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Symposia

S1- A ROAD MAP FOR THE DEVELOPMENT OF HIGH PRIORITY PHYSICAL FRAILTY RESEARCH.

Jeremy Walston *(Johns Hopkins University, Baltimore, Maryland, USA)*

Over the past 2 decades, great progress has been made in developing frailty assessment methods, understanding the consequences of frailty, and in identifying important biological characteristics related to physical frailty. Despite this progress, there remain considerable gaps in knowledge related to frailty measurement, biological etiologies, implementation of frailty into clinical practice, and public health measures to prevent and ameliorate frailty. A group of frailty-focused investigators centered at Johns Hopkins University have convened a bimonthly frailty working group and identified several major areas of frailty research that would benefit from increased focus. This symposium provides an overview of progress in physical frailty research to date, and a roadmap for future high priority frailty research in the biological, measurement, clinical implementation, and public health domains

Communication 1: *Biological Research Priorities,* Jeremy Walston (Johns Hopkins University, Baltimore, MD, USA)

Age-related molecular changes and dysregulation of physiological systems have long been hypothesized to drive the development of physical frailty. Chronic inflammation, mitochondria decline, altered energy metabolism, and dysregulated stress response systems and their potential etiological roles in frailty will be discussed. In addition, Dr. Walston will provide suggested directions for next generation of studies that would help to link specific molecular changes to dysregulated physiology and ultimately the frailty phenotype in these domains. Integration of large data sets that include omics and genetics data will also be considered. Finally, the utility of this biological progress will be considered in the context of prevention and intervention strategies targeting frailty in older adults.

Communication 2: *Future Implementation Research Priorities,* Qian-Li Xu (Johns Hopkins University, School of Public Health, Baltimore, MD, USA)

Despite being one of the most described Geriatric syndromes, and the broad knowledge that frailty is highly associated with early mortality and disability, there has to date been no broadly successful implementation of frailty into clinical practice. This may be in part due to (i) difficulty to implement new screening tools into specialty practices, (ii) heterogeneity of frailty etiology, and (iii) lack of randomized studies that show clear efficacy of frailty-focused interventions. Substantial barriers for frailty screening remain that include lack of optimal frailty instruments, poor agreement between assessment methods, insufficient evidence-based intervention strategies, and limited clinical resources. A key step in addressing this challenge is to gain a better understanding of frailty etiology and its heterogeneity. To help guide next generation of etiologic research, studies designed to identify markers of disease-specific pathology distinct from frailty manifestations are necessary in order to refute the possibility of frailty as merely a marker of disease severity with questionable added value. If frailty identified using existing tools represents heterogeneous medical conditions that share phenotypic characteristics, but with different causal mechanisms and natural history, no single intervention strategy is likely to be universally effective for everyone. Therefore, innovative trial designs including adaptive and pragmatic trials that prospectively account for heterogeneity should be actively pursued in intervention research. Dr. Xue will outline potential solutions to these issues, including ideas related to new implementation strategies and the development and testing of clinical management strategies that would buffer adverse health impact in frail, older adults.

Communication 3: *Public Health Research Priorities,* Karen Bandeen-Roche (Johns Hopkins University, Baltimore, MD, USA)

Identifying frail older adults promises to anchor personalized geriatric medicine for them; early intervention to forestall frailty itself promises to prolong healthy life for the older population. We identify three areas of urgently needed research to achieve this latter goal. First, improved methods are needed for identifying impending frailty before it becomes disabling. This entails both improved methods for ascertaining prefrailty and leveraging signal-intensive technologies to improve surveillance for frailty in free-living settings. Second, life course determinants of frailty are not well identified, yet their ascertainment will be crucial in order to forestall frailty beginning in midlife or earlier. Particularly little research has addressed attributable risks and years of healthy—yet these arguably are most important metrics for targeting public and community health efforts. Third, substantial disparities in frailty prevalence have been evidenced by social factors, but we have

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little insight on pathways by which to address these. Need remains not only to fully document disparities, but to explain these and develop strategies by which to intervene. Inequities in frailty assessment additionally have been evidenced. In this presentation Dr. Bandeen-Roche will elaborate each challenge and outline methods by which to begin addressing them.

S2- BIOMARKERS OF CELLULAR SENESCENCE: RESULTS FROM THE LIFE, CALERIE, AND HEALTH ABC STUDIES. Nathan K. LeBrasseur *(Mayo Clinic, Rochester, MN, USA))*

Identifying frail older adults promises to anchor personalized geriatric medicine for them; early intervention to forestall frailty itself promises to prolong healthy life for the older population. We identify three areas of urgently needed research to achieve this latter goal. First, improved methods are needed for identifying impending frailty before it becomes disabling. This entails both improved methods for ascertaining prefrailty and leveraging signal-intensive technologies to improve surveillance for frailty in free-living settings. Second, life course determinants of frailty are not well identified, yet their ascertainment will be crucial in order to forestall frailty beginning in midlife or earlier. Particularly little research has addressed attributable risks and years of healthy—yet these arguably are most important metrics for targeting public and community health efforts. Third, substantial disparities in frailty prevalence have been evidenced by social factors, but we have little insight on pathways by which to address these. Need remains not only to fully document disparities, but to explain these and develop strategies by which to intervene. Inequities in frailty assessment additionally have been evidenced. In this presentation Dr. Bandeen-Roche will elaborate each challenge and outline methods by which to begin addressing them.

Communication 1: *Biomarkers of Cellular Senescence Predict Onset of Mobility Disability and are Modifiable by Exercise in Older Adults with Mobility Limitations: Results from the Lifestyle Interventions for Elders (LIFE) Study,* Roger A. Fielding(1), Elizabeth J. Atkinson(2), Thomas A. White(3), Amanda A. Heeren(3), Michelle M. Mielke(4), Nathan K. LeBrasseur(3,5,6) ((1) Nutrition, Exercise Physiology and Sarcopenia Laboratory, Jean Mayer USDA Human Nutrition Research Center on Aging, Tufts University, Boston, USA; (2) Department of Quantitative Health Sciences, Mayo Clinic, Rochester, MN, USA; (3) Robert and Arlene Kogod Center on Aging, Mayo Clinic, Rochester, MN, USA; (4) Department of Epidemiology and Prevention, Wake Forest University School of Medicine, Winston-Salem, NC USA; (5) Department of Physical Medicine and Rehabilitation, Mayo Clinic, Rochester, MN, USA; (6) Paul F. Glenn Center for the Biology of Aging Research at Mayo Clinic, Rochester, MN, USA)

Background: Senescent cells develop in many tissues with advancing age in response to multiple forms of genotoxic, proteotoxic, metabolic, and inflammatory stress and are characterized by distinct changes in morphology, upregulation of cell cycle regulators and anti-apoptosis pathways, alterations in metabolism, and, notably, a marked and pluripotent senescence-associated secretory phenotype (SASP). **Objective:** Using samples obtained from the LIFE study we examined 27 biomarkers of cellular senescence and their association with major mobility disability, and whether these biomarkers were affected in participants randomized to a structured moderate intensity physical activity intervention (PA) compared to a healthy aging intervention (HA). **Methods and Results:** In 1,377 older females and males randomized to PA or HA, we observed significant associations between multiple SASP proteins and the onset of incident and persistent mobility disability. There was no significant difference in any of the SASP proteins between PA and HA at 12 or 24 months. However, when accelerometry assessed physical activity was separated by quartiles from lowest to highest moderate intensity activity (>760 counts/min) at 12 and 24 months, we found a significantly lower concentrations of 10 SASP proteins (eotaxin, IL-15, IL-6, IL-7, MMP1, MMP7, Osteopontin, TNF-a, TNF-R2, VEGF) by quartile of physical activity achieved. **Conclusion:** These data highlight an association between senescence biomarkers and the onset of mobility disability and the potential for physical activity to attenuate these effects in older adults.

Communication 2: *Caloric Restriction Reduces Biomarkers of Cellular Senescence in Humans,* Zaira Aversa(1,2), Beth Atkinson(3), Roger Fielding(4), Nathan K. LeBrasseur(1,2,5) ((1) Robert and Arlene Kogod Center on Aging, Mayo Clinic, Rochester, MN, USA; (2) Department of Physical Medicine and Rehabilitation, Mayo Clinic, Rochester, MN, USA; (3) Department of Quantitative Health Sciences, Mayo Clinic, Rochester, MN, USA; (4) Nutrition, Exercise Physiology and Sarcopenia Laboratory, Jean Mayer USDA Human Nutrition Research Center on Aging, Tufts University, Boston, USA; (5) Paul F. Glenn Center for the Biology of Aging Research at Mayo Clinic, Rochester, MN ,USA)

