following 2 weeks of exercise habituation. **Methods:** Sixteen healthy, exercise-naïve males (age, 23±1 y; BMI, 24±1 kg.m⁻²; VO₂max, 45±1 mL.kg⁻¹.min⁻¹) were randomly assigned to either CON-dominant (submaximal uphill running, n=8) or ECC-dominant (submaximal downhill running, n=8) exercise. Participants performed eight CON or ECC exercise bouts (30 min at a speed equivalent to 60% VO₂max) over a two-week 'habituation' period. Mitochondrial respiration was assessed via high-resolution respirometry in permeabilized vastus lateralis muscle biopsies collected at baseline (~2 weeks before first training bout) and 4 h after the first and final exercise training bouts. **Results:** Mitochondrial respiration coupled to phosphorylation supported by electron transport chain complexes I and II (PI+II) and maximal respiratory capacity (E) both acutely declined after the first bout of unaccustomed ECC exercise (P<0.1). Whereas PI+II returned to baseline values after 2 weeks ECC habituation, suppression of E remained after the final ECC bout (P<0.1). Conversely, whilst CON exercise had no effect on PI+II either pre- or post-habituation, E was increased after unaccustomed CON (P<0.1) but returned to baseline values after CON habituation. **Conclusion:** Short-term ECC and CON training induce opposing mitochondrial adaptations: ECC impairs mitochondrial respiratory capacity even after ECC habituation, whereas transient increases in mitochondrial function after CON are not maintained post-habituation. Contraction mode-specific mitochondrial responses might, therefore, contribute to alternate muscular adaptation to training modes and provide a potential framework for understanding sub-optimal muscular responses to exercise in ageing muscle.

C33- SALIDROSIDE SUPPLEMENTATION ASSOCIATED WITH INTERMITTENT EXERCISE ENHANCES PHYSICAL PERFORMANCE IN OLD MICE. Rémi Roumanille¹, Thomas Brioché¹, Théo Fovet¹, Corentin Guilhot¹, Pierre Delobel¹, Christelle Bertrand-Gaday¹, Ange le Chopard¹, Anne Bonnieu¹, Pascale Fanca-Berthon², Guillaume Py¹ ((1) *DMEM, Université Montpellier, INRAE, Montpellier, France*; (2) *Naturex SA, rue Pierre Bayle, Avignon, France*)

Background: Muscle wasting can be caused by numerous conditions including aging. Indeed, aging causes a decrease of muscle mass and strength, and an increase of fatigability (Brioché, 2016), which are associated with a poor quality of life. Exercise is currently the best strategy against muscle wasting (Montero-Fernandez, 2013), but sometimes it cannot be used or is insufficient and alternative methods are necessary to prevent muscle deconditioning. In partnership with a french society, we already showed that particular plant extracts coupled with exercise enhanced protein synthesis leading to greater performance in young rats. Salidroside, a molecule contained in the extracts is known to increase mTOR expression (Chen, 2016), decrease oxidative stress (Huang, 2009) and promote neovascularization (Zhang, 2017). **Objectives:** We aim to test the effects of salidroside coupled with exercise during sarcopenia, and elucidate the underlying molecular mechanisms. **Methods:** 40 C57BL/6J mice (18 months) were divided in four groups: Control (C), Control-Exercise (CE), Salidroside (S) and Salidroside-Exercise (SE). Mice were supplemented (drinking water) during 12 weeks and followed an intermittent exercise protocol : they ran at 100% of their Maximal Aerobic Speed (MAS) at 25% grade for 15s followed by 45s rest, repeated 15 times, 3 times a week. MAS and Maximal Force of the forelimb were assessed before and after treatment. Animals were sacrificed and gastrocnemius muscles harvested to investigate expression of key proteins via Western Blot and for histological examination. **Results:** Mice in CE and SE presented greater MAS than those in C (29.2 ±5.52 and 31.2 ±3.31 vs 24.5 ±4.16 m.min⁻¹, p<0.05). Salidroside treatment increased also Maximal Force in regard to C. SE showed a lower expression of p-PDHE1a than C (p=0.04) and S had a higher expression of HIF1-alpha than C (p=0.01). In comparison to C the CE, S and SE groups showed a dramatically greater expression of Sirtuin 1 (p<0.05). And further histological results will be presented. **Conclusion:** Salidroside associated with intermittent exercise enhanced performance following a chronic supplementation. This effect could be explained by a greater vascularization, different substrate utilization and implication of satellite cells. Salidroside coupled with exercise could limit aging effects and improve quality of life.

C34- LATE-ONSET NICOTINAMIDE RIBOSIDE SUPPLEMENTATION IMPROVES HEALTH-SPAN AND FUNCTIONAL PARAMETERS IN OLD MICE.

J. Vina¹, C. Arc-Chagnaud^{1,2}, A. Salvador-Pascual¹, A. De la Rosa Gonzalez¹, F. Millan¹, E. Garcia-Dominguez¹, A. Carretero¹, A.G. Correas¹, G. Olaso-Gonzalez¹, M.C. Gomez-Cabrera¹ ((1) *Freshage Research Group- Dept. Physiology-University of Valencia, CIBERFES-ISCIII, INCLIVA, Valencia, Spain;* (2) *University of Montpellier, INRA, UMR866, Dynamique Musculaire et Métabolisme, Montpellier, France*)

Background: Reduced NAD⁺ levels in skeletal muscle during aging alter mitochondrial bioenergetics and impair muscle mass, strength, and endurance. This suggests that low NAD⁺ levels in old individuals could directly contribute to sarcopenia and frailty. Dietary administration of NAD⁺ precursors, such as nicotinamide riboside (NR), have emerged as a new therapeutic strategy to restore NAD⁺ levels in muscle and other tissues. **Objectives:** The aim of our study was to evaluate the effects of NR supplementation for twelve weeks on performance, muscle metabolism, and oxidative damage in old C57BL6J mice. We also measured the levels of the pyridine nucleotides: NADP⁺, NADPH, NAD⁺ and NADH in liver and skeletal muscle in the supplemented animals. **Methods:** We divided C57BL6J old male mice (21 months old) in two groups: control (n=11) and supplemented with NR (n=10). The supplemented group received 400mg/kg/day of NR for 12 weeks in the drinking water. Mice were tested for functional and biochemical analyses in muscle and liver samples. **Results:** Our results show that supplemented mice exhibited higher liver levels of NADP⁺, NAD⁺ and NADH when compared with the controls. However, no changes in pyridine nucleotide levels were found in the skeletal muscle after the supplementation. Despite having no effects on the intramuscular pyridine nucleotide levels, NR-treated animals exhibited better motor coordination and endurance capacity than the controls. In vivo metabolism (VO₂, VCO₂ and the Respiratory Exchange Ratio, RER) was not affected after the supplementation. In muscle samples, protein content of PDK4 as well as the phosphorylated form of PDH were reduced in the supplemented mice. This resulted in a higher activation of the PDH complex that regulates pyruvate conversion into acetyl-CoA. Moreover, our results regarding lipid peroxidation (MDA) and protein oxidation (carbonylated proteins) clearly demonstrated that NR supplementation protects against skeletal muscle oxidative damage. **Conclusion:** Oral administration of nicotinamide riboside ameliorates functional deficits in old mice despite having no effect on the intramuscular pyridine nucleotide levels. NR reduces the skeletal muscle oxidative damage and activates the PDH complex. Supplementation with NR may represent a new therapeutic opportunity for an age-associated syndrome such as frailty.

C35- CAN WHEY-PROTEIN PLUS VITAMIN D SUPPLEMENTATION ENHANCE THE EFFECTS OF PROGRESSIVE RESISTANCE TRAINING ON MUSCLE HEALTH, GLYCAEMIC CONTROL, COGNITIVE FUNCTION AND RELATED RISK FACTORS IN OLDER ADULTS WITH TYPE 2 DIABETES? A 6-MONTH RANDOMIZED CONTROLLED TRIAL.

Eliza Miller¹, David W. Dunstan², Deborah A. Kerr³, David Menzies⁴, Caryl A. Nowson¹, Helen Macpherson¹, Robin M. Daly¹ ((1) *Institute for Physical Activity and Nutrition, Deakin University, Melbourne, VIC, Australia* ; (2) *Baker IDI Heart and Diabetes Institute, Melbourne, VIC, Australia*; (3) *School of Public Health, Curtin University, Perth, WA, Australia*; (4) *South Eastern Melbourne PHN, Melbourne, VIC Australia*)

Backgrounds: Type 2 diabetes (T2D), sarcopenia, and cognitive dysfunction are thought to be mutually associated, which is likely due to the presence of related risk factors (obesity, insulin resistance, inflammation, oxidative stress, physical inactivity and poor nutrition). Therefore, identifying interventions that address multiple risk factors are likely to provide the greatest health benefits. Progressive resistance training (PRT) is recommended to optimize glycaemic control, muscle mass/strength and cognition, but the benefits are dependent on adequate nutrition. Whether protein plus vitamin D can provide added benefits to PRT simultaneously on all these outcomes in people with T2D remains unknown. **Objectives:** To investigate whether whey-protein+vitamin D supplementation can enhance the effects of PRT on muscle mass/size, strength, glycaemic control, cognitive function and related risk factors [fat mass (FM), blood pressure (BP), lipids and inflammatory cytokines) in older adults with T2D. **Methods:** This was a 6-month, randomized controlled trial whereby 198 adults (50-75y) with T2D were prescribed PRT (2 d/week) and allocated to receive whey-protein (20g/d plus 20g/d post-exercise) plus vitamin D (2000IU/d) (PRT+ProD, n=98), or PRT without supplementation (PRT, n=100). Outcomes included glycated haemoglobin (HbA1c), DXA appendicular lean mass (ALM), totalbody FM, pQCT thigh muscle CSA, muscle strength, cognitive function (Cogstate battery), BP, lipids and inflammatory markers. **Results:** 168 (85%) participants completed the study. Exercise adherence was 67% in PRT+ProD and 58% in PRT. Whey-protein and vitamin D adherence was 79% and 92%, respectively. Mean basal serum 25(OH)D was 72 nmol/L and dietary protein 1.2g/kg/d. For PRT+ProD versus PRT, there was a trend for greater gains in ALM (mean change 0.34 vs 0.14 kg, P=0.06) and muscle CSA (3.5 vs 1.8%, P=0.09). Both groups experienced similar improvements in muscle strength (15-16%), FM (-0.6-0.9 kg), HbA1c (absolute -0.1-0.2%), global cognitive function (z-score 0.14 SD), working memory/learning (0.22-0.24 SD) and diastolic BP (P<0.05-<0.001). There was no effect of the intervention on blood lipids. Serum IL-10 (anti-inflammatory) and TNF-alpha (pro-inflammatory) increased in PRT+ProD versus PRT (P<0.05-<0.001). **Conclusion:** Daily whey-protein+vitamin D supplementation does not appear to enhance the benefits of resistance training on muscle mass, strength,

glycaemic control, cognitive function or other common risk factors in older people with T2D.

C36- THE EFFECT OF VITAMIN D SUPPLEMENTATION ON LOWER EXTREMITY POWER, STRENGTH AND PHYSICAL PERFORMANCE IN OLDER ADULTS: A RANDOMIZED CONTROLLED TRIA. Denise K. Houston¹, Anthony P. Marsh², Rebecca H. Neiberg¹, Jamehl L. Demons¹, Claudia L. Campos¹, Osvaldo Delbono¹, Stephen B. Kritchevsky¹, Janet A. Toozee¹ ((1) *Wake Forest School of Medicine, Winston Salem, NC, USA*; (2) *Wake Forest University, Winston Salem, NC, USA*)

Backgrounds: Low 25-hydroxyvitamin D (25[OH]D) concentrations (<30 ng/mL [<50 nmol/L]) have been associated with lower extremity muscle weakness and impaired physical performance in observational studies. However, the effect of vitamin D supplementation on changes in muscle strength and physical performance in randomized controlled trials has been mixed. **Objectives:** We conducted a 12-month randomized, placebo-controlled trial to determine the effect of vitamin D supplementation on lower extremity muscle power and strength and physical performance in low functioning older adults with low-normal 25(OH)D concentrations. **Methods:** In this single-center, double-blind randomized controlled trial, 136 adults aged 70 to 89 years with Short Physical Performance Battery (SPPB) scores ≤ 10 and 25(OH)D concentrations of 18 to <30 ng/mL were randomized to 2000 IU/day vitamin D3 or placebo for 12 months. Lower-extremity leg power (adjusted for body mass in kg), leg strength, SPPB, expanded physical performance battery (expPPB), and Timed Up and Go (TUG) were assessed at baseline, 4 and 12 months. A mixed effects model was used to examine change in power, strength and physical performance over time adjusted for age, gender, race, and season; linear contrasts were used to estimate the difference in change between the two groups between baseline and 12 months. **Results:** Participants' mean (SD) age, 25(OH)D concentration, and SPPB score at baseline were 73.4 (6.3) years, 24.5 (3.2) ng/mL, and 7.8 (1.8), respectively; 49.3% were female and 32.4% were African American. Randomization to vitamin D was successful in increasing 25(OH)D concentrations compared to placebo (15.4 vs. 1.1 ng/mL, $p < 0.0001$). However, there were no differences in change in leg power (-0.13 vs. -0.10 watts/kg, $p = 0.63$), leg strength (-8.09 vs. -3.84 Nm, $p = 0.08$), SPPB score (1.64 vs. 1.83, $p = 0.53$), expPPB score (0.19 vs. 0.17, $p = 0.75$), 4-m walk speed (0.07 vs. 0.08 m/sec, $p = 0.83$), or TUG (1.01 vs. 0.98 sec, $p = 0.92$) by intervention group over the 12-month intervention. **Conclusion:** In low functioning older adults with low-normal 25(OH)D concentrations, randomization to 2000 IU/day vitamin D3 supplementation did not result in improvements in lower extremity power, strength, or physical performance. Funded by the National Institutes of Health (R01 AG042411 and P30 AG021332).