Background: Calorie restriction (CR) with adequate nutrient intake has emerged as a potential geroprotective intervention. **Objective:** We investigated whether a two-year moderate CR intervention in non-obese young to middle-aged individuals influenced the circulating levels of biomarkers associated with cellular senescence, a state of cell growth arrest triggered by various stressors and implicated in the pathogenesis of aging conditions. We also examined whether the longitudinal changes in circulating senescence-related biomarkers predicted the longitudinal changes in parameters of metabolic health. **Methods:** We examined blood samples and clinical data obtained from the Comprehensive Assessment of Long-term Effects of Reducing Intake of Energy (CALERIE) Phase 2 Study, a two-year, multicenter, randomized controlled trial in healthy non-obese young to middle-aged individuals to examine the feasibility, safety, and effects of moderate CR compared to an ad libitum (AL) diet on predictors of longevity and disease risk factors. **Results:** We found that CR significantly

reduced the circulating levels of several candidate senescence biomarkers compared to an ad libitum diet at 12 and 24 months. By using a machine learning approach, changes in the circulating concentration of several biomarkers emerged as important predictors of the change in resting metabolic rate residual and insulin sensitivity index. Moreover, in a subset of participants, CR significantly reduced the enrichment of a novel gene set (SenMayo) of 125 secreted factors, transmembrane proteins, and intracellular proteins centered on cellular senescence and the senescence-associated secretory phenotype. **Conclusion:** Our results advance the understanding of the effects of CR in humans and suggest a potential link between cellular senescence and measures of metabolic health

Communication 3: *Biomarkers of Cellular Senescence are Associated with Adverse Clinical Outcomes and Mortality in Older Adults,* Steven Cummings(1,2), Lily Liu(2), Nathan LeBrasseur(3,4,5) ((1) Departments of Medicine, Epidemiology and Biostatistics, University of California San Francisco, San Francisco CA, USA; (2) Research Institute, California Pacific Medical Center, San Francisco, CA, USA; (3) Robert and Arlene Kogod Center on Aging, Mayo Clinic, Rochester, MN, USA; (4) Department of Physical Medicine and Rehabilitation, Mayo Clinic, Rochester, MN, USA; (5) Paul F. Glenn Center for the Biology of Aging Research at Mayo Clinic, Rochester, MN, USA)

Background: Senescent cells accumulate with advancing age and contribute to a multitude of aging-related conditions, in part, through their robust SASP (senescence-associated secretory phenotype). Protein components of the SASP that are detectable in the circulation have been used as blood-based biomarkers of systemic senescent cell burden. **Objectives:** Examine whether levels of SASP proteins predict important aging-related clinical outcomes. **Methods:** We studied a panel of 39 proteins that have been identified as components of the SASP in several experimental models. We measured the concentrations of these proteins in archived serum from a random sample of 1,681 participants 70-79 years old from the prospective Health ABC study. We assessed associations between protein levels (analyzed as quartiles (Q)) and the risk (hazard ratios (HR)) of selected clinical outcomes, adjusting for age, sex, race, and BMI. **Results:** We observed multiple associations between individual senescence biomarkers and risk for aging-related clinical outcomes. Notably, GDF-15 had the most consistent and strongest associations with mobility limitations, dementia, heart failure, hip fracture, and mortality, with significant HRs ranging from 1.9-2.6 for Q4 compared to Q1. Similar and significant findings were observed for TNFR1 (1.6-2.7), IL6 (1.8-2.3), MMP7 (1.4-2.0), and activin A (1.3-1.9). **Conclusion:** High serum levels of GDF15, TNFR1, IL6, MMP7, and activin A are associated with elevated risk for mortality, dementia, heart failure, mobility limitation, and hip fracture. These observations support the premise that cellular senescence is a fundamental mechanism of aging and high levels of SASP factors predict the risk of several aging-related conditions.

S3- SOMMA: REIMAGING FRAILTY AND SARCOPENIA.

Peggy M. Cawthon *(California Pacific Medical Center, Research Institute, San Francisco, CA, USA)*

Communication 1: *Classically defined phenotypic frailty and its relationship with muscle mitochondrial energetics in SOMMA,* Theresa Mau(1), Haley Barnes(1), Peggy M. Cawthon(1), Terri L. Blackwell(1), Philip A. Kramer(2), Sofhia V. Ramos(3), Paul M. Coen(3), Russell T. Hepple(4), Stephen B. Kritchevsky(2), Steven R. Cummings(1), Anne B. Newman(5) ((1) California Pacific Medical Center, Research Institute, San Francisco, CA, USA; (2) Wake Forest University, Winston-Salem, NC, USA; (3) Translational Research Institute, Adventist Health, Orlando, FL, USA; (4) ,University of Florida, Gainesville, FL, USA; (5) University of Pittsburgh, Pittsburgh, PA, USA)

A potential biological driver of phenotypic frailty is mitochondrial dysfunction. Age-associated declines in mitochondria have been linked to frailty in older adults, and studies have shown that muscle energetics, measured by 31P magnetic resonance spectroscopy (MRS), in pre-frail or sarcopenic older adults had decreased resting adenosine triphosphate (ATP) and ATPmax compared with age-matched participants. Leveraging data from the Study of Muscle, Mobility, and Aging (SOMMA) cohort (N=873, 58.4% women, 84.9% non-Hispanic white), we investigated phenotypic frailty (the 5 components were defined as follows; shrinking—lowest quintile of D3Cr muscle mass, exhaustion—CES-D questionnaire, weakness—lowest quintile of grip strength stratified by gender and BMI quartile, slowness—lowest quartile of 4-meter walk time stratified by gender and median height, and lowest quintile of physical activity from CHAMPS questionnaire) and its relationship with 2 different measures of muscle mitochondrial energetics: ATPmax determined by 31P MRS and maximal oxidative phosphorylation (Max OXPHOS) measured by high resolution respirometry of vastus lateralis permeabilized muscle fibers. Participants with score of 0 frailty components were considered robust (45.5%), 1 or 2 were pre-frail (47.0%), and 3+ components were frail (7.6%). After full model adjustments, the associations of ATPmax with phenotypic frailty were attenuated (adjusted ATPmax mean = 0.6(robust), 0.5(pre-frail), and 0.5(frail) mM/sec, p=0.22). Whereas, even after fully adjusting for age, gender, race, education, marital status, technician/site, adiposity, height, smoking, alcohol use, and number of morbidities, maximal respiration (OXPHOS) remained significantly associated with frailty status (p<0.001). The adjusted Max OXPHOS mean was 62.7pmol/s*mg (95%CI: 60.9, 64.6) for robust (N=397), 58.2pmol/s*mg (56.3, 60.0) for pre-frail (N=410), and 54.3pmol/s*mg (49.3, 59.3) for frail (N=66) older women and men. There was no gender-interaction between muscle mitochondrial energetics and frailty status. This data suggests that in older adults in SOMMA, higher skeletal muscle mitochondrial respiration is associated with decreased frailty prevalence.

Communication 2: *Relationship of Clinical Sarcopenia Definitions to Aging Muscle Biology in SOMMA,* Russell T. Hepple(1), Peggy M Cawthon(2), Osvaldo Delbono(3), Stephen B. Kritchevsky(3), Anne B. Newman(4), Paul M. Coen(5), Bret Goodpaster(5), Steven R. Cummings(2) ((1) University of Florida, Gainesville, FL, USA; (2) California Pacific Medical Center, Research Institute, San Francisco, CA, USA; (3) Wake Forest University, Winston-Salem, NC, USA; (4) University of Pittsburgh, Pittsburgh, PA, USA; (5) Translational Research Institute, Adventist Health, Orlando, FL, USA)

Sarcopenia was originally defined as the age-related loss of skeletal muscle mass and later evolved to include the reduction in strength with aging. To facilitate clinical research in this area, numerous operational definitions of sarcopenia have been adopted, but the extent to which any clinical sarcopenia definition relates to aging muscle biology is not well established. To this end, we used data generated by the Study of Muscle, Mobility and Aging (SOMMA) for walking speed, whole body muscle mass by D3Cr, quadriceps muscle volume by MRI, knee extensor strength and power, and vastus lateralis muscle histology data in 135 participants (74 women) to provide a means of determining how two current sarcopenia definitions put forth by Sarcopenia Definitions and Outcomes Consortium (SDOC) (Bhasin et al. J Am Geriatr Soc. 68[7]: 1410-18, 2020) and European Working Group on Sarcopenia in Older People (EWGSOP2) (Cruz-Jentoft et al. Age Ageing 48[1]: 16-31, 2019) relate to histological indices of aging muscle biology. Specifically, we used the proportion of grouped fibers (an index of motor unit remodeling consequent to denervation-reinnervation that increases with aging), the type II to type I fiber cross-sectional area ratio (declines with aging), and the proportion of very small muscle fibers (defined as the size corresponding to the first percentile size for healthy young adults and which increases with aging) as indices of aging muscle biology. Amongst the indices, the proportion of very small fibers demonstrated the strongest correlations with muscle strength, muscle power, and 400m walking speed in men ($r=-0.25$, -0.33, and -0.32, respectively, $p<.001$ for all), whereas the type II to type I fiber cross-sectional area ratio had the strongest correlation with quadriceps fat-free muscle mass ($r=-0.16$, $p<.001$ for all). In contrast, in women type II to type I fiber cross-sectional area ratio demonstrated the strongest correlation with muscle strength ($r=-0.15$), the proportion of very small fibers had the strongest correlations with muscle power ($r=-0.19$) and quadriceps fat free muscle mass ($r=-0.23$), and the proportion of grouped type I fibers had the strongest correlation with 400m walking speed ($r=0.18$, $p<.001$ for all).

Communication 3: *SOMMA Frailty: Advancing the Science of Frailty,* Anne B. Newman(1), Steven R. Cummings(2), Russell T. Hepple(3), Peggy M Cawthon(2), Paul M. Coen(4), Bret Goodpaster(4), Stephen B. Kritchevsky(5) ((1) University of Pittsburgh, Pittsburgh, PA, USA; (2) California Pacific Medical Center, Research Institute, San Francisco, CA, USA; (3) University of Florida, Gainesville, FL, USA; (4)Translational Research Institute, Adventist Health, Orlando, FL, USA; (5) Wake Forest University, Winston-Salem, NC, USA)

Physical frailty is a vulnerability to stressors, increasing with age. The frailty syndrome was originally defined using available measures in a cohort study. SOMMA has directly assessed many of the physiologic manifestations of frailty that could lead to more precise diagnostic criteria. We created a new SOMMA frailty scale using peak oxygen consumption, directly assessed muscle mass, leg power, fatigability, actigraphic assessment of physical activity. We will describe its relationship to measures of health and function, including skeletal muscle mitochondrial energetics, in the SOMMA cohort.

S4- DISENTANGLING RELATIONSHIPS AMONG RESILIENCE, FRAILTY, SELF-REPORTED HEALTH: LONGITUDINAL EVIDENCE FROM COMMUNITY AND CLINICAL STUDIES OF OLDER ADULTS.

Qian-Li Xue *(Department of Medicine Division of Geriatric Medicine and Gerontology, School of Medicine, Johns Hopkins University, Baltimore, MD, USA)*

Communication 1: *Frailty and Self-Reported Health as Surrogate Markers of Physiological Resilience: Findings from the SPRING-RESTORE Study,* Brian Buta(1), Fangyu Liu(2), Meredith Dobrosielski(1), Frederick Sieber(3), Julius Oni(4), Jeremy Walston(1), Karen Bandeen-Roche(1,5), Ravi Varadhan(6), Qian-Li Xue(1) ((1) Department of Medicine, Johns Hopkins University, Baltimore, MD, USA; (2) Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA; (3) Department of Anesthesiology and Critical Care Medicine, Johns Hopkins University, Baltimore, MD, USA; (4) Department of Orthopaedic Surgery, Johns Hopkins University, Baltimore, MD, USA; (5) Department of Biostatistics, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA; (6) Department of Oncology, Quantitative Sciences, Johns Hopkins University, Baltimore, MD, USA)

Background: Surrogate markers of physiological resilience capacity, the capacity of a system to recover to or improve upon a baseline level of function after clinical procedures such as total knee replacement (TKR), could be used to flag older patients at high risk for poor outcomes. These surrogates may include frailty and self-reported health (SRH). **Objectives:** We assessed the association between frailty (frail, prefrail, and robust) and SRH (poor/fair, good, very good/excellent) with a resilience phenotype – defined as change in Short Physical Performance Battery (SPPB) scores pre-and post-surgery – in the TKR arm of the Study of Physical Resilience and

agING (SPRING), known as RESTORE (RESilience in TOtal knee REplacement). **Methods:** Our analysis included 114 participants aged 60 and older at the time of recruitment who completed two baseline visits before TKR surgery. 91 and 63 of these participants completed one-month and 4-6-month follow-up visits post-surgery, respectively. The associations of frailty and SRH with SPPB were analyzed using linear regression after adjusting for age, sex, race, education, and number of diseases. **Results:** At baseline, pre-frail and frail participants had significantly lower SPPB score compared to robust participants (p-value=.03 and <.01, respectively), and the association remained significant after adjusting for SRH. The association between SRH and SPPB however was not statistically significant (p-value=.12). Compared to the excellent/very good SRH group, we found a significantly greater drop in SPPB at one-month post-surgery (p-value=.04) and significantly less recovery at 4-6 months after surgery in the fair/poor SRH group (p-value=.03), and the significance remained after adjusting for frailty. No significant differences in decline at one-month (p-value=.12) or recovery at 4-6-months post-surgery (p-value=.99) were found between the frail and the robust. **Conclusion:** Though physical frailty had a stronger association with SPPB than SRH at pre-surgery baseline, only poor or fair SRH status was statistically significantly associated with changes in SPPB scores at post-surgery follow-up visits. SRH likely reflects multidimensional factors, beyond physical function/frailty, that may improve prediction of less resilient phenotypic trajectories.

Communication 2: *Physical Frailty, Self-Reported Health and All-Cause Mortality: Implications for Resilience,* Qian-Li Xue(1,2,4), Nadia M. Chu(3,4), Chenkai Wu(5) Linda P. Fried(6) ((1) Department of Medicine Division of Geriatric Medicine and Gerontology, School of Medicine, Johns Hopkins University, Baltimore, MD, USA; (2) Center on Aging and Health, Johns Hopkins Medical Institutions, Baltimore, MD, USA; (3) Department of Surgery, School of Medicine, Johns Hopkins University, Baltimore, MD, USA; (4) Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA; (5) Global Health Research Center, Duke Kunshan University, Jiangsu, China; (6) Mailman School of Public Health, Columbia University, New York, NY, USA)

Background: Frailty and poor self-reported health (SRH) as potential surrogates of poor resilience are separately associated with all-cause mortality. Whether the associations are independent of each other, of physical disability, and of disease burden, and whether SRH remains predictive of mortality among frail older adults is unknown. **Objectives:** (I) To assess the associations of frailty and SRH jointly with all-cause mortality; (II) To assess the association between SRH and all-cause mortality among the frail subset. **Methods:** We leveraged NHATS, a prospective, nationally-representative cohort of older adult U.S. Medicare beneficiaries, followed annually (2011-2019). Individuals were assessed for frailty (robust, pre-frail, and frail by the physical frailty phenotype) and SRH (excellent/very good, good, or fair/poor) at baseline. Cox models were used to address the study objectives after adjusting for age, race, sex, education, number of diseases, and mobility disability. **Results:** Of 7,425 community-dwelling older adults at baseline, 1,306 (17.6%) were frail and 2,132 (28.7%) reported fair/poor health. Although being frail was positively correlated with fair/poor SRH, 12.4% of those deemed frail reported excellent/very good health and 8.5% reporting fair/poor health were deemed robust. Over a median 4.25-year follow-up, 29.1% of the 7,425 died. Compared to the robust, being pre-frail and frail were associated with 1.4- and 2.0-fold increase in the risk of mortality respectively after adjusting for SRH (p-value<0.01); and reporting good and excellent/very good health were associated with 23% and 36% reduction in mortality risk respectively after adjusting for frailty (p-value<0.01). No significant interaction between frailty and SRH was found (p-value=0.09). Among the frail subset, good and excellent/very good health respectively were associated 24% and 26% reduction in mortality risk (p-value<0.05). **Conclusion:** Physical frailty and SRH, although positively correlated, are not synonymous, a phenomenon resembling the well-being/disability paradox. Physical frailty and SRH were independently predictive of all-cause mortality; and SRH remained highly predictive among the frail. Future investigation into the determinants of positive SRH despite of being frail could provide important targets for intervention to improve resilience, and for risk screening of downstream outcomes in those most vulnerable.

Communication 3: *Interactions between Self-Reported Health and Free-Living Movement Patterns on Frailty Incidence,* Amal A. Wanigatunga(1), Brian Buta(2,3), Jennifer A. Schrack(1,3) Yurun Cai(4), Jeremy D. Walston(2,3), Karen Bandeen-Roche(5,3), Lawrence J. Appel(2,6), Qian-Li Xue(2,3 ((1) Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA; (2) Department of Medicine, School of Medicine, Johns Hopkins University, Baltimore, MD, USA; (3) Center on Aging and Health, Johns Hopkins Medical Institutions, Baltimore, MD, USA; (4) School of Nursing University of Pittsburgh School of Nursing, Pittsburg, PA, USA; (5) Department of Biostatistics, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA; (6) The Welch Center for Prevention, Epidemiology, and Clinical Research, Johns Hopkins Medical Institutions, Baltimore, MD, USA)

Background: Self-reported health (SRH) is emerging as a marker of physiological resilience defined as homeostatic recovery from adverse stressors and intervening events. Whether lower SRH leads to higher incidence of physical frailty (a severe form of homeostatic imbalance), and whether this relationship is modified by free-living patterns of everyday movement, have not been explored. **Objectives:** To examine whether SRH was associated with incident frailty, and whether accelerometer-derived movement patterns modified the relationship of SRH with incident frailty. **Methods:** Using STURDY (Study to Understand Fall Reduction and Vitamin D

in You) data from 476 robust/prefrail adults (mean age=76+5 years; 41% women), we examined whether SRH rated as either poor, fair, good, very good or excellent (treated as a continuous variable) was associated with incident frailty using Cox regression models. In addition, we tested whether accelerometer-derived activity counts/day, active minutes/day, activity fragmentation (e.g., less continuous active time), and sedentary fragmentation (e.g., less prolonged sedentary time) modified the relationship of SRH with incident frailty. Models were adjusted for demographics, body mass index, intervention, medical conditions, and device wear days. **Results:** Over 2 years of follow-up, 42 (9%) participants developed frailty. For each lower category of SRH, there was a 66% higher frailty risk (HR: 1.66; 95% CI: 1.08-2.55). An interaction between SRH and sedentary fragmentation on frailty risk was observed in that the protective effect of sedentary fragmentation on frailty risk was attenuated among those reporting poorer health compared to those reporting better health (p-value=0.04). The same was not observed for other activity metrics (interaction p-values>0.11 for all). **Conclusion:** The negative relationship between SRH and frailty incidence supports the hypothesis that self-reported health is a potential surrogate marker of resilience. The interaction between sedentary fragmentation and SRH suggests the protective association between breaking up sedentary behaviors and frailty incidence is strengthened with higher SRH. Further research is needed to show that the success of interventions that reduce sedentary behaviors or increase activity might rely on SRH.