C37- EWGSOP1 VERSUS EWGSOP2: WHAT IS THE IMPACT ON PREVALENCE AND HEALTH OUTCOMES? Fanny Petermann-Rocha^{1,2}, Frederick K Ho¹, Stuart R Gray², Jill P Pell¹, Carlos Celis-Morales² ((1) *Institute of Health and Wellbeing, University of Glasgow, Glasgow, UK*; (2) *British Heart Foundation Glasgow Cardiovascular Research Centre, Institute of Cardiovascular and Medical Science, University of Glasgow, Glasgow, UK*)

Background: Different operational definitions have been proposed to define sarcopenia, most based on the combination of three primary physical capability markers: low muscle mass, low muscle strength (grip strength) and slow walking pace (gait speed). In 2019, the European Working Group on Sarcopenia in Older People (EWGSOP) established a new operational definition and cut-off points for sarcopenia. **Objectives:** The aim of this study was, therefore, to compare the prevalence of sarcopenia and its associations with different health outcomes using the old (EWGSOP1) and new (EWGSOP2) definitions of sarcopenia in the UK Biobank cohort. **Methods:** Sarcopenia was defined as low grip strength plus low muscle mass. Using both EWGSOP cut-off points, we created specific sarcopenia variables. Prevalence of sarcopenia derived using both EWGSOP definitions was calculated and compared as well as prospective health outcomes including all-cause mortality as well as incidence and mortality from cardiovascular disease (CVD), respiratory disease, and chronic obstructive pulmonary disease (COPD). Associations between sarcopenia and health outcomes, by EWGSOP1 and EWGSOP2 criteria, were investigated using Cox-proportional hazard models. All analyses were adjusted for confounding factors, including socio-demographic covariates, prevalent diseases and lifestyle factors and were performed using STATA 15 statistical software. **Results:** The prevalence of sarcopenia based on the EWGSOP1 and EWGSOP2 classification was 8.14% and 0.36%, respectively. Sarcopenia defined by EWGSOP1 was associated with a higher risk of respiratory disease and COPD as well as mortality from all-cause, CVD, and respiratory diseases. However, only respiratory incidence remained associated with sarcopenia when EWGSOP2 was used (Hazard Ratio: 1.32 [95% confidence interval: 1.05 to 1.66]). Moreover, although individuals classified as sarcopenic using both classifications had the highest risk of all-cause mortality and respiratory disease, those with sarcopenia based on EWGSOP1 only, experienced a more extensive range of poorer health outcomes. **Conclusion:** Substantial changes in the estimate prevalence and association patterns were found between EWGSOP1 and EWGSOP2 definitions. Using the new operational guideline, the estimate prevalence of sarcopenia decreased considerably. Furthermore, although the new EWGSOP2 showed a higher magnitude of association with the health outcomes, many became not-significant.

C38- MALNUTRITION AS A STRONG PREDICTOR OF THE ONSET OF SARCOPENIA. Charlotte Beaudart¹, Dolores Sanchez-Rodriguez^{1,2}, Médéa Locquet¹, Jean-Yves Reginster^{1,3}, Laetitia Lengel¹, Olivier Bruyère¹ ((1) WHO Collaborating Centre for Public Health Aspects of Musculoskeletal Health and Aging, Division of Public Health, Epidemiology and Health Economics, University of Liège, Liège, Belgium; (2) Geriatrics Department, Parc Salut Mar. Rehabilitation Research Group, Hospital Del Mar Medical Research Institute (IMIM), Barcelona, Spain; (3) Prince Mutaib Chair for Biomarkers of Osteoporosis, Biochemistry Department, College of Science, King Saud University, Riyadh, Kingdom of Saudi Arabia)

Background: Our research group has followed the call to action launched by the Global Leadership Initiative of Malnutrition (GLIM) and the European Society of Clinical Nutrition and Metabolism (ESPEN) in order to shed light on the overlap between malnutrition and nutrition-related diseases such as sarcopenia. **Objectives:** We explored the association between malnutrition according to GLIM and ESPEN criteria and the 4-year onset of sarcopenia/severe sarcopenia. **Methods:** The prospective SarcoPhAge (Sarcopenia and Physical Impairment with advancing Age) cohort, which included 534 community-dwelling ≥ 65 -year-old volunteers followed annually, was used as dataset. Malnutrition was defined at baseline according to GLIM and ESPEN criteria. Outcome measure was the incidence of sarcopenia/severe sarcopenia (EWGSOP2) measured annually during a 4-year follow-up period, i.e. number of new cases each year, which were cumulated. Cox-regressions, giving the hazard ratio (HR) and 95% confidence interval (CI), and Kaplan-Meier curves with log-rank tests were performed. Analyses were adjusted on sex, age, and number of concomitant diseases, number of drugs, cognitive status and level of physical activity. **Results:** From the 534 participants in SarcoPhAge, 510 were free from sarcopenia at baseline, of which 336 had complete data to apply GLIM and ESPEN criteria (mean age 72.5 ± 5.8 years; 55.4% women). A significantly higher risk of developing sarcopenia/severe sarcopenia along the 4-year follow-up in presence of GLIM [sarcopenia: adjusted HR=3.23 (95%CI 1.73-6.05) ; severe sarcopenia: adjusted HR=2.87 (95%CI 1.25-6.56)] and ESPEN [sarcopenia: adjusted HR=4.28 (95%CI 1.86-9.86) ; severe sarcopenia: adjusted HR=3.86 (95%CI 1.29-11.54)] criteria was observed. Kaplan-Meier curves confirmed this significant impact of malnutrition on the onset of sarcopenia, regardless of the definition met (Log-rank $p < 0.001$ for all). **Conclusion:** Baseline malnutrition was associated with an approximately four fold higher risk of developing sarcopenia/severe sarcopenia during a 4-year follow-up.

C39- BIOCHEMICAL AND NEUROIMAGING MARKERS AS PREDICTORS OF INCIDENT FRAILITY IN THE ELDERLY: A SECONDARY ANALYSIS OF THE MAPT STUDY. Wan-Hsuan Lu¹, Philippe de Souto Barreto^{1,2}, Yves Rolland^{1,2}, Kelly Virecoulon Giudici¹, Bruno Vellas^{1,2} and the MAPT/DSA Group ((1) Gerontopole of Toulouse, Institute of Ageing, Toulouse University Hospital (CHU Toulouse), Toulouse, France; (2) UPS/Inserm UMR1027, University of Toulouse III, Toulouse, France)

Backgrounds: A broad range of physical and biochemical factors had shown associations with frailty among community-dwelling elderly. Nevertheless, most of studies were mainly focused on one or few types of risk factors. Furthermore, it is still unclear whether brain structure changes, especially cerebral cortical thickness, associate with frailty. **Objectives:** This study aimed to investigate predictive markers, in both biochemical and neuroimaging fields, for incident frailty among the elderly. We hypothesized that these biomarkers may be present in the frail older adults before the frailty phenotypes appear. **Methods:** This study included 1,394 adults ≥ 70 years who participated in the Multidomain Alzheimer Preventive Trial (MAPT) without frailty at baseline. Subjects were followed for 3 years. Incident frailty was defined according to Fried's criteria. The differences of clinical performance (the Mini Mental State Examination, the Geriatric Depression Scale, the Short Physical Performance Battery, the instrumental activity of daily living), biochemical factors (plasma vitamin D, C-reactive protein, homocysteine, omega-3 index), cognitive-related markers (Apolipoprotein E genotypes, beta-amyloid) and neuroimaging data (total intracranial volume, hippocampal volume, gray matter volume, white matter hyperintensities and cortical thickness) were compared between participants with incident frailty and those remained non-frail during the follow-up. The Cox proportional hazard model was used to evaluate the associations between biomarkers and the risk of frailty after adjusting for age-related confounders. **Results:** A total of 134 participants became frail during the 3-year follow-up (incidence of frailty: 38.5 cases per 1,000 person-years). Compared to people who remained non-frail, those with incident frailty tended to be vitamin D deficient (< 20 ng/mL) at baseline and to present low-grade inflammation (persistent C-reactive protein 3-10 mg/L). Note worthy, frail elderly differed significantly in the baseline hippocampal volume (median [IQR]: 2.59 [2.25-2.89] vs. 2.70 [2.46-2.92] cm³, $p = 0.036$) and the cortical thickness of Alzheimer's disease signature regions (2.79 [2.66-2.93] vs. 2.87 [2.76-2.99] mm, $p = 0.032$) compared to their non-frail counterparts. Associations with biomarkers did not persist after adjusting for confounders. **Conclusion:** Older adults who progressed to frailty presented different baseline biochemical and neuroimaging profiles from stably non-frail elderly. The hippocampal volume and cortical thickness might be potential early predictors for detecting incident frailty.

C40- DETECTING PREFRAILITY: COMPARING SUBJECTIVE FRAILTY ASSESSMENT AND THE PAULSON-LICHTENBERG FRAILTY INDEX. Heather Fritz, Malcolm Cutchin, Yi-Ling Hu (*Institute of Gerontology, Wayne State University, Detroit, MI, USA*)

Background: Validated frailty screening tools are seldom used in everyday practice. Clinicians often rely instead on subjective frailty assessment (SFA) when determining which patients to refer for additional services and supports. Existing studies of SFA do not provide insights into the validity of SFA as a tool to identify individuals at the intermediate, prefrail stage. In addition, those studies do not compare the validity of SFA among clinicians with differing levels of training (e.g., physicians versus nurses). **Objectives:** The goal of the proposed study was to examine the degree of agreement among a validated frailty screening questionnaire, the Paulson-Lichtenberg Frailty Index (PLFI), and geriatrician and geriatric nurse SFA for detecting health, prefrailty, and frailty among older African American patients recruited from a geriatric primary care clinic. **Methods:** PLFI derived frailty classifications were obtained for 202 older African American clinic patients. Next, and within 3 months of the patient's visit to the clinic, two geriatricians and two geriatric nurses were asked to classify participants into one of the same categories (healthy, prefrail or frail) based on SFA. Clinicians were only asked to classify patients in the dataset for whom they were listed as the attending physician or the nurse assigned to the patients care. The two geriatricians classified 58 and 65 patients respectively, and each of the geriatric nurses classified 58 and 69 patients respectively. Clinicians were blinded to the PLFI classifications. Clinicians could, however, use the patient's medical record to assist in their SFA. **Results:** Of the 202 participants (mean age: 76.7 +/- 8.6), 52 (26%) were prefrail and 57 (28%) were frail based on the PLFI. Geriatrician SFA aligned with the PLFI in 43.0% of prefrail and 65.7% of frail cases. Nurse SFA aligned with the PLFI in 43.9% of prefrail and 17.0% of frail cases. There was slight to fair agreement between SFA and PLFI (geriatrician Cohen's $k = .23$ [95% CI, -.40 to .52], $p < .001$; nurse Cohen's $k = .59$ [95% CI, -.33 to .46], $p = .001$). **Conclusion:** Clinician SFA did not align well with PLFI classifications. There was a significance difference on the deviation of SFA from PLFI between physicians and nurses.

C41- IMPACT OF PROTEIN INTAKE AND HIGH-FAT DIET ON BODY COMPOSITION AND MUSCLE LIPID INFILTRATION IN RELATION TO AGING IN RATS: INSIGHTS INTO SARCOPENIC OBESITY. Eleonora Poggiogalle, Aude Carayon, Jérôme Salles, Christophe Giraudet, Jean-Paul Rigaudière, Sarah de Saint-Vincent, Phelipe Sanchez, Olivier LeBacquer, Frédéric Capel, Stéphane Walrand, Yves Boirie, Christelle Guillet (*Italy, France*)

Background: Trajectories of body composition changes during the aging process are characterized by ectopic lipid infiltration and impaired muscle anabolic response. To which

extent protein intake can modulate protein anabolism in the presence of excess energy and high-fat feeding, and the interference of aging, has not been thoroughly understood. We hypothesized that the anabolic efficiency of dietary protein in skeletal muscle may affect age-related alterations in body compartments within the context of high-fat diet.

Objectives: The aim of the study was to investigate changes in body composition, with emphasis on sarcopenia and excess fat, and intramuscular lipid infiltration in response to two levels of protein intake combined to two levels of fat intake. **Methods:** Two groups of sixty adult and forty-nine old male Wistar rats were randomly divided into four groups: isocaloric standard diet (12% protein, 14% lipid, as STD12); isocaloric standard (high-protein) diet (25% protein, 14% lipid, STD25); hypercaloric high-fat (normal-protein) diet (12% protein, 45% lipid, HFD12); and hypercaloric high-fat (high-protein) diet (25% protein, 45% lipid, HFD25). The nutritional intervention lasted 10 weeks. Body weight was measured on a weekly basis, and body composition was assessed by magnetic resonance (Echo-MRI) at baseline (T0), week 5 (T1), and week 10 (T2). Lipid content in tibialis anterior (TA) muscle was assessed by chromatography. **Results:** Rats in the high-fat diet groups self-limited their food intake, so that energy intake was not different among the groups. Regarding changes in body compartments, a time effect ($p < 0.05$) for the increase in body fat was reported in all diet groups at all time-points regardless of age group. In adult rats and old rats body fat was increased at T1 and T2 in the HFD12 group compared to the STD12 and STD25 group (diet effect, $p < 0.05$), but not in the HFD25 group. Fat-free mass in the old HFD25 group was lower than STD25 group (diet effect, $p < 0.05$). Regardless of dietary interventions, TA muscle weight was lower in old groups compared to adult groups (all p values < 0.01). An age effect was detected in all groups when total hindlimb muscle weight was considered (all $p < 0.05$); a diet effect was observed in adult HFD12 (18.96 ± 2.06 g) and HFD25 (19.12 ± 2.0 g) groups compared to the adult STD25 group (15.52 ± 2.02 g), $p < 0.05$. Only old rats in the HFD12 group exhibited increased intramuscular triacylglycerols in TA (age effect: $p = 0.02$; diet effect: HFD12 vs. STD12: 2.04 ± 1.74 vs. 0.83 ± 0.49 ug/g, $p = 0.02$). **Conclusion:** In isocaloric conditions, high-protein intake combined with high-fat diet limited lipid infiltration in the skeletal muscle, but did not ameliorate age-related anabolic resistance and sarcopenia in old rats fed a high-fat diet.