S5- TRANSLATIONAL GEROSCIENCE IN SARCOPENIA AND FRAILTY: BIOLOGY, BIOMARKERS AND BIG DATA. John A. Batsis *(School of Medicine (Geriatric Medicine) and Gillings School of Global Public Health (Nutrition), University of North Carolina at Chapel Hill, Chapel Hill, NC, USA)*

This symposium aims to highlight the importance of translational geroscience in sarcopenia and frailty through aging biology, biomarkers, and big data. Professor Duque will begin by describing the geroscience hypothesis as a framework for conceptualizing how aging biology may contribute to age-related changes in muscle, bone, and fat. This hypothesis theorizes that pathophysiological changes observed with age result from perturbations in one of several fundamental biological processes. These changes alter musculoskeletal, metabolic, and stress response physiology, resulting in common geriatric syndromes, including osteoporosis, sarcopenia and frailty. In this talk, we will outline how the geroscience hypothesis has contributed to an increased understanding of the interconnected relationship between changes that occur in muscle, bone, and fat with aging. He will summarize current state of the science and outline promising areas of future research. This will be followed by a presentation by Dr. Justice. She will elaborate and describe the geroscience hypothesis that posits that understanding and addressing chronic diseases, functional decline, and frailty requires a “root cause” approach: to focus on dysregulation of fundamental aging processes rather than individual diseases or conditions. The promise of the geroscience approach is supported by specific examples of translational research models. We are now testing the geroscience hypothesis in clinical trials of pharmacologic (e.g. metformin, senolytics) and lifestyle interventions that may improve healthspan and prevent or delay frailty. This requires new clinical trial frameworks, aging outcomes, and biomarkers. In this session we will outline how geroscience studies have advanced frailty science. She will also provide an overview of promising geroscience interventions, and considerations for trials to test specific approaches in translational research and interventions testing. Finally, the symposium will conclude with Dr. Batsis, who will describe the importance of lifestyle interventions, including diet and exercise. These can mitigate such adverse outcomes associated with sarcopenia and frailty; however, differential response to treatment is often observed due to clinical and biological heterogeneity. Tailoring interventions based on individual characteristics may optimize response. However, there is little evidence to guide such strategies. Precision medicine analytics can be leveraged to explore the biological mechanism underlying the heterogeneity observed in treatment responses. It can also facilitate the targeting of interventions in novel adaptive trial designs. In this session we will review how precision medicine and geroscience principles have been combined in frailty and sarcopenia research and outline potential avenues for future studies.

Communication 1: *How Geroscience can help us understand the muscle-bone-fat interaction,* Gustavo Duque (Division of Geriatric Medicine, McGill University, Montreal, Canada)

The geroscience hypothesis offers a framework for conceptualizing how aging biology may contribute to age-related changes in muscle, bone, and fat. This hypothesis theorizes that pathophysiological changes observed with age result from perturbations in one of several fundamental biological processes. These changes alter musculoskeletal, metabolic, and stress response physiology, resulting in common geriatric syndromes, including osteoporosis, sarcopenia and frailty. In this talk, we will outline how the geroscience hypothesis has contributed to an increased understanding of the interconnected relationship between changes that occur in muscle, bone, and fat with aging. We will summarize current state of the science and outline promising areas of future research.

Communication 2: *Translational Geroscience in Frailty and Sarcopenia – the past, present, and future,* Jamie Justice (Section on Gerontology and Geriatrics, Department of Internal Medicine, and Sticht Center on Healthy Aging and Alzheimer’s Prevention, Wake Forest University School of Medicine (WFUSM), Winston Salem, NC, USA)

The geroscience hypothesis posits that understanding and addressing chronic diseases, functional decline, and frailty requires a “root cause” approach: to focus on dysregulation of

fundamental aging processes rather than individual diseases or conditions. The promise of the geroscience approach is supported by specific examples of translational research models. We are now testing the geroscience hypothesis in clinical trials of pharmacologic (e.g. metformin, senolytics) and lifestyle interventions that may improve healthspan and prevent or delay frailty. This requires new clinical trial frameworks, aging outcomes, and biomarkers. In this session we will outline how geroscience studies have advanced frailty science. We will also provide an overview of promising geroscience interventions, and considerations for trials to test specific approaches in translational research and interventions testing.

Communication 3: *The interplay between Precision Medicine and Geroscience in Aging Research,* John A. Batsis (Division of Geriatric Medicine and Department of Nutrition, University of North Carolina at Chapel Hill, NC, USA)

Lifestyle interventions, including diet and exercise, can mitigate such adverse outcomes associated with sarcopenia and frailty; however, differential response to treatment is often observed due to clinical and biological heterogeneity. Tailoring interventions based on individual characteristics may optimize response. However, there is little evidence to guide such strategies. Precision medicine analytics can be leveraged to explore the biological mechanism underlying the heterogeneity observed in treatment responses. It can also facilitate the targeting of interventions in novel adaptive trial designs. In this session we will review how precision medicine and geroscience principles have been combined in frailty and sarcopenia research and outline potential avenues for future studies.

S6- INNOVATIVE FRAILTY AND SARCOPENIA RESEARCH UPDATE FROM ASIA. Hidenori Arai *(National Center for Geriatrics and Gerontology, Tokyo (Japan))*

As Asians have different physiques and cultural and social backgrounds compared to people in Europe and the U.S., we have been seeking our approaches regarding sarcopenia and frailty. For example, the AWGS diagnostic criteria for sarcopenia, revised in 2019, takes a slightly different approach than the EWGSOP, whereas Japan has issued diagnostic criteria for sarcopenic dysphagia and Taiwan has issued the physio-cognitive decline syndrome, which focuses on the interaction between skeletal muscle and brain. We hope that this symposium will also lead to global innovation by introducing new and unique concepts and interventions related to sarcopenia and frailty.

Communication 1: *Muscle-Brain Crosstalk in Healthy Aging,* Liang-Kung Chen (Center for Healthy Longevity and Aging Sciences, National Yang Ming Chiao Tung University, Hsin-Chu, Taiwan; Center for Geriatrics and Gerontology, Taipei Veterans General Hospital. Taipei, Taiwan; Taipei Municipal Gan-Dau Hospital Taipei, Taiwan)

Background: Healthy aging is defined as the process of developing and maintaining the functional ability that enables well-being in older age. The core elements of the so-defined "functional ability" consist of physical, cognitive, sensory, and social dimensions. In epidemiological studies and intervention trials, exercise has been reported to play important role in preventing the development of disability and dementia. Despite the well-evidenced favorable effects of exercise in preventing cognitive declines, the molecular mechanisms remain less clear. Studies have identified several myokines secreted by skeletal muscle, e.g., cathepsin B and irisin, contribute to the regulation of neuron senescence and hippocampal function. Besides, exercise also increases the PGC1α-dependent muscular expression of kynurenine aminotransferase enzymes, which leads to the beneficial balance between the neurotoxic kynurenine and the neuroprotective kynurenic acid that reduces depression-like symptoms. Meanwhile, atrophic skeletal muscle fibers secrete exosomes containing miR-29b-3p that induce senescence of human neurons prepared by the iPSC platform. The circulatory miR-29b-3p appears in dexamethasone-induced skeletal muscle atrophy and in the plasma of older people with sarcopenia. Hence, the muscle-brain crosstalk clearly disclosed the substantial interactions between muscle and brain through circulation instead of the nervous systems. Therefore, an integrated approach to promoting healthy aging by preventing the development of disability and dementia with a more comprehensive mechanistic understanding would benefit the clinical efficacy of healthy aging interventions.

Communication 2: *Innovative approaches for sarcopenic dysphagia: Japan's experiences,* Keisuke Maeda (Department of Geriatric Medicine, Hospital, National Center for Geriatrics and Gerontology, Aichi, Japan)

Older adults may face a risk of swallowing problems. The novel etiology of dysphagia, sarcopenic dysphagia, is gathering great attention in the field of geriatric nutrition. In 2019, four academic societies in Japan published a position paper focusing on the concept, definition, and diagnostic criteria of sarcopenic dysphagia. Current proposed diagnostic criteria for sarcopenic dysphagia include the presence of sarcopenia and dysphagia without apparent cause of dysphagia, such as stroke or neurodegenerative disease, and the presence of low tongue strength. The prevalence of sarcopenic dysphagia has been reported as 13-42% in older inpatients. The risk factors for developing sarcopenic dysphagia are poor physical function, malnutrition, and highly advanced sarcopenia. Since sarcopenic dysphagia develops in association with sarcopenia and many factors are associated with the development of sarcopenic dysphagia, physical and nutritional interventions may improve

swallowing muscle function. We recently reported the impact of physical intervention and nutritional intake on increasing tongue strength. The results indicated that physical intervention with nutritional support in addition to swallowing exercises would be necessary to treat sarcopenic dysphagia. Furthermore, another study reported that aggressive nutrition therapy for patients with sarcopenic dysphagia could contribute to better swallowing function in a rehabilitation hospital. In the statistical model, swallowing function and rates of achieved the minimal clinically important difference of activities of daily living at discharge from the hospital were significantly higher in the mean provided energy ≥ 30 kcal/day (kg) group (p=.004 and P<.001, respectively). Aggressive nutritional support for sarcopenic dysphagia would be vital to improve swallowing function. In summary, we would like to focus on new mechanisms of sarcopenic dysphagia in Japan. In addition, its prevention and treatment require a systemic approach, and the strategy differs somewhat from conventional dysphagia rehabilitation. Physical and nutritional care combined with traditional intervention will probably be essential candidates.

Communication 3: *Renovation of DXA, BIA for diagnosis of sarcopenia,* Chang Won Won (Department of Family Medicine College of Medicine, Kyung Hee University, Seoul, South Korea)

Some Studies show that "measuring muscle mass is not helpful in prediction of bad outcomes and raised uselessness of muscle mass measurement by DXA or BIA in diagnosis of sarcopenia. However, lean mass by CT is significantly associated with outcomes. Therefore, muscle itself is not a culprit, but the modality for muscle measure matters. Then how can we improve correctness of DXA, BIA in assessing skeletal muscle mass through make-up for its shortcomings? 1. BIA : With an advent of multi-frequency BIA from 1 kHz to 1 MHz, more accurate analysis of body composition without relying on empirical estimations became possible. But, it still has inaccuracy. Recently developed high-frequency BIA use the 3 MHz high-frequency measurement technology seems to increase the accuracy of muscle mass analysis. 2. DXA: Though DXA is a recommended method of appendicular lean mass(ALM) measure, it does not assess muscle mass directly, and the ALM assessed includes intramuscular fat, and connective tissue, and therefore overestimates skeletal muscle mass. If we can estimate intramuscular fat, we could improve the correctness of DXA for muscle measure.

S8- CONCEPTUALIZATION, ASCERTAINMENT AND IMPLICATIONS OF PREFRAILTY AS A PUBLIC HEALTH PRIORITY.

Karen Bandeen-Roche *(Department of Biostatistics, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA)*

Communication 1: *Pre-Frailty as an Important Public Health Condition,* Rónán O'Caoimh (University College Cork and Mercy University Hospital, Cork, Ireland)

There is a growing recognition that frailty is a public health priority. Hence, early identification of frailty is important to prevent or at least mitigate its adverse consequences, particularly functional decline and disability at both individual and population-level. Recent research has focused on understanding the nature of frailty at its earliest prodromal stage, often referred to as pre-frailty. This may represent an optimal target for public health interventions. However, it currently lacks a recognised definition, which is particularly important to support comparability across populations and types of interventions. A recent international Delphi consensus conducted by this research team suggests that pre-frailty is an aged-associated, multi-factorial, multi-dimensional, and non-linear prodromal risk-state associated with one or more of physical impairment, cognitive decline, nutritional deficiencies and socioeconomic inequalities, predisposing to the development of frailty. Differences in the operationalisation of pre-frailty present a marked challenge to understanding its epidemiology as prevalence, incidence and outcome rates vary considerably by definition. For example, the prevalence of pre-frailty in population-level studies varies from as low as 24% with the Edmonton Frail Scale to as high as 50% with the deficit accumulation model (frailty index). However, the number and type of studies using different measures of pre-frailty vary markedly introducing significant heterogeneity. This research communication provides an up-to-date overview of pre-frailty in a public health context, examining its core features including proposed definitions, current epidemiology, and data exploring its clinical associations and outcomes.

Communication 2: *Next-generation prefrailty assessment in the Physical Frailty Phenotype,* Karen Bandeen-Roche, Charlotte Clapham (Department of Biostatistics, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA)

Regular frailty assessment has been recommended for older adults' health management. To maintain health, prefrailty assessment is as important. With the physical frailty phenotype (PFP), prefrailty defined as 1-2 PFP criteria has been shown to predict adverse health outcomes, but its reliance on a low number of criteria may limit its psychometric strength and diagnostic specificity. A recent international Delphi consensus study affirmed need for improved assessment of pre-frailty as an initially silent risk state which predisposes to frailty onset, disability, and adverse outcomes if poorly managed; the PFP further hypothesizes as etiology an unraveling network of physiological systems governing stress response. This paper

explores potential for an improved schema by which to evaluate candidate pre-frailty measures adhering to these concepts—by (1) considering alternative prefrailty assessments employing measures underlying PFP criteria differently than the current definition, or augmenting these; and (2) evaluating reliability and predictive validity for incident frailty and selected downstream outcomes of the candidate measures. Analyses leverage the Women's Health and Aging Studies (WHAS) I and II. Exemplifying approaches: An alternative prefrailty assessment was created by distinguishing 3 population subclusters via latent profile analysis: An intermediate cluster was similar to a most frail cluster on grip strength and relatively similar on energy (both distinguished from a robust cluster); relatively similar to a robust subcluster on physical activity and weight change (both distinguished from a frail subcluster); and distinguished in a stepwise fashion across clusters by gait speed. Downstream outcomes to be considered in predictive validity analyses include onset of frank frailty, mobility dependence and mortality. The project aims to inform design of (a) a formal conference to elicit further expert opinion/ identify research gaps and (b) a de novo study to develop next-generation measures.

Communication 3: *Effects of Pre-frailty in Working Middle-aged and Older Adults in Europe,* Duygu Sezgin (University of Galway, Galway, Ireland)

People with chronic conditions may develop pre-frailty while still being of working age and this may affect their performance. As the dependency ratio increases in many developed countries, more people must continue working for longer. Extending the working age is also essential for many individuals to minimise income loss and subsequent medical debt associated with managing chronic conditions. To date, studies investigating the link between pre-frailty and work ability of middle-aged and older individuals who work despite suffering from chronic diseases are limited. Further, it is not yet well-known how chronic diseases and pre-frailty affect the perceptions of working middle-aged and older adults on their ability to work despite having health issues and therefore having plans for early retirement. We conducted a study to identify the prevalence of pre-frailty and investigate the association between pre-frailty, fear of health limiting ability to work, and plans for early retirement in working middle-aged and older adults. Data from 29 European countries was gathered using waves 1-8 of the Survey of Health, Ageing and Retirement in Europe (SHARE, 2004-2020). We included participants aged 50 years and over with data on employment and frailty status in the data analyses. Pre-frailty was identified using a modified version of the Fried et al. criteria. A total of 38,220 participants (mean age 55.7±3.8) were included. Thirty-six per cent (13,909) were pre-frail, 46% (17,614) looked for early retirement, and 30% (11,406) were afraid that their health would limit their ability to work. After adjusting for age and sex, logistic regression analyses indicated that those with pre-frailty were more likely to have a fear of health limiting their ability to work and were more likely to have plans for early retirement. We found that pre-frailty may limit middle-aged and older individuals' ability to work and may lead to plans for early retirement. It is important to understand the significance of early frailty in work life so that effective preventative measures and management strategies can be implemented.

Oral Communications

OC1- THE APELIN RECEPTOR AGONIST BGE-105 PREVENTS MUSCLE ATROPHY INDUCED BY BED REST IN HEALTHY VOLUNTEERS AGED ≥ 65 YEARS. Ann Neale(1), Eric Wang(1), Eric Morgen(1), Kristen Fortney(1), Patrick Martin(1), Kristen Reiman(1), Paul Rubin(1), William Evans(2) *((1) BioAge Labs, Richmond, CA, USA; (2) Nutrition Sciences & Toxicology, University of California Berkeley, CA, USA)*

Background: The apelin peptide promotes regeneration and repair of skeletal muscle. BioAge's AI-driven analysis of human aging profiles revealed that people with higher apelin pathway activity as they age live longer and healthier lives. Loss of apelin activity with age is correlated with multiple morbidities. **Objectives:** BioAge tested the small molecule BGE-105, an apelin receptor agonist, in a Phase 1b clinical trial for prevention of muscle atrophy in older people. **Methods:** Healthy volunteers 65 or older were subjected to a 10-day course of strict bed rest, during which they received daily intravenous infusions of BGE-105 (n=11) or placebo (n=10). Thigh circumference, ultrasound measurements of the vastus lateralis, Goutallier grade (an index that quantifies fatty degeneration in muscle), and muscle protein synthesis were recorded before and after bed rest. **Results:** Bed rest resulted in muscle atrophy on day 10 of the study. BGE-105 improved all muscle parameters relative to placebo: thigh circumference (placebo: -6.4% vs. baseline; BGE-105: +0.8% vs baseline; $p < 0.001$), vastus lateralis diameter (placebo: -21.2%; BGE-105: -5.7%; $p < 0.01$); and vastus lateralis cross-sectional area (placebo: -19.5%; BGE-105: -8.0%; $p < 0.05$). Goutallier grade worsened in 8 of 10 volunteers on placebo vs. 1 of 11 volunteers receiving BGE-105 ($p < 0.005$). Bed rest decreased synthesis of muscle proteins, and this effect was significantly ameliorated by BGE-105 (placebo: 15.9%; BGE-105: 22.0%; $p < 0.005$). All percentages are relative to baseline before initiation of bed rest. No severe adverse effects were observed. **Conclusion:** Daily treatment with BGE-105 significantly improved multiple metrics of muscle atrophy in healthy older people on bed rest. BGE-105 may have prevented reductions in muscle dimensions by increasing the rate of muscle protein synthesis. Diseases associated with muscle atrophy, including acute myopathies in mechanically ventilated ICU patients and chronic illnesses driven by progressive loss of muscle function with age, affect millions of people each year. Given that there are no effective therapies for diseases of muscle aging, the trial data warrant further clinical investigation of BGE-105 for acute and chronic indications.