C42- TRIMETAZIDINE ATTENUATES DEXAMETHASONE-INDUCED MUSCLE ATROPHY AND PYROPTOSIS VIA TARGETING SIRT3/FOXO3A PATHWAY. Li Wang^{1,2}, Yue Wang^{1,2}, Xi-Yu Shen^{1,2}, Kang-Zhen Zhang^{1,2}, Xiang Lu^{1,2}, Wei Gao^{1,2} ((1) *Department of Geriatrics, Sir Run Run Hospital, Nanjing Medical University, China*; (2) *Key Laboratory for Aging & Disease, Nanjing Medical University, Nanjing, China*)

Background: Skeletal muscle atrophy is one of the major side adverse effects of high dose or the sustained usage of glucocorticoids. Pyroptosis is a novel pro-inflammatory form of

pro-inflammatory programmed cell death that may contribute skeletal muscle atrophy. Recent evidence suggests that trimetazidine can also improve skeletal muscle performance both in human and mice. **Objectives:** We sought to explore the role and underlying mechanisms of trimetazidine in the regulation of pyroptosis in dexamethasone-induced muscle atrophy model. **Methods:** Eight-week-old mice were randomly administered saline, dexamethasone, trimetazidine, or dexamethasone plus trimetazidine by intraperitoneal injection for 10 days. Running tolerance test was evaluated at the end of the treatment and muscles of hind legs were excised for analyses after sacrifice. The C2C12 mouse myoblast cells were differentiated and treated with dexamethasone for 24h, and then co-cultured with trimetazidine or vehicle for 6h. Small interfering RNA (siRNA) targeting FoxO3a and Sirt3 inhibitor 3-TYP were applied to identify whether the effects of trimetazidine on dexamethasone-induced muscle atrophy was mediated by Sirt3/FoxO3a pathway. Markers of muscle atrophy and pyroptosis were assessed by Western Blot and Real-time quantitative PCR. Diameter of myotubes was analyzed by immunofluorescence. **Results:** Dexamethasone-induced muscle atrophy was attenuated by trimetazidine treatment in mice, indicated by improved exercise tolerance, and increased skeletal muscle mass. The expression of muscle atrophy markers Atrogin-1 and MuRF1 were increased and pyroptosis was induced by dexamethasone treatment, but were mitigated by with trimetazidine treatment both in vivo and in vitro. Dexamethasone-induced reduction of myotubes diameter was also ameliorated by trimetazidine. Mechanically, trimetazidine could reverse dexamethasone-induced activation of FoxO3a phosphorylation and inhibition of Sirt3-mediated FoxO3a deacetylation. In contrast, knockdown of FoxO3a or inhibition of Sirt3 abolished the protective effects of trimetazidine on dexamethasone-induced muscle atrophy and pyroptosis. **Conclusion:** Our present study demonstrated that trimetazidine could attenuate dexamethasone-induced skeletal muscle atrophy and pyroptosis via targeting Sirt3/FoxO3a pathway.

ORAL COMMUNICATIONS

OC1- SARA PROGRAM: PRELIMINARY FINDINGS & IMPLICATIONS FROM SARA-OBS STUDY AND ITS IMPACT ON SARA-INT STUDY. Waly Diah¹, Cendrine Tourette¹, Carole Margalef¹, Amy Chen², René Lafont^{1,3}, Pierre Dilda¹, Stanislas Veillet¹, Samuel Agus² ((1) *Biophytis, Sorbonne Université – BC9, Paris, France*; (2) *Biophytis, Inc., Cambridge, MA, USA*; (3) *Sorbonne Université, CNRS - Institute de Biologie Paris Seine (BIOSIPE), Paris, France*)

Backgrounds: Sarcopenia is a prevalent, progressive muscle disorder in which the onset increases with age and may lead to mobility disability. SARA-OBS, an observational trial, and SARA-INT, an ongoing phase II interventional trial, are part of a clinical program that strives to provide better understanding of the sarcopenia population and to develop a viable treatment option. SARA-OBS included community

dwelling sarcopenic adults similar to the target population in SARA-INT which is testing the safety and efficacy of an investigational drug, BIO101. Findings from SARA-OBS have provided insight on the natural decline in physical functions of the target population and suggest modifications necessary to the current SARA-INT study design. **Objectives:** The objective is to better understand the physical performance and the body composition changes in this population within 6 months and use this knowledge to improve the design for the SARA-INT study. **Methods:** Older adults ≥ 65 years with a SPPB ≤ 8 and lean body mass based on the FNIIH criteria (ALM/BMI < 0.789 in men and 0.512 in women, or ALM < 19.75 kg in men and < 15.02 kg in women) were recruited. Evaluation of the changes in physical performance and body composition from baseline were based on 400m walk test, 6-minute walk test, SPPB, handgrip strength test, stair climb power test and DXA scans. **Results:** Preliminary analysis shows a decrease in the gait speed (0.9 vs 0.84 ; $p < 0.0036$), decrease in distance walked (298.84 m vs 279.56 m; $p < 0.0012$) but no change in the SPPB total score (6.67 vs 6.99 ; $p < 0.0915$). A non-significant trend for decreased strength is also detected for the handgrip and the stair climb tests. These findings led to an amendment in the study design for SARA-INT as follows: 1) increase in the value set for the expected difference between treatment groups, 2) subsequent change in sample size, 3) change of a key secondary endpoint and 4) introduction of a 'promising zone' interim analysis. **Conclusion:** SARA-OBS study contributes to better understanding of the at-risk sarcopenic individuals. This knowledge led to improving the design of a comparative clinical trial that will hopefully accelerate the development of BIO101, a medical treatment for age-related sarcopenia.

OC2- ACCELEROMETER-DETERMINED PHYSICAL ACTIVITY AND SEDENTARY BEHAVIOUR ARE ASSOCIATED WITH SARCOPENIA BUT NOT 12-MONTH INCIDENT FALLS IN COMMUNITY-DWELLING SWEDISH OLDER ADULTS. David Scott¹, Jonas Johansson², Anoohya Gandham¹, Peter Ebeling¹, Peter Nordstrom², Anna Nordstrom² ((1) *Monash University, Clayton, VICTORIA, Australia*; (2) *Umeå University, Umeå, Sweden*)

Background: It is unclear how the total time and number of bouts performing physical activity (PA) at different intensities relates to likelihood of sarcopenia and falls in older adults. Determining whether threshold effects exist in the relationships between PA, sarcopenia and falls may be important for public health messaging. **Objectives:** We aimed to determine associations of accelerometer-determined total time and number of bouts of sedentary behaviour, light-intensity PA and moderate to vigorous intensity PA (MVPA) with sarcopenia and its components (according to the revised European Working Group on Sarcopenia in Older People definition; EWGSOP2), and incidence of 12-month falls. **Methods:** 3,334 Swedish 70-year-olds had appendicular lean mass (ALM; kg) estimated by dual-energy X-ray absorptiometry. Handgrip strength (HGS) and timed up-and-go (TUG) were assessed, and sarcopenia was defined according to EWGSOP2

criteria (probable or confirmed sarcopenia). Accelerometers estimated total time in sedentary behaviour, light-intensity PA and MVPA, and also the total number of bouts of increasing duration, over seven days. Incident falls were self-reported 6 and 12 months later. **Results:** Only 61 (1.8%) participants had probable or confirmed sarcopenia and 14% of participants with complete 12-month follow-up at a reported a fall. After multivariable adjustment, including for other levels of activity, greater MVPA was associated with reduced likelihood of having low HGS, and greater light-intensity PA and MVPA were both associated with lower likelihood of having low ALM and slow TUG time (all $P < 0.05$). Greater sedentary behaviour was associated with higher likelihood of having slow TUG time (odds ratio: 1.04; 95% CI 1.01-1.08 per additional hour). Only greater MVPA was associated with lower likelihood of probable or confirmed sarcopenia (0.80; 0.71-0.91 per additional hour). Similar associations were observed for the number of bouts of activity, and there was no evidence of a threshold for effects of higher duration bouts. There were no associations between total time or bouts of activity and incident falls (all $P > 0.05$). **Conclusion:** Higher total amounts of accelerometer-determined MVPA are consistently associated with reduced likelihood of sarcopenia and its components, but not incident falls, regardless of the length of activity bouts or total amounts of sedentary behaviour.

OC3- ACTIVITY PATTERN VARIANCE: STATISTICAL NOISE OR INSIGHT INTO FRAILTY? Megan Huisingscheetz¹, Kristen Wroblewski², Linda Waite³, Elbert Huang⁴, Donald Hedeker⁵, L. Philip Schumm⁶ ((1) *University of Chicago, Department of Medicine, Section of Geriatrics and Palliative Medicine, Chicago, IL, USA*; (2) *University of Chicago, Department of Public Health Sciences, Chicago, IL, USA*; (3) *University of Chicago, Department of Sociology and NORC, Chicago, IL, USA*; (4) *University of Chicago, Department of Medicine, Section of General Medicine, Chicago, IL, USA*; (5) *University of Chicago, Department of Public Health Sciences, Chicago, IL, USA*; (6) *University of Chicago, Department of Public Health Sciences, Chicago, IL, USA*)

Background: Prior work has shown activity patterns across the day vary by frailty status. Morning rather than afternoon or evening hourly activity best differentiates frail, pre-frail, and robust adults using free-living accelerometry data. However, there is great variability in hourly activity patterns among older adults not otherwise explained by frailty status, demographics or comorbidities. Residual variance can be estimated as an indicator of model robustness but is rarely the main objective of analyses. Yet, residual activity variance also reflects the consistency of activity patterns between and within subjects, and we hypothesized that frail older adults would demonstrate more inconsistent hourly activity patterns across the day compared to robust adults. **Objectives:** The objective of this study was to determine whether frailty status is associated with hourly activity variance across the day. **Methods:** Using wrist accelerometry data collected from the National Social Life,

Health and Aging Project (n=651), we employed a mixed effect location scale model to simultaneously determine whether an adapted phenotypic frailty scale was significantly associated with the logarithm of mean hourly counts per minute (CPM) as well as between and within subject activity variance, adjusting for demographic and health characteristics, season, day of week, and time of day. **Results:** We demonstrated that higher frailty scores were associated with modestly lower mean hourly activity; each frailty point (0–4) corresponded to a ~7% lower mean hourly CPM ($\beta = -0.03$, $p < 0.001$), and the effect of frailty on activity was greatest in the morning. Increasing frailty was also significantly associated with increasing between ($\beta = 0.22$, $p < 0.001$) and within subject ($\beta = 0.02$, $p = 0.03$) hourly activity variance. The frailty effect on within subject activity variance was strongest in the morning. **Conclusion:** These findings indicate that frail adults have more inconsistent accelerometry-measured activity behavior across the day compared to robust adults. Activity consistency may be a novel marker of older adult health. Future research exploring factors explaining activity variability including sleep and napping patterns are warranted.

OC4- ASSESSING HEART RATE DYNAMICS DURING PHYSICAL ACTIVITY: A NEW MARKER OF FRAILTY AMONG OLDER ADULTS. Authors: Kayleigh Ruberto¹, Ben Carpenter¹, Hossein Ehsani¹, Saman Parvaneh², Jane Mohler^{1,3}, Nima Toosizadeh^{1,3,4} ((1) *Department of Biomedical Engineering, College of Engineering, University of Arizona, USA*; (2) *Philips Research North America, Cambridge, USA*; (3) *Arizona Center of Aging, University of Arizona, USA*; (4) *Division of Geriatrics, General Internal Medicine and Palliative Medicine, Department of Medicine, University of Arizona, USA*)

Background: In addition to physical function decline, alterations in heart rate dynamics with aging and frailty has been previously demonstrated. However, it is not clear how frailty can influence heart response to demanding physical activities such as walking-based frailty assessment methods among elders. **Objectives:** Determine the association between heart rate dynamics and frailty in response to physical activity. **Methods:** Older adults, aged 65 and above, were recruited and categorized into frailty groups based on the Fried phenotype. The influence of physical activity on heart rate was assessed during normal and rapid speed walking over a distance of ~10m, using wearable ECG/accelerometer sensor (360° eMotion Faros). Using the accelerometer data, the time periods of walking tasks were identified, and the time to peak heart rate and the percentage change in heart rate due to activity initiation were calculated as outcomes. Differences between outcomes among frailty groups were tested using ANOVA model, adjusted with age, BMI, and sex. **Results:** Ninety-four participants were recruited, including 30 non-frail (age=78±7.11) and 64 pre-frail/frail (age=81±8.02). The percent change in heart rate in response to normal speed walking were significantly different between groups (12.60±9.74% for pre-frail/frail and 19.79±15.94% for non-frail; $p = 0.02$).

Similarly, the percent heart rate change for rapid walking was significantly different between groups ($15.01 \pm 11.32\%$ for pre-frail/frail and $26.14 \pm 22.23\%$ for non-frail; $p < 0.01$). The time to peak heart rate in response to normal walking was significantly different between groups (8.785 ± 3.546 and 6.124 ± 2.33 seconds for pre-frail/frail and non-frail; $p < 0.01$); however, this outcome was not significantly different within the rapid walking condition ($p = 0.08$). **Conclusion:** This study showed that heart response to physical activity was weaker and slower among pre-frail/frail individuals, which may happen due to the lack of cardiovascular strength and overall physiological reserve. Accordingly, measures of heart rate dynamics may provide meaningful markers for improving frailty screening. These findings also suggest that lack of quick heart response to walking initiation among frail elderly may in turn expose them to a higher risk of falling. These hypotheses need to be investigated in future studies to provide a potentially robust tool for screening frailty, considering multi-dimensional aspects of functional decline.

OC5- INCIDENT COGNITIVE DECLINE IN SARCOPENIC OBESITY: DATA FROM THE NATIONAL HEALTH AND AGING TRENDS SURVEY.