OC2- IMPACT OF L-CITRULLINE SUPPLEMENTATION AND LOW-INTENSITY RESISTANCE TRAINING ON LEG ENDOTHELIAL FUNCTION, LEAN MASS, AND STRENGTH IN POSTMENOPAUSAL WOMEN WITH HYPERTENSION.
Arturo Figueroa(1), Arun Maharaj(2), Stephen M. Fischer(1), Katherine N. Dillon(1), Mauricio A. Martinez(1), Yejin Kang(1) *((1) Department of Kinesiology and Sport Management, Texas Tech University, Lubbock, TX, USA; (2) Department of Epidemiology and Cancer Control, St. Jude Children's Research Hospital, Memphis, TN, USA)*

Background: Sarcopenia is associated with reduced endothelial function (flow-mediated dilation [FMD]) and hypertension. L-citrulline (CIT), an arginine and nitric oxide precursor, has improved blood pressure in hypertensive women and lean mass (LM) in malnourished older women. Low-intensity resistance training (LIRT) has increased strength but not LM in older women. CIT supplementation combined with aerobic training increased muscle strength but not LM in dynapenic older adults. **Objectives:** The aim of this study was to test the hypothesis that CIT supplementation combined with LIRT would have additive benefits on leg endothelial function, LM, and muscle strength in postmenopausal women with hypertension. **Methods:** Twenty-four postmenopausal women aged 50-75 years were randomized to either 10g/day of CIT (n= 13) or placebo (PL, n= 11) alone for 4 weeks and combined with LIRT (CIT+LIRT or PL+LIRT) for another 4 weeks. Leg endothelial function was measured using superficial femoral FMD. Leg LM was measured using DEXA. Muscle strength was measured using leg curl 10RM. LIRT consisted of 3 sets of four leg exercises at 40-50% of 1RM, 3 days/week. Measurements were performed at 0, 4, and 8 weeks. **Results:** CIT supplementation increased FMD compared to PL after 4 weeks (CIT:1.8$\pm$0.3% vs. PL:-0.2$\pm$0.5%, P=0.004) and 8 weeks (CIT+LIRT:2.7$\pm$0.5% vs PL+LIRT:-0.02$\pm$0.5, P=0.003). CIT alone for 4 weeks did not improve leg LM or strength. CIT+LIRT increased leg LM compared to PL+LIRT (0.5$\pm$0.2 kg vs 0.1$\pm$0.1 kg, P=0.046). The increase in leg curl strength from baseline was greater after CIT+LIRT compared to PL+LIRT (6.9$\pm$0.9 kg vs. 3.3$\pm$0.9 kg, P=0.04). There was a significant correlation between changes in FMD and leg LM (r= 0.44, P= 0.03) but not with changes in leg strength (r= 0.32, P= 0.13) during the combined interventions. **Conclusion:** CIT supplementation alone for 4 weeks improved leg endothelial function but not leg LM and strength. CIT supplementation had and additive effect on leg muscle strength. Our findings suggest that CIT supplementation combined with LIRT induced greater increases in leg LM via improved endothelial function in postmenopausal women with hypertension.

OC3- LIVING LONGER BUT FRAILER? TRENDS IN LIFE EXPECTANCY AND FRAILTY IN OLDER SWEDISH ADULTS.
Clare Tazzeo(1), Debora Rizzuto(1,2), Amaia Calderón-Larranaga(1,2), Serhiy Dekhtyar(1,2), Alberto Zucchelli(1,3), Xin Xia(1), Laura Fratiglioni(1,2), Davide Liborio Vetrano(1,2) (*(1) Aging Research Center, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet and Stockholm University, Stockholm, Sweden; (2) Stockholm Gerontology Research Center, Stockholm, Sweden; (3) Department of Information Engineering, University of Brescia, Brescia, Italy)*

Background: Frailty – a clinical syndrome characterized by physiological vulnerability to stressors – is one of the greatest threats to healthy aging. However, it is unclear whether there has been an expansion or compression of frailty over time with increases in life expectancy. **Objectives:** This study aims to: 1) examine frailty state transitions by birth year, and 2) assess whether there has been an expansion or compression of years of life spent frail across birth cohorts. **Methods:** We analyzed approximately 15 years of follow-up data from 2941 individuals, aged 60+ years, participating in the Swedish National study on Aging and Care in Kungsholmen (SNAC-K; baseline 2001-2004). A 40-deficit frailty index (FI) was built, and three frailty states were identified: robust (FI $\leq$ 0.125), mild frailty (0.125 < FI $\leq$ 0.25), and moderate & severe frailty (FI > 0.25). Multi-state survival analyses were implemented to compute frailty-state transitions; hazard ratios for the transitions were obtained with birth year and sex as predictors, also adjusting for age. Frailty state-specific life expectancies for robust persons at age 60 were estimated by birth cohort and sex. **Results:** Forecasted life expectancy increased, but a greater proportion of life was spent frail, in later birth cohorts. Hazards of transitioning from mild frailty to death (hazard ratio [HR]: 0.89; 95% confidence interval [CI]: 0.83-0.97) and moderate and severe frailty to death (HR: 0.98; 95% CI: 0.97-0.99) were lower with later birth year. Unfavourable transitions from robust to mild frailty (HR: 0.81; 95% CI: 0.70-0.93), mild frailty to moderate and severe frailty (HR: 0.80; 95% CI: 0.68-0.93), and moderate and severe frailty to death (HR: 0.68; 95% CI: 0.59-0.78) were less likely among women. Women had a greater predicted life expectancy than men, but more time was spent frail; this difference attenuated over time. **Conclusion:** Our results point to an expansion of frailty in older Swedish adults and an attenuation in discrepancies in life expectancy by sex. As population aging continues, it is more important than ever that we continue to monitor frailty trends to inform resource allocation and preventive strategies that promote resiliency and independence in older adults.

OC4- IDENTIFICATION OF BIOMARKERS OF FRAILTY IN SILICO. Kristina Tomkova, Adewale Adebayo, Gavin Murphy, Marcin Wozniak *(Department of Cardiovascular Sciences, University of Leicester, Leicester, UK)*

Introduction: Frailty is a syndrome characterised on a symptomatic level by loss of muscle mass, weakness, low energy levels and overall vulnerability to stressors. However, the lack of a molecular definition of frailty presents a barrier for researchers and clinicians in developing effective interventions or specialised care for patients suffering from this syndrome. **Objectives:** This study aimed to identify gene expression signatures and potential biomarkers characteristic of frailty. **Methods:** Transcriptomic profiles from frail, non-frail, old and young individuals were retrieved from the NCBI Gene Expression Omnibus repository using E-utilities. Differential gene expression analysis was performed using the LIMMA pipeline, gene set enrichment analysis using Reactome annotations, highly correlated genes were identified using weighted correlation network analysis, and a random forest algorithm was used to identify the most discriminatory transcripts. **Results:** Ten studies with 553 individual samples, each examining 13 991 genes, were included. This data comprised of 315 peripheral blood mononuclear cell (PBMC) samples, 28 CD8 cell samples, and 209 muscle tissue samples. Genes involved in nucleolar processes, mitochondrial function, translation and muscle contraction were most affected in samples from frail patients (FDR < 0.001). Small nucleolar RNAs (SNORDs) were the most discriminatory and predicted frailty with high accuracy. The results also indicated that frailty is an independent phenomenon compared to biological ageing. Old age affected a wide variety of pathways including protein translation, immunity, and cell cycle, while frailty affected a more specific portfolio of pathways revolving around nucleolar processes, mitochondrial function and muscle contraction. Further analysis indicated that frailty might be tissue specific. **Conclusion:** Our results suggest that nucleolar processes, including ribosomal assembly, mainly driven by SNORDs, are potentially a frailty-specific mechanism that likely lead to dysregulation of mitochondrial function and changes in the expression of muscle proteins.