John A. Batsis^{1,2,3}, Christian Haudenschild^{1,3}, Robert M. Roth¹, Meredith Roderka², Travis Masterson¹, John Brand¹, Tyler Gooding², Matthew C. Lohman⁵, Todd A. Mackenzie^{1,2,3} ((1) Geisel School of Medicine at Dartmouth, Hanover, New Hampshire, USA; (2) Department of Medicine, Dartmouth Hitchcock Medical Center, Lebanon, New Hampshire, USA; (3) The Dartmouth Institute for Health Policy, Lebanon, New Hampshire, USA; (4) Neuropsychology Program, Department of Psychiatry, Dartmouth-Hitchcock, USA; (5) University of South Carolina, Department of Epidemiology and Biostatistics, Columbia, SC, USA)

Backgrounds: The prevalence of obesity in combination with sarcopenia (the age-related loss of muscle mass, strength or physical function) is increasing in adults aged ≥ 65 years. This geriatric syndrome places individuals at risk for synergistic complications from both sarcopenia and obesity that leads to long-term functional decline. **Objectives:** As certain the relationship between sarcopenic obesity and incident long-term cognitive function in a representative population in the United States. **Methods:** We identified 5,822 participants ≥ 65 years with grip strength and body mass index measures without baseline cognitive impairment from the longitudinal National Health and Aging Trends Survey in the United States. Sarcopenia was defined using the Foundation for the NIH Sarcopenia Project grip strength cut points (males < 26 kg; females < 16 kg), and obesity was defined using standard body mass index (BMI) categories. Impaired global cognition was defined as NHATS-defined impairment in the Alzheimer's Disease-8 score or immediate/delayed recall, orientation, clock-draw test, date/person recall. Cox-proportional hazard models and linear mixed-effects modeling ascertained the risk of cognitive impairment over 8-years, adjusting for age, sex, smoking status, education, co-morbidities, and an ability to walk. Our referent variable was non-obese, non-sarcopenia. A

sensitivity analysis was re-run using waist circumference as an obesity variable, and using grip strength normalized for BMI. **Results:** Of the 5,822 participants (55.7% female), median age category was 75-80, and mean grip strength and BMI were 26.4kg and 27.5kg/m², respectively. Prevalence of sarcopenic obesity was 12.9%. We observed 45.7% of participants with impaired cognition at follow-up. Compared to those without sarcopenia or obesity, the risk of impaired cognition was no different in obesity alone (HR 0.89 [95%CI:0.73,1.08]), but was significantly higher in sarcopenia (HR 1.65 [1.45,1.89]) and sarcopenic obesity (HR 1.33 [1.12,1.58]). Using waist circumference as a measure for obesity, we found significant risk of developing cognitive impairment for both sarcopenia (HR 1.68 [1.39-2.03]) and sarcopenic obesity (HR 1.61 [1.35-1.92]). Grip strength normalized for BMI demonstrated a higher risk of impaired cognition (HR 1.37 [1.22-1.53]). Using linear mixed-effects modeling, similar results were observed. There was no observed interaction between sarcopenia and obesity. **Conclusion:** Both sarcopenia and sarcopenic obesity are associated with an increased long-term risk of cognitive impairment.

OC6- RELATIONSHIP OF INTRACELLULAR WATER WITH MUSCLE STRENGTH, FUNCTIONAL PERFORMANCE AND FRAILTY IN AGED POPULATION. ANALYSES IN TWO INDEPENDENT POPULATION-BASED SAMPLES.

Mateu Serra-Prat¹, Isabel Lorenzo¹, Mateu Cabré², Emili Burdoy³, Maria Bartolomé³, Mònica Papiol³ ((1) Research Unit. Consorci Sanitari del Maresme, Spain; (2) Internal Medicine Department. Hospital of Mataró. Consorci Sanitari del Maresme, Spain; (3) Primary Care Department. Consorci Sanitari del Maresme, Spain)

Background: Age-related loss of muscle mass only partially explains age-related loss of muscle strength. In aged population, strength depends more on muscle quality than on muscle quantity. Intracellular water (ICW) decreases with age and has been suggested as possible indicator of muscle quality. **Objectives:** To assess the relationship of ICW content in lean mass (ICW/LM ratio) with muscle strength, functional capacity and frailty in aged population. **Methods:** Body composition (bioelectrical impedance analysis), hand grip strength (dynamometer), functional capacity (Barthel score, gait speed, timed up and go test -TUG- and unipodal station test), frailty (Fried criteria) and other socio-demographic characteristics and co-morbidities were assessed in two independent population-based samples without severe or terminal diseases: A) people over 75 years old, and B) people 65-75 years with a BMI between 30 and 40. A cross-sectional analysis was performed. **Results:** In sample A (n=324, mean age 80y): The ICW/LM ratio was correlated with age ($r_s = -0.249$), hand grip ($r_s = 0.397$), Barthel score ($r_s = 0.317$), gait speed ($r_s = 0.311$), and TUG ($r_s = -0.326$). The ICW/LM ratio was associated with sex (417 in men vs 398 in women), the unipodal station test (411 able vs 399 not able) and the frailty state (411 in non frail vs 391 in frail). A higher ICW/LM ratio was associated with greater muscle

strength, better functional capacity, and a lower frailty risk, even when adjusted by age, sex, n° of co-morbidities, and LM. In sample B (n=305, mean age 70y): The ICW/LM ratio was correlated with TUG (rs=-0.45), gait speed (rs=0.35) and the hand grip (rs=0.13), but not with the Barthel score or with age. The ICW/LM ratio was associated with sex (435 in men vs 421 in women), the unipodal station test (429 able vs 406 not able) and the frailty state (433 in robust, 422 in pre-frail and 386 in frail). The multivariate analyses showed an effect of the ICW/LM ratio (independent of age, sex and muscle mass) on gait speed and unipodal station capacity. **Conclusion:** ICW content in LM may influence muscle strength, functional capacity and frailty in the elderly. However, further studies are needed to confirm this hypothesis.

OC7- ASSOCIATION OF MUSCLE AND METABOLIC BIOMARKERS WITH TRANSITIONS IN GAIT SPEED AND COGNITIVE STATUS IN OLDER ADULTS.

Debra L. Waters^{1,2}, Lara Vlietstra¹, Clifford Qualls², John E. Morley³, Bruno Vellas⁴ ((1) University of Otago, Dunedin, New Zealand; (2) University of New Mexico School of Medicine, Albuquerque, USA; (3) Saint Louis University, St. Louis, USA; (4) Gerontopole, CHU de Toulouse, UMR 1027 INSERM, University Toulouse III, Toulouse, France)

Background: Age-related gait speed and cognition changes are consistently reported as a progressive decline. However, transitory states reveal complex trajectory of decline with implications for timely interventions. **Objectives:** Determine relationships between biomarkers and gait speed and cognition transitions over a 9 year follow up. **Methods:** 216 males (72.7 + 8.07 years) and 384 females (71.1+ 8.44 years) from New Mexico Aging Process Study with annual gait speed, cognition (3MSE), body composition (DXA) and numerous serological biomarkers. Poisson regression assessed individual transitions with total transition count for all categories. Transition categories were “stable” (normal to normal, 0-0), “protective” (abnormal to normal, 1-0), or “harmful” (normal to abnormal, 0-1). Analyses stratified by sex and adjusted for age and APOE4 (plus education for cognition). **Results:** Stable gait speed (0-0) in females was associated with lower percent body fat (IRR 0.793, p=0.001, 95%CI 0.691-0.910) and lower lactate dehydrogenase (LDH) (IRR 0.623, p=0.00, 95%CI 0.514-0.752). In males it was associated with higher cholesterol (IRR 1.394, p=0.001, 95%CI 1.154-1.684). Gait speed transitions (low to normal, 1-0) associated with higher insulin in females (IRR 1.325, p=0.022, 95%CI 1.041-1.685) and lower creatinine in males (IRR 0.520, p=0.01, 95%CI 0.310-0.870). Stable cognitive function (0-0) associated with lower LDH in females (IRR 0.276, p=0.013, 95%CI 0.099-0.765) and higher appendicular skeletal muscle mass (APSM) in males (IRR 1.52, p=0.02, 95%CI 1.076-2.135). Improving cognitive (1-0) associated with higher leptin (IRR 7.5, p=0.03, 95%CI 1.282-44.34) and lower triglyceride (IRR 0.299, p=0.017, 95%CI 0.110-0.809) in males only. Harmful gait speed transitions (0-1) in males associated with IGF-1 (IRR 1.74, p=0.022, 95%CI 1.08-2.79) and leptin in females (IRR

1.39, p=0.043, 95%CI 1.01-1.91). No biomarkers considered were associated with harmful cognitive transitions (0-1). **Conclusion:** Of all biomarkers investigated, biomarkers of muscle (LDH, Creatinine) and metabolism (% fat, insulin and cholesterol) were associated with “protective” or “stable” gait speed changes. “Harmful” gait transition had fewer metabolic and muscle markers (leptin in females and IGF1 in males). Muscle and metabolic biomarkers were also associated with positive or stable cognition (APSM, leptin and triglycerides) in males only. This suggests there are sex-specific, modifiable biomarkers that could be targeted for interventions

OC8- THE APPLICATION OF DIFFERENT SARCOPENIA CUTOFF POINTS IN CHINESE OLDER PEOPLE: A CROSS-SECTIONAL OBSERVATIONAL STUDY.

Qin Du¹, Wei Chen², Sheng Ge³, Xianfeng Zhao¹ ((1) Abbott Nutrition Research and Development, Shanghai, China; (2) Peking Union Medical College Hospital, Beijing, China; (3) The Sixth People's Hospital Affiliated Shanghai Jiaotong University, Shanghai, China)

Objectives: The cut-off points of sarcopenia have been established worldwide. The optimal criteria applied to older Chinese people have not been defined. **Objectives:** We aimed to evaluate how existed different definitions of sarcopenia impact the prevalence of sarcopenia and set up Chinese people based sarcopenia definition. **Methods:** A total of 2821 older people (men 1398, women 1423) aged ≥ 60 years were recruited from Beijing and Shanghai, and their anthropometrics, body compositions, hand grip strength, and gait speed were assessed. **Results:** Prevalence of sarcopenia were 5.01% and 7.38% in males and females using AWGS (Asia Working Group for Sarcopenia) cut-off values, and were 6.65% and 7.17% in males and females using IWGS (International Working Group on Sarcopenia) cut-off values, and were 2.43% and 2.88% in males and females using EWGSOP (European Working Group on Sarcopenia in Older People) cut-off values, and were 0.64% and 0.63% in males and females using FNIH (Foundation for the National Institutes of Health, US) cut-off values. **Conclusion:** Our findings firstly demonstrated the existed sarcopenia definition resulted in low prevalences in Chinese older people. Hence, we suggest that the cut-off points of sarcopenia should be established based on specific diagnosis criteria data in Chinese population.

OC9- PARKIN, A NEW THERAPEUTIC TARGET TO COUNTER SARCOPENIA AND SEPSIS-INDUCED MUSCLE WASTING. Jean-Philippe Leduc-Gaudet^{1,2,3}, Olivier Reynaud^{1,2}, Felipe Eduardo Broering³, Dominique Mayaki³, Sabah NA Hussain^{3,4}, Gilles Gouspillou^{1,2,3,5} ((1) *Département de Sciences de l'activité physique, Faculté des Sciences, UQAM, Québec, Canada*; (2) *Groupe de recherche en Activité Physique Adaptée, Québec, Canada*; (3) *Department of Medicine and Division of Experimental Medicine, McGill University, Québec, Canada*; (4) *Research Institute of the McGill University Health Centre, Québec, Canada*; (5) *Centre de Recherche de l'Institut Universitaire de Gériatrie de Montréal, Québec, Canada*)

Backgrounds: Skeletal muscle aging is characterized by a progressive loss of muscle mass and strength, a process termed sarcopenia. It is now widely recognized that sarcopenia involves an accumulation of mitochondrial dysfunction. Recent data suggest that mitophagy, the process removing dysfunctional mitochondria, is impaired in aged skeletal muscles. However, whether stimulating mitophagy can attenuate sarcopenia remains unknown. **Objectives:** To test whether stimulating mitophagy can attenuate sarcopenia, we investigated the impact of Parkin over expression, Parkin being a key regulator of mitophagy, in skeletal muscles of young and old mice. We also investigated whether Parkin overexpression could attenuate sepsis-induced muscle atrophy, a devastating condition often encountered in the elderly. **Methods:** Parkin overexpression was achieved using intramuscular injection of Adeno-Associated Viruses (AAV) in skeletal muscles of young and late middle-aged mice. In our AAV construction, the expression of Parkin was driven by the muscle specific promoter MCK (Muscle Creatine Kinase). A control AAV, containing a sequence coding for the green fluorescent protein, was injected in the contralateral leg. Sepsis was induced by cecal ligation and perforation (CLP). SHAM operated animals were used as controls. **Results:** Overexpressing Parkin for 4 months in skeletal muscle of young and old mice resulted in higher muscle mass, fiber cross-sectional area and complex II activity. In old animals, Parkin overexpression lead to an upregulation of PGC-1alpha expression and a higher mitochondrial content. Parkin overexpression also attenuated aging-related increases in makers of oxidative stress, apoptosis and fibrosis. Lastly, parkin overexpression also attenuated muscle wasting in septic animals. **Conclusion:** Our findings indicate that Parkin could represent an effective therapeutic target to counteract sarcopenia and to positively impact muscle mass and function in young adults. Our findings also place Parkin as a potential therapeutic target to attenuate sepsis-induced muscle wasting.

OC10- SARCOPENIA PREVENTION BY CALORIC RESTRICTION IN RHESUS MONKEYS: MOLECULAR AND FUNCTIONAL NETWORKS. Timothy W. Rhoads, Josef P. Clark, Ricki J. Colman, Rozalyn M. Anderson (*GRECC D5214 William S Middleton Memorial Veterans Hospital, Madison, USA*)

Background: Caloric restriction (CR) improves survival in nonhuman primates and delays the onset of age-related morbidities including sarcopenia, the age-related loss of muscle mass and function. The mechanisms behind the protective effect of CR are currently unknown; however, a shift in metabolism occurs in advance of the onset of muscle mass loss in nonhuman primates, pointing to a potential role for energetic pathways in precipitating the phenotypes of age and in their prevention through CR. **Objectives:** Here we investigate the impact of CR on aging outcomes at biometric, systemic, and tissue levels, including muscle composition, the cellular metabolic environment, and gene expression, to determine the role each plays in delayed skeletal muscle aging. **Methods:** This study involved monkeys from the longitudinal Aging and Caloric Restriction study. Measures of body composition, physical activity, glucoregulatory function, were captured through 30 years of study. Vastus lateralis biopsies from aged control and CRmonkeys (~28years of age) were used to establish the impact of CR phenotypes of cellular aging, including energy profiles and gene expression profiling. **Results:** Bioinformatic analysis linked delayed aging by caloric restriction to proteostasis, RNA processing, and lipid synthetic pathways. At the tissue level, CR maintained contractile content and attenuated age-related metabolic shifts among individual fiber types. CR was associated with higher mitochondrial activity, altered redox metabolism, and smaller intracellular lipid droplet size. Biometric and metabolic rate data confirm preserved metabolic efficiency in CR animals that correlated with attenuation of age-related muscle mass and physical activity. **Conclusion:** These data are consistent with a role for energy metabolism in the biology of skeletal muscle aging in rhesus monkeys and suggest that CR-induced reprogramming of metabolism plays a role in delaying sarcopenia onset and progression.

OC11- FIBER TYPE 2 ATROPHY IS ASSOCIATED WITH SARCOPENIA IN HIP FRACTURE PATIENTS. Fabiana Tanganelli¹, Lisa Baber¹, Stefanie Jarmusch¹, Fabian Hofmeister¹, Carl Neuerburg³, Stefan Mehaffey³, Stefan Hintze², Peter Meinke², Uta Ferrari¹, Benedikt Schoser², Michael Drey¹ ((1) *Geriatrics, Department of Medicine IV, University Hospital, LMU Munich, Germany*; (2) *Friedrich Baur Institute at the Department of Neurology, University Hospital, LMU Munich, Germany*; (3) *Department of General, Trauma and Reconstructive Surgery, University Hospital, LMU Munich, Germany*)

Background: In the past a lot of effort was put in the definition of sarcopenia. Very little is known about histological

changes in sarcopenic patients. **Objectives:** The aim of the study was to find out correlations between histomorphometric findings and sarcopenia in hip fracture patients. **Methods:** Muscle biopsies of the vastus lateralis muscle were taken from 41 patients (age: 81.1 ± 7 years, 26 women) who underwent operative treatment by osteosynthesis or endoprosthesis implantation, due to a proximal femur fracture. Serial cross sections of skeletal muscle were labeled with Myosin Heavy Chain slow (fiber type 1) and fast (fiber type 2) antibodies. The presence of sarcopenia was defined according to the EWGSOP2 criteria by using bioelectrical impedance analysis and handgrip strength measurement. In addition, a Z-score was calculated as a measure of the degree of sarcopenia. Multiple linear regression analysis was used to identify associations between histomorphometrical findings and the degree of sarcopenia. For all tests, the statistical significance was set at $p < 0.05$. **Results:** There was a significant association between the degree of sarcopenia and the fiber type 2 diameter ($\beta = -0.756$ $p = 0.002$), and between the degree of sarcopenia and the atrophy factor for fiber type 2 ($\beta = 0.744$ $p = 0.002$) in men. **Conclusion:** Type 2 muscle fiber atrophy might be a histological marker for sarcopenia in men. Further histological and biochemical investigations are necessary to gain more insight in the genesis of muscle loss.

OC12- PRECLINICAL EVALUATION OF AN ARTIFICIAL INTELLIGENCE DISCOVERED PEPTIDE NETWORK FOR MUSCLE HEALTH. Roi Cal, Heidi Davis, Alish Kerr, Ian Holyer and Nora Khalidi (*Nuritas, Joshua Dawson House, Dublin, Ireland*)

Backgrounds: Skeletal muscle accounts for approximately 40% of total human body weight and for 30–50% of whole-body protein turnover. Skeletal muscle health is a complex multifactorial process aimed at maintaining the balance between muscle protein synthesis and degradation. Dysregulation of this process can have devastating effects such as muscle atrophy, commonly associated with immobilisation, sarcopenia, cachexia and other wasting disorders. The ability to modulate muscle metabolism not only addresses atrophy associated with such muscle disorders but also presents an opportunity for building muscle mass in the general population. **Objectives:** Using an integrative AI approach, we identified a natural peptide network, NPN_1, and determined in vitro and in vivo effects on protein synthesis and muscle atrophy. **Methods:** NPN_1 was tested in cell culture assays to evaluate safety and muscle metabolism related effects. Oral bio availability and stability were assessed using simulated in vitro gastrointestinal digestion and human plasma studies. A hindlimb suspension murine model was used to determine the in vivo effects of NPN_1 on soleus wet weight, myogenic and inflammatory biomarkers, and on integrated muscle fibre density. **Results:** NPN_1 treatment exhibited no adverse effects on cell viability and demonstrated an increase on mTOR associated phosphorylated S6 in C2C12 cells, indicative of protein synthesis. We noted bioactive peptides within NPN_1 survive gastric and intestinal digestion with the potential to cross the GI tract. Additionally, these

peptides exhibited substantial stability in human plasma studies. We carried out an induced atrophy murine model, where following 18 days of NPN_1 treatment, animals exhibited significant attenuation of muscle loss in the soleus, increased expression of a myogenesis biomarkers and reduced circulating IL-6. Additionally we observed enhanced integrated density of Type I and Type II soleus muscle fibres suggesting increased oxidative capacity and improved skeletal muscle performance. **Conclusion:** In vitro and in vivo testing confirmed that NPN_1 is a safe and active ingredient, with significant muscle metabolism modulating effects. Currently, work is ongoing to provide translatable insight into PK/PD properties of peptides within NPN_1 across different species, to establish clinically relevant biomarkers and further MOA evidence.

OC13- AGE-ASSOCIATED SEM CELL EXHAUSTION PROMOTES FRAILTY. Ander Matheu, Leire Moreno-Cugnon, Miren Revuelta, Manuel Moreno-Valladares, Alex Arrieta (*Cellular Oncology Laboratory, Biodonostia Institute, San Sebastian, Spain*)

Backgrounds: Stem cell exhaustion is a critical process involved in the decline of the regenerative capacity of tissues with age but its impact on longevity and frailty requires further investigation SOX2 marks and maintains the activity of stem and progenitor cell populations in multiple adult tissues. **Objectives:** Our aim is to study the impact of SOX2 in frailty, longevity and age-associated stem cell exhaustion. **Methods:** To study SOX2 function in frailty and longevity, we took advantage of Sox2EGFP mouse model, in which one copy of Sox2 was replaced by GFP. **Results:** By naturally aging Sox2GFP heterozygous mice, we found that aged Sox2GFP haplo insufficient mice present generalized tissue impairment and signs of accelerated aging including tissues where Sox2 activity is linked to stem cells (stomach, lung, testes) or are relevant for aging (kidney, spleen). At the organismal level, they display aggravated cognitive decline and frailty, however longevity seems to be partially affected (maximal lifespan is not altered). At cellular level, we found diminished number of neurospheres in Sox2EGFP mice. Furthermore, we observed that type A and B neural stem cells (NSCs) together with neuroblasts were decreased in Sox2EGFP mice in vivo in old, but not young mice and this correlated with increased accumulation of DNA damage and oxidative stress, as well as decreased telomere length in the subventricular zone. Moreover, SOX2 reactivation in neurospheres from 2-years mice rejuvenated NSCs activation. **Conclusion:** A together, our results confirm that SOX2 plays a major role in stem cell exhaustion, frailty and aging.

OC14- CELLULAR SENESENCE AND CHRONOLOGICAL AGE IN VARIOUS HUMAN TISSUES: A SYSTEMATIC REVIEW AND META-ANALYSIS. C.S.L. Tuttle¹, M.E.C. Waaijer², M.S. Slee-Valentijn³, T. Stijnen⁴, R.G.J. Westendorp⁵, A.B. Maier^{1,6} ((1) *Department of Medicine and Aged Care, @AgeMelbourne, Royal Melbourne Hospital, University of Melbourne, Victoria, Australia;* (2) *Department of Gerontology and Geriatrics, Leiden University Medical Center, Leiden, the Netherlands;* (3) *Geriatric Rehabilitation, Cordaan, Amsterdam, the Netherlands;* (4) *Department of Biomedical Data Sciences, Leiden University Medical Center, Leiden, the Netherlands;* (5) *Department of Public Health and Centre for Healthy Ageing, University of Copenhagen, Copenhagen, Denmark;* (6) *Faculty of Behavioural and Movement Sciences, Department of Human Movement Sciences, @AgeAmsterdam, Vrije Universiteit, Amsterdam Movement Sciences, Amsterdam, the Netherlands*)

Backgrounds: Senescent cells in tissues and organs are considered to be pivotal to not only the ageing process but also the onset of chronic disease. Accumulating evidence from animal experiments indicate that the magnitude of senescence can vary within and between aged tissue samples from the same animal. **Objectives:** Whether this variation in senescence translates across to human tissue samples is unknown. **Methods:** To address this fundamental question, we have conducted a systematic review and meta-analysis of all available literature investigating the magnitude of senescence and its association with chronological age in human tissues samples. **Results:** While senescence is higher in aged tissue samples, the magnitude of senescence varies considerably depending upon tissue type, tissue section and marker used to detect senescence. These findings echo animal experiments demonstrating that senescence levels may vary between organs within the same animal. **Conclusion:** These findings echo animal experiments demonstrating that senescence levels may vary between organs within the same animal.

OC15- UTILIZING THE PARABIOSIS-DETACHMENT MODEL TO INVESTIGATE LASTING EFFECTS OF HETEROCHRONIC PARABIOSIS. David E. Lee, Akshay Bareja, Lauren H. Katz and James P. White (*Duke University Medical Center, Durham, NC, USA*)

Background: The rejuvenating effects of “youthful circulation” has been shown through heterochronic parabiosis and blood plasma transfer models. In the mouse, these effects are seen across many tissues of the aged recipient, including cardiac, brain, liver and skeletal muscle. Despite these compelling observations, there are several questions that have yet to be addressed, including investigation of the lasting effects of heterochronic parabiosis after the youthful circulation is discontinued. We hypothesize long-term exposure to youthful circulation will slow the aging process and have continued health benefits after discontinuation of the parabiosis. **Objectives:** The objective of this study was to investigate the lasting effects of heterochronic parabiosis on lifespan and

muscle healthspan after detachment. **Methods:** This study utilized the parabiosis-detach model to determine lasting effects on the aged mice. The aged mice were paired starting at 20 months, just before the onset of sarcopenia in the C57Bl/6 mouse and detached at 23 months. After one month of recovery, the detached mice were assessed for longevity and aspects of sarcopenia, including muscle mass, regenerative capacity and function. **Results:** After detachment from heterochronic pairing, the aged mice showed an extension of lifespan in comparison to the detached mice from isochronic pairs. The detached heterochronic aged mice had an increased exercise capacity along with voluntary activity. Moreover, the heterochronic, detached mice had increased grip strength and neuromuscular performance. Lastly, the heterochronic aged mice had increased muscle regenerative capacity one month after detachment, which included enhanced muscle stem cell function. **Conclusion:** The use of the parabiosis-detach model is effective to measure lasting effects of youthful circulation. Prolonged exposure to youthful circulation appears to extend both lifespan and healthspan in aged mice after discontinuation from parabiosis.

OC16- PREVALENCE OF SARCOPENIA IN A NORTHERN SCANDINAVIAN POPULATION ACCORDING TO UPDATED EWGSOP2 THRESHOLDS FOR UPPER-BODY OR LOWER-BODY STRENGTH: THE TROMSØ STUDY. Jonas Johansson¹, Bjørn Heine Strand³, Bente Morseth², Laila Hopstock¹, Sameline Grimsgaard¹ ((1) *Department of Community Medicine, UiT The Arctic University of Norway, Tromsø, Norway;* (2) *School of Sport Sciences, UiT The Arctic University of Norway, Tromsø, Norway;* (3) *Norwegian Institute of Public Health, Oslo, Norway*)

Background: Sarcopenia was recently recognized formally as a muscle disease, and the European Working Group on Sarcopenia in Older People (EWGSOP) has updated the European criteria with emphasis on upper- and lower body muscle strength as primary defining measures. However, the updated criteria should be evaluated in various populations. **Objectives:** Investigate the prevalence of sarcopenia in a large population based cohort and explore whether prevalence varies based on the two recommended criteria for muscle strength. **Methods:** This cross-sectional analysis included grip strength (Jamar+ Digital dynamometer), 5-repetition chair stands, Dual-Energy X-ray Absorptiometry (GE Lunar Prodigy), Short Physical Performance Battery and Timed-Up-and-Go from 3515 community-dwelling participants from the 7th wave of the Tromsø Study aged 40-84 years. Thresholds established in the EWGSOP2 definitions determined sarcopenia prevalence. **Results:** Prevalence of probable sarcopenia (low muscle strength only) was 3.4% based on grip strength, and 5.7% based on chairstands. Prevalence of confirmed (addition of low appendicular lean mass) and severe sarcopenia (further addition of low physical function) ranged between 0.5-1.0% and 0.0-0.3% respectively, depending on EWGSOP2 criteria combination. Among 65-79 year-olds, grip strength defined

1.8-5.7% participants as having probable sarcopenia, while corresponding chair stand prevalence was 4.5-10.6%. After age-adjustment, chair stands defined significantly more women as having probable sarcopenia compared to men (7.2% vs. 3.5%, $p < 0.001$) while no statistical sex-difference was found for grip strength (3.8% vs. 2.9%, $p = 0.139$). Participants with grip strength-based probable sarcopenia expressed lower weight ($p < 0.001$), body mass index (BMI; $p = 0.050$), and waist circumference (WC; $p = 0.056$) than their non-sarcopenic counterparts. In contrast, participants meeting the sarcopenic thresholds for chair stands were of similar weight ($p = 0.155$), had higher BMI ($p < 0.001$) and WC ($p < 0.001$) compared to their non-sarcopenic counterparts. **Conclusion:** The lower-body strength criteria roughly doubled the prevalence of probable sarcopenia among 65-79 year-olds and included significantly more women, compared to the upper-body strength criteria. Furthermore, the two criteria defined individuals of contrasting anthropometrics to have probable sarcopenia. Researchers should further evaluate the sex-specific thresholds and consequences of using different strength measures to define sarcopenia.