OC5- ASSOCIATION BETWEEN DEPRESSIVE SYMPTOMS AND FRAILTY BY DIFFERENT PHYSICAL ACTIVITY LEVELS IN EUROPEAN COMMUNITY-DWELLING OLDER ADULTS ENROLLED IN THE DO-HEALTH TRIAL – A THREE-YEAR PROSPECTIVE OBSERVATIONAL ANALYSIS. Michael Gagesch(1,2), Stephanie Gängler(1,2), Michèle Mattle(1,2), Reto W. Kressig(3), Bruno Vellas(4), Gregor Freystätter(1,2), Heike A. Bischoff-Ferrari(1,2,5) for the DO-HEALTH investigators *((1) Department of Aging Medicine and Aging Research, University Hospital Zurich and University of Zurich, Zurich, Switzerland; (2) Centre on Aging and Mobility, University Hospital Zurich, City Hospital Zurich Waid and University of Zurich, Zurich, Switzerland; (3) University Department of Geriatric Medicine FELIX PLATTER, Basel, Switzerland; (4) Gérontopôle, Toulouse University Hospital, University of Toulouse, UMR INSERM 1027, Toulouse, France; (5) University Clinic for Acute Geriatric Care, City Hospital Waid and Triemli, Zurich, Switzerland)*

Background: Mechanisms leading to frailty root in multi-system dysregulations. In addition, mental health has been associated with an increased frailty risk. Prior studies indicate a bidirectional association of frailty and depressive symptoms. However, longitudinal data as well as data on potential modifiers including physical activity (PA) and sedentary behavior (SB) are limited. **Objectives:** We aim to investigate a) the association of baseline depressive symptoms (DS) in robust participants with incident pre-frailty/frailty over 3 years, and b) the association of change in DS from baseline to year 3 with time, and the incidence of pre-frailty/frailty in the same timeframe. Additionally, we will investigate these associations stratified by different baseline PA and SB levels. **Methods:** This is a prospective observational analysis of 1,137 DO-HEALTH participants robust at baseline (mean age, 74.3 years; 56.5% women, mean gait speed 1.18 m/s). DO-HEALTH is a multi-center clinical trial in community-dwelling European adults aged 70+. We operationalized frailty by the Fried physical frailty phenotype (robust/pre-frail/frail). DS were assessed with the Geriatric Depression Scale 15 items (GDS-15). Levels of PA and SB were classified based on the Nurses' Health Study Physical Activity Questionnaire. **Results:** We will present population characteristics overall and by DS status at baseline. To report the association of baseline GDS-15 scores and incident pre-frailty/frailty we will present odds ratios and 95% confidence intervals from a generalized estimating equation model for repeated binary outcomes for each outcome after adjustments. Predefined adjustments are age, sex, BMI, study center, cognitive function, presence of pain, use of antidepressant drugs, faller status at baseline, DO-HEALTH treatments, time, and their interaction. A stratified analysis by level of PA and SB will be performed, i.e. meeting WHO PA guidelines vs. not meeting WHO PA guidelines; and high vs. low reporting of sedentary behavior. **Conclusion:** Our analysis aims to contribute important knowledge on the association of incident pre-frailty/frailty and DS at baseline and DS change

over three years of follow up in generally healthy participants aged 70+, recruited from five European countries. Additionally, novel data on the influence of different levels of PA and SB on the exposure-disease relationship will be discussed.

OC6- ASSOCIATION BETWEEN THE SEVERITY OF THE DISEASE AND THE RISK OF SARCOPENIA IN PEOPLE WHO RECOVERED FROM COVID-19. Ester Wiggers(1), Gabriel Peinado Costa(2), Paulo Giusti Rossi(3), Átila Alexandre Trapé(2) *((1) Geriatric Department, University of São Paulo, Ribeirão Preto, São Paulo, Brazil; (2) School of Physical Education and Sport of Ribeirão Preto, University of São Paulo, Ribeirão Preto, São Paulo, Brazil; (3) Department of Physical Therapy, Federal University of São Carlos, São Carlos, Brazil)*

Background: Some studies have investigated the relationship between anthropometric variables, such as body mass index and waist circumference, with the severity of COVID-19. However, more specific body composition assessments, such as the one performed through Dual-energy X-ray absorptiometry (DXA), have yet to be explored to study the relationship with the severity of COVID-19. Objectives: To verify the association between the severity of COVID-19 and the risk of sarcopenia in recovered COVID-19 patients. **Methods:** Descriptive and cross-sectional study. Volunteers (aged 30-69 years old) were selected from the community between September and October 2020, about 30 days after recovery from clinical signs or medical discharge. We assessed body composition at baseline by DXA, with the measurement of the skeletal mass index (SMI), physical fitness by 30-s chair stand (CS), and agility and dynamic balance (AGI). Information related to sex and age was collected. COVID-19 severity was classified into four categories: mild: common flu-like symptoms without dyspnea (n=16), moderate: common flu-like symptoms with dyspnea (n=49), severe: hospitalization (n=10), and critical: hospitalization with intensive care (respirator) (n=8). The risk of sarcopenia was classified following the criteria of Janssen et al. into three categories: regular grade, grade 1 risk, and grade 2 risk. Quantitative variables are presented as mean (standard deviation), and categorical variables are presented as relative frequency. The association has been verified by Fisher's exact test, and correlation strength was verified through Pearson (continuous variables) and Spearman (discrete variables), with a 5% significance level. Results: The sample consisted of 83 participants aged 48.5(9.8) without a difference ($p>0.05$) between groups. An association between COVID-19 severity and sarcopenia risk could be observed ($\chi2=13.5$; $df=3$; $p<0.05$), as severity mild, moderate, severe, and critical had 24.5%, 70.7%, 2.4%, and 2.4% for no risk of sarcopenia, respectively, versus 14.3%, 47.6%, 21.4%, and 16.7% for grade 1 sarcopenia risk. Additionally, CS (number of repetitions) correlated positively (r=0.49), and AGI (time to complete the circuit) correlated negatively (r=-0.54) to SMI. **Conclusion:** The COVID-19 severity was associated with SMI classification, with severity 3 and 4 more frequent for grade 1 sarcopenia risk. Additionally, the SMI score correlated moderately with physical fitness. **Keywords:** sarcopenia, COVID-19, body composition.

OC7- BIOCHEMICAL MARKERS OF MUSCULOSKELETAL HEALTH AND AGING TO BE ASSESSED IN CLINICAL TRIALS OF DRUGS AIMING AT THE TREATMENT OF SARCOPENIA. Aurélie Ladang(1), Charlotte Beaudart(2), Jean-Yves Reginster(2,3), Nasser Al-Daghri(3), Olivier Bruyère(2), Nansa Burlet(2), Matteo Cesari(4,5), Antonio Cherubini(6), Mario Coelho da Silva(7), Cyrus Cooper(8), Alfonso J. Cruz-Jentoft(9), Francesco Landi(10), Andrea Laslop(11), Stefania Maggi(12), Ali Mobasheri(2,13-15), Sif Ormarsdottir(16), Régis Radermecker(17), Marjolein Visser(18), Maria Concepcion Prieto Yerro(19), René Rizzoli(20), Etienne Cavalier(1) *((1 Department of clinical chemistry, CHU de Liège, University of Liège, Liège, Belgium; (2) WHO Collaborating Center for Public Health aspects of musculo-skeletal health and ageing, Division of Public Health, Epidemiology and Health Economics, University of Liège, Belgium; (3) Chair for Biomarkers of Chronic Diseases, Biochemistry Department, College of Science, King Saud University, Riyadh, Saudi Arabia; (4) Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy; (5) Geriatric Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; (6) Geriatric Unit, IRCCS Istituti Clinici Scientifici Maugeri, Milan, Italy; (7) Laboratory of Clinical and Therapeutical Pharmacology, Portugal; (8) MRC Lifecourse Epidemiology Unit, University of Southampton UK; (9) Servicio de Geriatría. Hospital Universitario Ramón y Cajal (IRYCIS). Madrid, Spain; (10) Department of Geriatrics, Neurosciences and Orthopedics, Catholic University of the Sacred Heart, Rome, Italy; (11) Scientific Office, Federal Office for Safety in Health Care, Vienna, Austria; (12) CNR Aging Branch-IN, Padua, Italy; (13) State Research Institute Centre for Innovative Medicine, Vilnius, Lithuania; (14) Research Unit of Medical Imaging, Physics and Technology, Faculty of Medicine, University of Oulu, Oulu, Finland; (15) Department of Joint Surgery, The First Affiliated Hospital of Sun Yat-sen University, Guangzhou, China; (16) Landspitali, University Hospital of Iceland, Reykjavik, Iceland; (17) Department of Diabetes, Nutrition and Metabolic Disorders, Clinical Pharmacology, University of Liege, CHU de Liège, Liège, Belgium; (18) Vrije Universiteit Amsterdam, Department of Health Sciences, Amsterdam, the Netherlands; (19) Agencia Española de Medicamentos y Productos Sanitarios, Madrid, Spain; (20) Service of Bone Diseases, Faculty of Medicine, Geneva University Hospitals, Geneva, Switzerland)*

Background: In clinical trials, biochemical markers provide useful information on drug's mode of action, on therapeutic response and side effect monitoring, and can act as surrogate endpoints. In pharmacological intervention development for sarcopenia management, there is an urgent need to identify biomarkers that should be measured in clinical trials and

could be used in the future in clinical practice. **Objective:** The objective of this consensus report is to provide a clear list of biochemical markers of musculoskeletal health and ageing that can be recommended to be measured in Phase II and Phase III clinical trials evaluating new chemical entities for sarcopenia treatment. **Methods:** The European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Disorders (ESCEO ASBL) jointly with the Centre Académique de Recherche et d'Expérimentation en Santé (CARES SRL) organized in September 2022, under the auspices of the World Health Organization Collaborating Center for Epidemiology of Musculoskeletal Health and Aging, a working group including scientists, specialists in Laboratory medicine and clinicians expert in the field of biochemical markers and sarcopenia as well as representatives of the regulatory bodies. Following a systematic literature review on the existing evidences, all experts met during a face-to-face meeting to discuss and agree on recommendations. **Results:** the group proposed to classify biochemical markers into 2 series: biochemical markers evaluating musculoskeletal status and biochemical markers evaluating causal factors. For series 1, the group agreed on 4 biochemical markers that should be assessed in Phase II or Phase III trials (i.e. Myostatin-Follistatin, Brain Derived Neurotrophic Factor, N-terminal Type III Procollagen and Serum Creatinine to Serum Cystatin C Ratio – or the Sarcopenia Index). For series 2, the group agreed on 6 biochemical markers that should be assessed in Phase II trials (i.e. the hormones Insulin-like growth factor-1 (IGF-I), dehydroepiandrosterone sulfate, and cortisol, and the inflammatory markers C-reactive protein (CRP), interleukin-6 and tumor necrosis factor-α), and 2 in Phase III trials (i.e. IGF-I and CRP). The group also proposed optional biochemical markers that may bring insights on the mode of action of pharmacological therapies. **Conclusion:** Further research and development of new methods for biochemical marker assays may lead to the evolution of these recommendations.