OC17- THE EFFECT OF EXERCISE ON ACTIVITIES OF DAILY LIFE AND QUALITY OF LIFE IN FRAIL OLDER ADULTS: A SYSTEMATIC REVIEW. Evan Campbell¹, Fanny Petermann-Rocha^{2,3}, Paul Welsh³, Carlos Celis-Morales^{2,3}, Stuart R Gray³ ((1) *Healthcare Improvement Scotland, NHS Scotland*; (2) *Institute of Health and Wellbeing, University of Glasgow, Glasgow, UK*; (3) *British Heart Foundation Glasgow Cardiovascular Research Centre, Institute of Cardiovascular and Medical Science, University of Glasgow, Glasgow, UK*)

Background: While the positive effects of exercise on frailty is well documented there has not been a systematic review of the effect of exercise on Quality of Life (QoL) and Activities of Daily Living (ADL) in frail older adults. **Objectives:** To systematically review the evidence of the effect of exercise on QoL and ADL in frail older adults. **Methods:** Embase, MEDLINE, CENTRAL, PEDro and Web of Science Core Collections were searched using relevant MeSH terms. Inclusion criteria: controlled trial, articles in English, populations included frail older adults, frailty measured quantitatively, interventions included exercise, and QoL or ADL measurements (PROSPERO:CRD42018106173). **Results:** 17 studies were identified: 16 randomised controlled trials and one controlled trial. Sample size ranged from 27-771 (total $n=3,195$). Nine studies used a recognised frailty measure. While nine trials conducted power calculations, only one of the concerned ADL. Thirteen QoL and ADL measures and 37 other outcome measures were used across the 17 studies. Nine studies had exercise only interventions, six were multi-modal, and two were multi-armed trials that included multi-modal and exercise only arms. All exercises interventions, bar one, were multi-component. All studies included strength training, 12 balance training, ten aerobic training, five flexibility, and four included functional exercises. Trial length ranged from

3-52 weeks. Training frequency ranged from twice to five times a week. Thirteen of the interventions were supervised. Improvements in QoL or ADL were seen in 11 studies ($p < 0.05$), with seven of these studies reporting differences between groups. All studies, but three, reported significant differences between group effects for other outcome measures. There were no associations between methodological variables, results of other outcome measures, and QoL or ADL outcomes. **Conclusion:** The available evidence is heterogeneous for the effects of exercise on QoL or ADL in frail older adults. This is in contrast to the clear positive effect of exercise studies in non-frail older adults. However, just one of the studies had QoL and ADL as a primary outcome measure. Further long-term large randomised controlled trials focussing on QoL and ADL are required to fully investigate the effects of exercise on QoL and ADL.

OC18- WALK SPEED AND MUSCLE MASS ESTIMATED BY THE D3-CREATINE DILUTION METHOD ARE IMPORTANT COMPONENTS OF SARCOPENIA ASSOCIATED WITH INCIDENT MOBILITY DISABILITY IN OLDER MEN: A CLASSIFICATION AND REGRESSION TREE ANALYSIS. Jesse Zanker¹, Terri Blackwell², Sheena Patel², Kate Duchowny^{2,3}, Sharon Brennan-Olsen¹, Steven R. Cummings^{2,3}, William J. Evans^{4,5}, Eric S. Orwoll⁶, David Scott^{1,7}, Sara Vogrin¹, Gustavo Duque¹, Peggy M. Cawthon^{2,3} ((1) *Department of Medicine-Western Health, University of Melbourne, Melbourne, Victoria, Australia*; Australian Institute for Musculoskeletal Science (AIMSS), University of Melbourne and Western Health, Melbourne, Victoria, Australia; (2) *Research Institute, California Pacific Medical Center, San Francisco*; (3) *Department of Epidemiology and Biostatistics, University of California, San Francisco*; (4) *Department of Nutritional Sciences and Toxicology, University of California, Berkeley*; (5) *Department of Medicine, Duke University, Durham, North Carolina*; (6) *Department of Medicine, Oregon Health and Science University, Portland*; (7) *Department of Medicine, School of Clinical Sciences at Monash Health, Monash University, Clayton, Victoria, Australia*.)

Background: It is unknown whether muscle mass measured by the D3-creatinine dilution method is a relatively more important predictor of incident mobility disability than current components of sarcopenia definitions (including grip strength, walking speed, appendicular lean mass). **Objectives:** To determine the relative importance of strength, physical performance, lean-, fat- and muscle mass, in predicting incident mobility disability in older men. **Methods:** This study used data from the Osteoporotic Fractures in Men (MrOS) longitudinal cohort study. Muscle mass was assessed by D3-creatinine dilution (D3Cr muscle mass) in 1098 men (mean age 83.7 ± 3.7 years). Participants also completed anthropomorphic measures, walk speed (6m), grip strength (kg), chair stands in 10 seconds, and dual x-ray absorptiometry (DXA) appendicular lean mass (ALM) and total body fat percentage. Men self-reported incident mobility disability defined by inability to

complete at least one of walking 2-3 blocks, climbing 10 steps, or carrying 10 pounds, over 2.2 + 0.3 years. Classification and regression tree analysis was conducted to determine relative variable importance and algorithm cutpoints for predicting incident mobility disability. Given the proximity of objectively-determined walk speed with the primary outcome (self-reported mobility disability), analyses were conducted with and without walk speed. **Results:** Walk speed followed by D3Cr muscle mass were the most important variables (variable importance: 53% and 12% respectively) in the prediction of self-reported incident mobility disability. D3Cr muscle mass was the most important variable in predicting incident mobility disability when walk speed was excluded, followed by chair stands (variable importance: 35% and 33%, respectively). Body fat percentage, ALM and grip strength had low or negligible variable importance in both models. **Conclusion:** This study has provided valuable insights into the importance of different variables in predicting incident mobility disability in older men. D3Cr muscle mass may be a key tool for predicting risk of negative outcomes in older adults in the future.

OC19- PREVALENCE OF LOW MUSCLE MASS, MUSCLE STRENGTH AND UPPER-BODY MUSCLE QUALITY IN COMMUNITY-LIVING OLDER ADULTS LIVING IN AUCKLAND, NEW ZEALAND. Anne N Hiol, Pamela R von Hurst, Cathryn A Conlon, Jamie V de Seymour, Kathryn L Beck (*School of Sport, Exercise, and Nutrition, Massey University, New Zealand*)

Background: Age-related changes in muscle strength are the result of a decline in muscle mass, as well as a reduction in muscle quality. To date, no studies have investigated these factors in older adults living in New Zealand. **Objectives:** To describe and evaluate the prevalence of low muscle mass, muscle strength and upper muscle quality in older community-living adults in New Zealand. **Methods:** Adults aged 65-74 years living independently were recruited from the cross-sectional Researching Eating Activity and Cognitive Health (REACH) study. Appendicular skeletal muscle mass (ASM) and the upper-body appendicular lean mass (ALM, kg) were measured using Dual-energy X-ray Absorptiometry (DXA; Hologic, Discovery QDR series). The ASM index was calculated by dividing ASM (kilograms by height (meters) squared. The maximum muscle (grip) strength was measured on the dominant hand using a hand-grip dynamometer (JAMAR HAND). Upper-body muscle quality (Upper-body-MQ) was calculated by dividing the maximum handgrip strength by upper body ALM. **Results:** Participants (n=369; 64% female) were 69.7±2.6 (mean ± SD) years. Low muscle mass (<5.5kg/m² and <7kg/m²) was observed in 6.3% and 2.3% of women and men respectively. Low muscle strength (<16kg women; <27kg men) was observed in 4.6% of women and 1.5% of men using the Revised European Working Group on Sarcopenia in Older People cut-off values. Low upper-body MQ (<5.475kg/kg women; <5.76 kg/kg men, Cooper et al. cut-off values) was observed in 51.3% and 75.2% of women and men respectively. Muscle strength showed a small but significant

positive correlation with muscle mass in both men and women (R²=0.038, P<0.001 and R²=0.055, P<0.001, respectively). **Conclusion:** In this cohort of older adults, the prevalence of low upper-body muscle quality exceeded the prevalence of low muscle mass and low muscle strength. These results suggest that changes in muscle quality may precede loss of muscle mass and muscle strength. Therefore, identifying poor muscle quality before 65 years of age could be important in identifying individuals at risk of age-related loss of muscle function.

OC20- EFFECTS OF SCREENING AND SELECTIVE FALL PREVENTION INTERVENTIONS FOR REDUCING FRACTURES, FALLS AND FRAILTY. Sarah E Lamb¹, Julie Bruce², Anower Hossain³, Ji Chen², Roberta Longo⁴, Ranjit Lall², Chris Bojke⁴, Claire Hulme¹, Emma Withers², Susanne Finnegan², Martin Underwood^{2,5} on behalf of the Prevention of Fall Injury Trial (Pre-FIT) Study Group ((1) *Institute of Health Research, College of Medicine and Health, University of Exeter, Exeter, United Kingdom;* (2) *Warwick Clinical Trials Unit, Division of Health Sciences, University of Warwick, Coventry, United Kingdom;* (3) *Institute of Statistical Research and Training (ISRT), University of Dhaka, Bangladesh;* (4) *Leeds Institute of Health Sciences, Worsley Building, 6 Clarendon Way, University of Leeds, Leeds, United Kingdom;* (5) *University Hospitals of Coventry and Warwickshire, Clifford Bridge Rd, Coventry, United Kingdom*)

Background: Community prevention strategies can reduce falls. Effects on fractures, frailty and health-related quality of life are unknown. **Objectives:** To estimate the effectiveness of commonly used fall prevention interventions in primary care on fractures, frailty and falls over an 18 month period. **Methods:** In a three-arm, cluster randomized controlled trial we estimated the effect of postal advice and falls risk screening with selective: interventions (multi-factorial risk intervention or exercise) for people at higher risk of falls in comparison to postal advice only. We randomised 9803 people aged 70 years and older from 63 general practices across England. The primary outcome was fracture rate over 18 months using routinely collected health data. Other outcomes included falls, frailty, and health-related quality of life. **Results:** Completed falls risk screeners were returned by 2925/3279 (89%) for exercise, and 2854/3301 (87%) for MF. Of these 37% (2153/5779) were at higher risk and invited for treatment. Fracture data were available for 9802/9803 participants. Neither intervention reduced fracture rates (exercise versus advice rate ratio (RaR) 1.20 (95% CI 0.91 to 1.59, in favour of advice) and multifactorial versus advice RaR 1.30 (95% CI 0.99 to 1.71, in favour of advice)). Exercise was associated with a short-term reduction in falls rate, small gains in health-related quality of life and lowest overall costs. There was no long term effect (18 months) on frailty outcomes. **Conclusion:** Postal screening followed by an exercise intervention does not reduce fractures or frailty but had a small positive effect on falls. Screening followed by a multifactorial intervention does not reduce falls or impact other outcomes. (Funder, National Institute of Health

Research, clinical trials registration ISRCTN71002650).

OC21- THE ASSOCIATION OF FRAILTY WITH MEDICATIONS WITH HIGH ANTICHOLINERGIC BURDEN IN COMMUNITY DWELLING US OLDER VETERANS. Sergio J. Ruiz¹, Victor Cevallos¹, Michael J. Mintzer^{1,2}, Jorge G. Ruiz^{1,2} ((1) *Miami VAHS GRECC, USA*; (2) *Dept. of Medicine, U of Miami Miller School of Medicine, USA*)

Background: Anticholinergic drugs are prescribed to treat a variety of medical and mental health conditions. Anticholinergics medications pharmacological actions oppose the actions of acetylcholine throughout the body. Anticholinergics may contribute to frailty by causing cognitive, functional and physical impairment. Medications with recognized and clinically significant high anticholinergic burden (ACB3) may be particularly deleterious to older adults. **Objectives:** Determine the cross-sectional association of frailty with medications with high anticholinergic burden (ACB3) among community-dwelling US older Veterans. **Methods:** This is a cross-sectional study of 17,216 community-dwelling Veterans 65 years and older whose frailty status was assessed between October 2018 and October 2019. The use of medications (never/active/inactive) with high anticholinergic burden scale (ACB3) were obtained from electronic health records. A 31-item VA Frailty Index (VA-FI) was generated as a proportion of all potential variables (morbidity, function, sensory loss, cognition and mood, and others) at the time of the assessment. We dichotomized the groups into non-frail (robust $FI \leq .10$ and prefrail $FI > .10, < .21$) and frail ($FI \geq .21$) patients. After adjusting for age, gender, race, marital status, median household income, and BMI, odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using binomial logistic regression with frailty as the dependent variable and anticholinergic medications (ACB3) as independent variables. **Results:** Patients were 71.1% White, 97.4% male, mean age 75.45 (SD=7.984, range 65-104) years, 11.1% (n=1975) were taking ACB3 medications (active), 30.9% (n=5316) took them in the past (inactive) and 57.6% (n=9925) never took them (never). The proportion of robust, pre-frail and frail patients was 31.3% (n=5396), 37.4% (n=6440) and 31.3% (n=5380) respectively. In binomial logistic regression, compared with individuals who never took ACB3 anticholinergics, those individuals on inactive and active ACB3 medications showed a higher risk for frailty, adjusted OR=3.207, 95%CI=2.497-3.490, $p < .0005$ and OR=4.876, 95%CI=4.345-5.473, $p < .0005$, respectively. **Conclusion:** This study shows that the use of medications with high anticholinergic burden was cross-sectionally associated with frailty in older community-dwelling Veterans. Longitudinal cohort studies may further clarify whether anticholinergic medications indeed contribute to the development of frailty.

OC22- AUGMENTED EXERCISE IN HOSPITAL IMPROVES PHYSICAL PERFORMANCE AND REDUCES NEGATIVE POST HOSPITALIZATION EVENTS: A RANDOMIZED CONTROLLED TRIAL. Ruth McCullagh¹, Eimear O'Connell², Sarah O'Meara³, Darren Dahly^{4,5}, Eilis O'Reilly⁴, Kieran O'Connor⁶, N. Frances Horgan⁷, Suzanne Timmons¹ ((1) *Centre for Gerontology & Rehabilitation, University College Cork, Ireland*; (2) *Physiotherapy Department, Mercy University Hospital, Cork, Ireland*; (3) *Clinical Research Facility, Mercy University Hospital, Cork, Ireland*; (4) *School of Public Health, University College, Cork, Ireland*; (5) *Clinical Research Facility, Cork, University College, Cork, Ireland*; (6) *Department of Geriatric Medicine, Mercy University Hospital, Cork; Ireland*; (7) *School of Physiotherapy, Royal College of Surgeons in Ireland, Dublin, Ireland*)

Background: It is well known that frail patients are potentially most at risk of functional decline following a hospital admission. **Objectives:** To measure the effects of an augmented prescribed exercise programme versus usual care, on physical performance, quality of life and healthcare utilisation for frail older medical patients in the acute setting. **Methods:** This was a parallel single-blinded randomised controlled trial. Within two days of admission, older medical inpatients with an anticipated length of stay ≥ 3 days, needing assistance/aid to walk, were blindly randomly allocated to the intervention or control group. Until discharge, both groups received twice daily, Monday-to-Friday half-hour assisted exercises, assisted by a staff physiotherapist. The intervention group completed tailored strengthening and balance exercises; the control group performed stretching and relaxation exercises. Length of stay was the primary outcome measure. Blindly assessed secondary measures included readmissions within three months, and physical performance (Short Physical Performance Battery) and quality of life (EuroQOL-5D-5L) at discharge and at three months. Time-to-event analysis was used to measure differences in length of stay, and regression models were used to measure differences in physical performance, quality of life, adverse events (falls, deaths) and negative events (prolonged hospitalisation, institutionalisation). **Results:** Of the 199 patients allocated, 190 patients' (aged 80 ± 7.5 years) data were analysed. Groups were comparable at baseline. In intention-to-treat analysis, length of stay did not differ between groups (HR 1.09 (95% CI, 0.77-1.56) $p=0.6$). Physical performance was better in the intervention group at discharge (difference 0.88 (95% CI, 0.20-1.57) $p=0.01$), but lost at follow-up (difference 0.45 (95% CI, -0.43 – 1.33) $p=0.3$). An improvement in quality of life was detected at follow-up in the intervention group (difference 0.28 (95% CI, 0.9 – 0.47) $p=0.004$). Overall, fewer negative events occurred in the intervention group (OR 0.46 (95% CI 0.23 – 0.92) $p=0.03$). **Conclusion:** Improvements in physical performance, quality of life and fewer negative events suggest that this intervention is of value to frail medical inpatients. Its effect on length of stay remains unclear.

OC23- SOCIOECONOMIC DISPARITIES IN FRAILTY: A 14 YEAR LONGITUDINAL COHORT STUDY.

Ruby Yu, Cecilia Tong, Jason Leung, Jean Woo (*Yasumoto International Academic Park, The Chinese University of Hong Kong, Shatin, Hong Kong, Hong Kong*)

Background: The prevalence of frailty varies among socioeconomic groups. However, longitudinal data for the association between subjective socio economic status (SES) and frailty is limited. **Objectives:** To examine whether subjective SES was associated with incident frailty. **Methods:** Data were from the 14-year cohort of Chinese men and women aged 65 years and older participating in the MrOs study, a longitudinal study on osteoporosis and general health in Hong Kong. Subjective SES at baseline (2001-2003) was assessed by asking participants to place a mark on a picture of an upright ladder with ten rungs, with the lowest rung being the most undesirable and the highest as the most desirable state with respect to their standing in the community. Incident frailty at the 14-year follow-up (2015-2017) was defined as proposed by Fried and colleagues. Multiple regressions were used to examine the association between subjective SES and incident frailty. **Results:** Of the 712 participants who were robust at baseline and retained in the 14-year follow-up, 429 and 217 developed pre-frailty and frailty at year 14, respectively. After adjustment for age, sex, marital status, objective SES (educational level, maximum lifetime income), medical history (hypertension, diabetes, stroke), lifestyle (smoking, alcohol intake, physical activity, diet quality, body mass index), mental and cognitive functions, participants with lower subjective SES at baseline was associated with a higher risk of developing frailty over time (OR 2.4, 95% CI 1.2-4.6) compared to those with higher subjective SES at baseline. In sex-stratified analysis, the social gradient in frailty was greater in men than women. For men, lower (OR 3.6, 95% CI 1.5-8.4) and medium (OR 2.2, 95% CI 1.3-3.8) subjective SES at baseline were associated with a higher risk of developing frailty at year 14 compared to those with higher subjective SES. For women, the risk increased with medium subjective SES only (OR 2.0, 95% CI 1.1-3.8). **Conclusion:** This study provides evidence for a social gradient in the development of frailty especially in men. The greater social inequality in frailty in men relative to women supports interventions specific to gender inequality and frailty. Integrating social determinants of health into the prevention and monitoring of frailty trends would ensure that interventions reach and benefits populations with the greatest need.

OC24- AN INTRINSIC CAPACITY SCORE TO PREDICT THE MORTALITY RISK IN A POPULATION IN ELDERLY POPULATION OF COSTA RICA. Luis Miguel Gutiérrez-Robledo, Rosa Estela García Chanes, Mario Ulises Pérez Zepeda (*Instituto Nacional de Geriatria, México*)

Background: The intrinsic capacity (IC) is defined with a set of physical and mental abilities that the individual has that could have an influence as well in lifespan and healthspan. This concept emphasizes the positive attributes and reserve of

individuals throughout life. Based on the evidence reviewed, Cesari and colleagues (2018) propose five domains of intrinsic capacity: cognition, psychological, sensory, vitality and locomotion, which must be viewed in an integrated manner. Based on this proposal, Gutierrez and colleagues (2019) proposed an operationalization of intrinsic capacity in populations whose predictive value remains to be demonstrated.

Objectives: To analyze the relationships between baseline intrinsic capacity and mortality through 5 years of follow up of an elderly population in Costa Rica. **Methods:** The source of information were the three waves (2005-2009) of the «Longevity and Healthy Aging Study Costa Rica» (CRELES). Intrinsic capacity was operationalized with a summary index of the five domains with a score ranging between 0 and 10 points in wave 1. Each domain was built with indicators selected by means of a principal component's analysis and stratification in three levels for each component was defined based on cluster analysis. Survival analyses techniques were used to examine the risk ratios for the level of the intrinsic capacity. Kaplan-Meier estimates were obtained as well as a cox proportional hazards model. **Results:** A total of 1,777 persons were included in the analysis. Cox proportional hazards models shows that with increasing IC, the risk of dying decreases up to 20% adjusted by sex, age, socioeconomic level, and number of health conditions. **Conclusion:** We observed an association between a lower intrinsic capacity and a greater probability of death. These findings contribute to strengthen the view stating that intrinsic capacity can be used to assess the integral capacities of older persons.

OC25- PRELIMINARY ESTIMATION OF RESIDUAL WORKING CAPACITIES CRITERIA FOR PREVENTING FRAILTY AND SARCOPENIA IN THE ELDERLY PERSONS. Tomarevska Olena, Poliakov Oleksandr, Bezrukov Vladyslav (*Institute of Gerontology by D.F. Chebotarev of National Academy of Medical Sciences of Ukraine, Kyiv, Ukraine*)

Background: The rapid development of information technologies has coincided remarkably with increasing percentage of elderly people. Meanwhile the increasing numbers of elderly people cannot fully use the advantages of modern technologies. **Objectives:** The purpose of the study was to develop the instrument for quantifying physiological possibilities of elderly people to enable realization of their residual working capacities. **Methods:** Anthropometric and functional parameters of respiration, physical performance, mental and psychomotor activities, sensory skills, ergometric indices, labor and social status as well as the rate of functional aging were studied in 307 persons aged 20 -104 years. **Results:** According to physiological and ergometric tests and subsequent clustering, correlation and regression analyses, the method for determining the residual physical and mental capacities of persons 60+ was developed. The level 90-100% of working capacities is evidencing that elderly workers can work during 8 hours, they have abilities to learn and improve skills; 70-89% - working time 4 hours; 50-69% - working time 2 hours;

20-49% - unable to work (functional decline); 0.01-19% - frailty and sarcopenia. It was found that elderly workers (45-59 years) possess 91.7% of working abilities, the age group 60-74 years - 64.6%, the age group 75-89 years - 30.5%, the group of centenarians - 9.5%. The impact factors defining residual capacities were: chronological age - 61.4% in the age group 60-89 years old and 3.6% in centenarians, body mass index - 5.4% and 10.5%, sit-to-stand 29.7% and 41.8%, frequency of walking in the street -13.0% and 14.9%, light housework or physical activity - 16.7% and 20.4%, educational level - 9.8% and 6.9%, years of study in secondary school - 25.7% and 6.9% - accordingly. Gerontechnology optimization approaches to work and daily activities of elderly persons allowed to use residual mental and physical capacities for realistic performance of the elderly. **Conclusion:** The method was developed for present and prognostic evaluation of the working abilities of persons at retirement age, as well as for regulation of their labor activities. It allows to arrange optimal schedule of working hours, to preserve worker's health, to promote longevity, and last but not least - to get second demographic dividend.

OC26- FRAILTY INDEX, HOSPITAL ADMISSION AND LENGTH OF HOSPITAL STAY IN NURSING HOME RESIDENTS: RESULTS FROM THE INCUR STUDY.

Simo Nadine¹, Cesari Matteo^{2,3}, Tchiero Huidi⁴, Yves Rolland⁵, Dartigues Jean-François⁷, Vellas Bruno⁵, Tabue-Tegu Maturin^{1,6} ((1) *CHU de Guadeloupe, Université des Antilles, Guadeloupe, France*; (2) *Geriatric Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, Italy*; (3) *Department of Clinical Sciences and Community Health, University of Milan, Milano, Italy*; (4) *CH de Saint Martin, Saint-Martin, France*; (5) *Gérontopôle, Centre Hospitalier Universitaire de Toulouse, INSERM UMR1027, Université de Toulouse III Paul Sabatier, Toulouse, France*; (6) *INSERM 1219, Bordeaux Population Health Research Center, Université de Bordeaux, Bordeaux, France*)

Background: Frailty Index (FI) is associated with negative outcome. In the present article, it is hypothesized that the FI may have an important role at discriminating the most vulnerable people to negative outcomes (ie, hospital admission) **Objectives:** To investigate the predictive capacity of an age-related deficit accumulation index (the so-called Frailty Index [FI] proposed by Rockwood) for hospital admission (HA) and length of hospital stay (LHS) among nursing home residents. **Methods:** Design, setting and participants: Data are from a longitudinal cohort study (i.e., the Incidence of pNeumonia and related. Consequences in nursing home Residents [INCUR]) of 768 older persons (75.4% women) living in 13 nursing homes in France. **Measurements:** The FI was computed taking into account as the ratio between 30 possible deficits the participant might have presented at the baseline visit. Hospital admissions were defined as all urgent and involuntary admissions including unplanned readmissions. The length of stay was the total number of days spent by the resident in the hospital. Cox proportional hazard models and survival analysis in the presence of competing risks (death) were performed to

study the relationship between the FI and HA over a 12-month follow-up. A Zero-inflated negative binomial regression was performed to study the association between the FI and LHS. **Results:** Results: Mean age of participants was 86.7 (standard deviation [SD] 6.9) years, with a mean FI was 0.37 (SD 0.11). At the end of the follow-up, 238 (30.9%) UHA events were recorded. Positive associations of the FI with LHS and UHA were reported (per 0.01 FI increment: age- and gender-adjusted hazard ratio 1.15, 95% confidence interval 1.020-1.297, p=0.02 and OR 1.209 (1.075 - 1.359, p<0.001, respectively). **Conclusion:** The FI is a strong predictor of negative health-related outcomes as HA and LHS events, even in very old and complex nursing home residents.

OC27- SOCIAL VULNERABILITY AND LIFESTYLE BEHAVIORS, THEIR IMPACT ON FRAILTY: RESULTS OF THE CANADIAN LONGITUDINAL STUDY ON AGING. Ulises Perez-Zepeda, Olga Theou, Kenneth Rockwood, Melissa Andrew, Andrea Mayo, Judith Godin, Scott Kehlerd (*Dalhousie University, Halifax, Canada*)

Background: Frailty is a well-known condition affecting older adults' health, with high impact on the individual, their families and society. The impact of different aspects of life on frailty are still a matter of continuous research. Social vulnerability and lifestyle behaviors are of particular interest, since their modification have the potential of changing the outcomes of individuals facing this condition. **Objectives:** To describe the impact of social vulnerability and lifestyle behaviors on frailty in middle aged and older Canadian adults. **Methods:** We conducted a secondary analysis of the baseline assessment of the Canadian Longitudinal Study on Aging (2015). This study, comprises two cohorts of individuals 45 to 85 years old, from the 10 provinces of the country. A frailty index (FI) was constructed with standardized procedures. Centiles for age and sex were calculated, and merged, having the possibility of a score from 0 to 100; being 0 the worst possible category and 100 the best possible one. A social vulnerability index (SVI) was integrated, with variables from the social dominion; in order to have one variable going from 0 (lowest social vulnerability) to 1 (highest social vulnerability). Physical activity, nutrition, toothbrushing, use of tobacco, binge alcohol drinking, multivitamin use, coffee drinking and cognitive training were included as lifestyle behaviors. Descriptive, bivariate and multivariate analyses were performed. **Results:** From a total of 51,338 individuals included in CLSA, the age mean was 62.9 (standard deviation [SD] ±10.4) and 50.9% (n=26,155) were women. A 52-item FI was calculated with a mean of 0.08 (SD ±0.05). Regarding the SVI, 46 items were included and the mean was 0.32 (± SD 0.11). According to the multivariate results, higher physical activity levels and cognitive training were independently associated with higher scores of the FI centiles. While SVI, nutritional risk and tobacco use were associated with lower FI centile scores. Toothbrushing and binge alcohol drinking were not significantly associated. **Conclusion:** Frailty is considered to be a progressive condition, however, changing factors that impact

it could have the potential of delaying its progression.

OC28- HIGH VERSUS LOW DIETARY PROTEIN INTAKE AND BONE HEALTH IN OLDER ADULTS: A SYSTEMATIC REVIEW AND META-ANALYSIS. Inge Groenendijk¹, Laura den Boeft¹, Luc J.C. van Loon², Lisette C.P.G.M. de Groot¹ ((1) *Division of Human Nutrition and Health, Wageningen University & Research, Wageningen, the Netherlands*; (2) *Department of Human Biology, NUTRIM School of Nutrition and Translational Research in Metabolism, Maastricht University Medical Centre+, Maastricht, the Netherlands*)

Background: Protein may play a beneficial role in the prevention of bone loss and in slowing down osteoporosis. The effect of dietary protein may be different in older adults compared to younger adults, since this population has a greater need for protein. **Objectives:** The aim of this systematic review and meta-analysis was to investigate the impact of a dietary protein intake above the Recommended Dietary Allowance (RDA) of 0.8 g/kg body weight/day from any source on Bone Mineral Density (BMD)/Bone Mineral Content (BMC), bone turnover markers, and fracture risk in older adults compared to a lower dietary protein intake. **Methods:** A systematic search was conducted through October 2018 in 3 databases: CENTRAL, MEDLINE, and EMBASE. We included all prospective cohort studies and Randomized Controlled Trials (RCTs) among adults aged ≥ 65 years that examined the relation between protein intake on bone health outcomes. Two investigators independently conducted abstract and full-text screenings, data extractions, and risk of bias assessments. Authors were contacted for missing data. **Results:** After screening of 523 records, twelve cohort studies and one RCT were included. Qualitative evaluation showed a positive trend between higher protein intakes and higher femoral neck and total hip BMD. Meta-analysis of four cohort studies showed that higher protein intakes resulted in a significant decrease in hip fractures (pooled hazard ratio: 0.89; 95% confidence interval: 0.84, 0.94). **Conclusion:** This systematic review supports that a protein intake above the current RDA may reduce hip fracture risk and may play a beneficial role in BMD maintenance and loss in older adults.

OC29- THE LOW-GRADE INTESTINAL INFLAMMATION POTENTIATES SARCOPENIA IN OLD ADULTS THAT CAN BE RESTRAINED BY A PROBIOTIC: STREPTOCOCCUS THERMOPHILUS CNRZ160. Isabelle Savary-Auzeloux¹, Marianne Jarzaguet¹, Jérémie David¹, Carole Migné¹, Marcela De Azevedo², Jean-Marc Chatel², Dominique Dardevet¹ ((1) *Université Clermont Auvergne, INRA, UNH, Unité de Nutrition Humaine, CRNH Auvergne, France*; (2) *Micalis, INRA, AgroParisTech, Université Paris Saclay, Jouy en Josas, France*)

Background: Aging is characterized, at the systemic level, by the development of low-grade inflammation, which has been identified as a determinant for sarcopenia by

preventing post prandial muscle anabolism. The origin of this “inflammaging” is still not clearly defined. An increase in intestinal permeability, a microbiota dysbiosis and subsequent generation of a micro- and then generalized inflammation has been hypothesized. **Objectives:** The objective of our study is to test in vivo during aging, if 1) a chronic low grade intestinal inflammation can lead to anabolic resistance and muscle loss and 2) if a bacterial strain presenting anti-inflammatory properties could prevent these adverse effects. **Methods:** To generate low grade intestinal inflammation, elderly rats (18m) were treated with chronic adapted Dextran Sodium Sulfate (DSS) ingestion for 28 days with (CNRZ group) or without (DSS group) *S. Thermophilus* CNRZ160 (109 CFU / day) previously shown to present an intestinal anti-inflammatory potential in vitro. They were compared to pair fed control (PF). Body composition was measured in vivo by EchoMRI whereas muscle and colon weights and protein synthesis (using ¹³C Valine) were at slaughter. Groups were compared using ANOVA and Fisher posthoc test (p <0.05). **Results:** Body weight, lean mass and to a lesser extent fat losses were significantly greater in DSS compared to PF controls (-110 vs -86g, -51 vs -36g and -65 vs -47g, respectively). Similarly, gastrocnemius and tibialis muscles were smaller by 12% and 10% vs PF respectively. In contrast, colon was increased by 13% with DSS. Our probiotic allowed: 1) to maintain normal colon weight (2.09 for CNRZ vs 2.14g for PF) by preventing increase in protein synthesis 2) to limit the loss of lean body mass like in the PF (-36g for CNRZ vs -38g for PF), 3) to limit the loss of muscle which is explained by a better maintenance of post prandial muscle protein synthesis. **Conclusion:** In the elderly, the loss of lean and muscle mass associated with low-grade intestinal inflammation can be reduced by the ingestion of *S. Thermophilus*. Preliminary data in adult rats showed that CNRZ160 prevented TNF α and IL1 β up-expression in DSS-treated adult colon by 78 and 92%. CNRZ160 could therefore be considered as an efficient probiotic to modulate muscle mass loss and limit sarcopenia during aging.

OC30- LEVELS OF FRAILTY AMONG PEOPLE WITH OSTEOARTHRITIS. Olga Theou^{1,2}, Mario Ulises Pérez Zepeda², D Scott Kehler¹, Rebecca Moyer¹, Cheryl Kozey¹, Kenneth Rockwood¹ ((1) *Physiotherapy, Dalhousie University, Halifax, NS, Canada*; (2) *Geriatric Medicine, Dalhousie University, Halifax, NS, Canada*)

Background: People with osteoarthritis, the most common type of arthritis, are at a higher risk of developing premature mobility disability. Even so, evidence on the impact of osteoarthritis on frailty level is limited. **Objectives:** The purpose of this study was to examine levels of frailty of middle aged and older people with osteoarthritis and how frailty levels differ based on the duration of osteoarthritis, the joints affected, multimorbidity, and whether people participate in physical activity. **Methods:** We included data from 47,261 people from the Canadian Longitudinal Study on Aging (CLSA baseline cohort) and 27,211 people from the National Health and Nutrition Examination Survey (NHANES 1999-2016 cohorts)

aged 45-84 years. Osteoarthritis was self-reported, and we also examined its co-existence with cardiovascular disease, stroke, diabetes, chronic obstructive pulmonary disease, cancer, kidney problems, thyroid problems, and other arthritis. We constructed a 40-item frailty index (FI) from the CLSA data and a 37-item FI from the NHANES data excluding all items related to arthritis and the eight chronic conditions examined. **Results:** The proportion of people who had only osteoarthritis and the proportion of those with osteoarthritis and other conditions was 8.5% and 22.5% in CLSA and 4.8% and 9.8% in NHANES, respectively. The weighted mean (\pm standard error) FI of those with only osteoarthritis was 0.07 ± 0.001 for CLSA and 0.15 ± 0.004 for NHANES whereas the mean FI of those with osteoarthritis and other conditions was 0.09 ± 0.001 for CLSA and 0.22 ± 0.003 for NHANES; for both groups FI increased with increasing age. Levels of frailty was higher among those who had osteoarthritis for more than 20 years. Having osteoarthritis in multiple joints was associated with a higher FI score and those who had osteoarthritis in three joints (knee, hand, and hip) had the highest FI scores across all age groups. Those who participated in 300+ min/week in moderate-vigorous physical activity had the lowest frailty index scores across all age groups. **Conclusion:** Frailty levels are high among people with osteoarthritis. Multimorbidity, long duration of osteoarthritis, and osteoarthritis in multiple joints were associated with higher levels of frailty whereas physical activity was associated with lower levels of frailty.

OC31- PROSPECTIVE VALIDATION OF OUR NEW SELECTION CRITERIA CONSIDERING BODY COMPOSITIONS WITH PERIOPERATIVE NUTRITION AND REHABILITATION IN LIVING DONOR LIVER TRANSPLANTATION. Toshimi Kaido^{1,2}, Yuhei Hamaguchi², Shinji Uemoto² ((1) *Department of Gastroenterological Surgery, Saint Luke's International University and Hospital, Tokyo, Japan*; (2) *Department of Hepato-Biliary-Pancreatic Surgery and Transplantation, Kyoto University, Kyoto, Japan*)

Background: Based on our previous findings that preoperative impaired body compositions were independent risk factors after living donor liver transplantation (LDLT), we established new selection criteria for LDLT considering pre-transplant body compositions with perioperative nutrition and rehabilitation therapy. **Objectives:** In the present study, we prospectively validated the usefulness of the new strategy. **Methods:** 1) Establishment: We evaluated pre-transplant skeletal muscle mass, muscle quality, and visceral adiposity using skeletal muscle mass index (SMI), intramuscular adipose tissue content (IMAC), and visceral-to-subcutaneous adipose tissue area ratio (VSR) for 277 consecutive patients who underwent adult LDLT between January 2008 and July 2016 in our institute. We investigated the impact of these three parameters on survival after LDLT. Based on the findings of this study, we have implemented new selection criteria for LDLT since October 2016. 2) Validation: We examined overall survival of 110 consecutive patients who underwent LDLT between October 2016 and October 2019. **Results:**

1) Establishment: Overall survival rates of patients with low SMI, high IMAC, and high VSR (abnormal factors) were significantly lower than those with high SMI, low IMAC, and low VSR, respectively. On multivariate analysis, low SMI, high IMAC, and high VSR were identified as independent risk factors for mortality after LDLT. One-year overall survival rate of patients with no abnormal factor, each one factor, two factors, three factors were 98%, 78%, 60%, and 41%, respectively. Based on these findings, we have established new selection criteria for LDLT: 1) to exclude patients with three abnormal factors, 2) to perform perioperative nutrition and rehabilitation therapy especially for patients with one or two abnormal factors. 2) Validation: One-year overall survival after LDLT under new criteria was 99%. **Conclusion:** We have first established and implemented new selection criteria for LDLT considering pre-transplant body compositions with perioperative nutrition and rehabilitation therapy and validated the usefulness of the new criteria.

OC32- A NOVEL ORAL NUTRITIONAL SUPPLEMENT IMPROVES GAIT SPEED AND OXIDATIVE PHOSPHORYLATION IN DUTCH OLDER ADULTS WITH (RISK OF) UNDERNUTRITION. P. Grootswagers, E.T.H.C. Smeets, A.B. Oteng, C.P.M.G. de Groot (*Department of Human Nutrition and Health, Wageningen University, Wageningen, The Netherlands*)

Background: Oral nutritional supplements are effective in enabling body weight gain. However, their effects on muscle health and performance are controversial and may depend on the composition of the supplements. Altering the composition of oral nutritional supplements might induce additional benefits on body composition and physical performance. **Objectives:** To test the effects of a novel oral nutritional supplement on body weight, lean body mass and physical performance. **Methods:** Older (>65y) participants with (risk of) undernutrition (n=82) were randomly allocated to 12 weeks of supplementation with the intervention product (586 kcal, 22 g protein of which 50% whey and 50% casein, 205 mg ursolic acid, 12 g BCAAs, 11 μ g vitamin D) or standard care (600 kcal, 24g protein of which 100% casein, 6 g BCAAs, 4 μ g vitamin D). Body composition and physical function were measured at baseline and after 12 weeks. Changes over time were assessed by linear mixed models. **Results:** Body weight increased significantly, both in the intervention group and in the standard care group. Lean body mass increased on average with 252 ± 112 g, without differences between groups. Standard care showed a larger increase in fat mass over time as compared to intervention. Walking performance on 4m and 400m improved over time in the intervention group, where the standard care showed no improvements, leading to significant time*treatment effects. Knee extension force, handgrip strength and total SPPB score did not change in the two groups. Microarray analyses on muscle biopsy tissue show upregulated gene sets related to different mitochondrial processes and oxidative phosphorylation in the intervention group. **Conclusion:** A 12-week intervention with a novel nutritional supplement

containing ursolic acid, whey protein, BCAAs and vitamin D improved walking performance both on short and long-distance as compared to standard care, explained by improved oxidative phosphorylation.

OC33- THE EFFECT OF AGEING ON SKELETAL MUSCLE AS ASSESSED BY QUANTITATIVE MR IMAGING: AN ASSOCIATION WITH FRAILTY AND MUSCLE STRENGTH. Matt Farrow^{1,2}, John Biglands^{2,3}, Steven Tanner^{2,3}, Andy Clegg⁴, Lesley Brown⁴, Paul Emery^{1,2}, Ai Lyn Tan^{1,2} ((1) *Leeds Institute of Rheumatic and Musculoskeletal Medicine, Chapel Allerton Hospital, University of Leeds, UK*; (2) *NIHR Leeds Biomedical Research Centre, Leeds Teaching Hospitals NHS Trust, Leeds, UK*; (3) *Medical Physics and Engineering, Leeds Teaching Hospitals NHS Trust, Leeds, UK*; (4) *Academic Unit of Elderly Care and Rehabilitation, University of Leeds, Bradford UK*)

Background: Skeletal muscles undergo changes with ageing, including myosteatosis, fatty infiltration, atrophy and changes in muscle microstructure. These changes are associated with decreased muscle function. Quantitative MRI may detect these changes by measuring fat fraction, T2, muscle volume and diffusion, which could help improve the understanding of muscle pathology and provide non-invasive methods to monitor the effects of interventions. **Objectives:** To investigate whether MRI-based measurements of quantitative T2, fat fraction (FF), diffusion tensor imaging (DTI) and muscle volume can detect differences within the muscles between young, middle-aged and older participants and to assess how these measures compare with frailty index, gait speed and muscle power measurements. **Methods:** 18 young (range 18-30 years), 18 middle-aged (31-68 years) and 18 older (69+ years) participants had an MRI scan of their dominant thigh. MR images of the mid-thigh

were acquired using a STEAM-EPI imaging sequence to assess diffusion, 2-point Dixon imaging to assess fat fraction and a fat-suppressed turbo-spin echo (TSE) sequence to measure T2. In addition to MRI, all participants had knee extension and flexion power and handgrip strength measured. In addition to this, the frailty index and gait speed was measured in older participants. **Results:** Fat fraction, mean diffusivity and T2 values were significantly higher in the older age group compared to the young group. In the quadriceps, the difference in fat fraction was 4%, the difference in mean diffusivity was $0.11 \times 10^{-3} \text{mm}^2/\text{s}$, the difference in T2 was 4.3ms. Muscle volume and muscle power were significantly lower in the older group compared to the young group. There was a difference in muscle power extension of 56W between the old and young group, the difference in muscle volume was 411cm³. The differences in the hamstrings are similar to those seen in the quadriceps. The differences between young and middle-aged, and middle-aged and older participants follow this same trajectory. Quantitative MRI measurements significantly correlated with frailty index, gait speed and muscle power. **Conclusion:** We have identified significant differences in muscle properties as assessed by quantitative MRI and muscle power in young, middle-aged and older participants. The study demonstrates the potential of quantitative T2, FF, diffusion, and muscle volume and muscle power as measures of the health of muscles during ageing to detect sarcopenia and monitor muscle health. This study has also shown a significant correlation between quantitative MRI measurements for T2, FF and muscle volume with an independent measure of frailty. This shows that frailty, as well as age, are detectable with quantitative MRI. This work will inform future efforts to validate quantitative MRI measurements as a diagnostic and management tool in the normal ageing of muscle.