OC8- ASSOCIATION BETWEEN THYROID FUNCTION AND LOWER LIMB COMPOSITION IN OLDER ADULTS: ANALYSIS FROM THE BALTIMORE LONGITUDINAL STUDY OF AGING. Hamza Ibad(1), Shadpour Demehri(1), A. Zenobia Moore(2), Eleanor M Simonsick(2), Jennifer SR Mammen(3) *((1) Johns Hopkins University School of Medicine, Department of Radiology, Baltimore MD, USA; (2) National Institute on Aging, National Institutes of Health, Baltimore MD, USA; (3) Johns Hopkins University School of Medicine, Department of Medicine, Division of Endocrinology, Diabetes, and Metabolism, Baltimore MD, USA)*

Background: In older adults, higher thyroid hormone levels have been associated with slower gait speed, lower endurance and higher fatigability. As thyroid hormone is catabolic, higher levels have the potential to accelerate age-related functional decline including loss of muscle mass and development of sarcopenia. Furthermore, thyroid hormone treatment is the most common cause of thyroid hormone excess. Therefore, any negative impact of higher thyroid hormone levels on sarcopenia would have implications for the clinical use of thyroid hormone replacement in older adults and especially in those with frailty. **Objectives:** Investigate the association between thyrotropin (TSH) and thyroid hormone levels and lower limb composition measured by dual-energy X-ray absorptiometry (DEXA) in participants of the Baltimore Longitudinal Study of Aging (BLSA). **Method:** Clustered-robust standard errors linear regression models were used to estimate crosssectional relationships between visit-specific thyroid function tests and lower limb composition, adjusted for levothyroxine use, age, race, sex, BMI, smoking, alcohol intake, total cholesterol, systolic blood pressure, and self-reported history of type II diabetes mellitus or knee osteoarthritis. **Results:** 1168 participants, 51% female and 73% white, made a total of 4669 eligible visits between 2003 and 2019, with 63.8% of participants making at least 3 visits. Mean age across all observations was 78 years, and levothyroxine (LT4) was in use for thyroid hormone replacement at 14% of visits. Knee osteoarthritis was reported at 36% of visits. Mean TSH was 2.4 mU/L and mean Free T4 (FT4) was 1.0 ng/dL. FT4 was negatively associated with lean mass (beta: -118.57, p-value <0.01) and positively associated with fat mass (beta: 98.16, p-value < 0.01) in fully adjusted models. Excluding visits at which participants were on LT4 did not change the associations between FT4 and body composition (FT4 and lean mass beta: -143.33, p-value <0.001). Neither TSH nor Free T3 were significantly associated with body composition. **Conclusion:** The association between higher FT4 and lower lean and higher fat mass suggests that higher thyroid hormone levels maybe a modifiable risk factor for sarcopenia that warrants further investigation. Prospective studies with a sufficient exposure time-frame are needed to assess for causality

OC9- AGING TRANSCRIPTOMIC SIGNATURES OF HIGH INTENSE EXERCISE AFFECTING MUSCLE BIOENERGETICS. Stefano Donega(1), Nirad Banskota(1), Julian Candia(1), Yulan Piao(1), Chee Chia(1), Supriyo De(1), Ranjan Sen(1), Luigi Ferrucci(1) *((1) National Institute on Aging, National Institutes of Health, Baltimore, MD, USA)*

Background: Mitochondrial mass and function decline with aging in humans and such decline affects many biological processes, in particular the capacity of organisms to expand the proteome in response to exterior stimuli or unfavorable metabolic conditions. There is evidence that some of these molecular changes involve the production of alternative RNA splicing variants, either directly or indirectly in response to those that modulate master regulators of the energy crisis response, namely AMPK. Mechanisms that maintain an optimal steady-state level of ATP are only partially understood but there is initial evidence in multiple model species that while mitochondrial mass and function decline with age, compensatory mechanisms are activated including alternative splicing. **Objectives:** Skeletal muscles require high amount of energy to function properly and muscle tissue is an ideal model to understand changes that occur in the absence and in

the presence of sufficient energy availability. **Methods:** The Genetic and Epigenetic Signatures of Translational Aging Laboratory Testing (GESTALT), a cross-sectional study that investigated relationships between aging and biomarkers of human blood/tissue, enrolled healthy individuals dispersed over a wide age-range (n=92, age 22-89). In this study, we investigated the relationship between muscle bioenergetics - measured by skeletal muscle oxidative capacity (kPCr) using 31P magnetic resonance spectroscopy - and the emergence of splicing variants. **Results:** In fully adjusted regression models, transcripts enriched for mitochondria- and respirasome- processes were lower at older ages and were higher in individuals with high mitochondrial function estimated by KPCr. Interestingly, when we compared the aging transcriptome in donors with low and high mitochondrial function - we detected pre-mRNA pathways to be up-regulated in poorer mitochondrial function donors, indicating possible key-role for specific mRNA isoforms governing muscle damage homeostasis with age. **Conclusion:** The association between spliceosome transcripts and age were substantially more evident in those individuals with low mitochondrial function (low kPCr) that in those with high mitochondrial function (high kPCr). We are currently investigating possible interactions with RNA subtype regulatory elements such lncRNAs, circRNAs and miRNAs, as well as contribution of Transposable Elements (TEs) and Epigenetic changes, since methyltransferase activity has been previously shown to be affected by physical activity.

OC10- BIOPHYTIS BIO101: A CANDIDATE TREATMENT FOR LONG COVID AFTER HOSPITALIZATION? Cendrine Tourette(1), Waly Dioh(1), Sandrine Rabut(1), Mounia Chabane(1), Serge Camelo(1), Myriem Louze(1), Jean Mariani(1,2), Rob Van Maanen(1), Stanislas Veillet(1) *((1) Biophytis - Sorbonne Université, BC9, Paris, France; (2) Sorbonne Université, CNRS - Institute de Biologie Paris Seine (UMR B2A), Paris, France)*

Background: BIO101 (20-hydroxyecdysone) is an investigational product that activates Mas receptor (MasR), part of the renin-angiotensin system (RAS), downstream of the SARS-CoV-2 virus receptor (ACE2) and involved in several protective pathways including muscle metabolism and structure. **Objectives:** Assessment of safety and efficacy of BIO101 treatment in 2 vulnerable populations: sarcopenic seniors and hospitalized severe COVID-19 patients. **Methods:** SARA-INT was a randomized three-arm interventional study (BIO101 175 mg or 350 mg bid / placebo) with planned treatment duration of 6 Months (up to 9 months in 50 subjects). Eligibility criteria for sarcopenia: meeting FNIH criteria and SPPB score ≤ 8/12 in community-dwelling seniors. Primary endpoint was the 400-meter walking test (400MWT), secondary endpoints being other physical activity assessments. COVA trial was a randomized, placebo-controlled phase 2/3 trial. Hospitalized adults ≥45 years with respiratory decompensation due to SARS-CoV-2 were randomized 1:1 to placebo or BIO101 (350 mg bid), up to 28 days or endpoint. Primary endpoint was proportion of patients dying or requiring high-flow oxygen, mechanical ventilation or ECMO; key secondary endpoint was proportion of patients recovered and discharged; both analysed using Cochran-Mantel-Haenszel (CMH) test. **Results:** Besides the promising results of SARA-INT, COVA included 233 participants in the ITT population (63.5% male, mean age 62.8 years). Primary (CMH) analysis at day 28 showed a statistically significant difference favouring BIO101 (BIO101: 15.8%, placebo: 26.0%), adjusted difference -11.4% (p=0.042), a relative risk (RR) reduction of death or respiratory failure of 44.0%. Kaplan-Meier (KM) analysis of difference in proportion of patients with death or respiratory failure over 28 days was nominally statistically significant favouring BIO101 at day 28 (10.9%, p=0.023), a 45.0% RR reduction. In both studies, safety and tolerability of BIO101 was very good: less patients treated with BIO101 350mg bid experienced adverse events (AEs) compared to placebo. **Conclusion:** BIO101(20E), targeting the MasR, is a candidate to treat vulnerable populations (sarcopenic seniors and severe hospitalized COVID-19 patients), with meaningful efficacy data and very good safety profile at the dose of 350 mg bid and may be a potential pharmacological strategy against physical performance deterioration associated with COVID-19.

OC11- DESIGN, METHODS AND PRELIMINARY FINDINGS FOR THE ENGAGE TRIAL: AN EXERCISE AND SOCIAL ENGAGEMENT INTERVENTION FOR MULTIMORBID, HOMEBOUND AFRICAN AMERICAN OLDER ADULT-CARE PARTNER DYADS DELIVERED OVER VOICE-ACTIVATED TECHNOLOGY. Megan Huisingh-Scheetz(1), Brittni Bryant(1), Corliss Taylor(1), Brandon Foster(1), Brad Appelhans(2), Marshini Chetty(1), Margaret Danilovich(3), Elizabeth Davis(2), Nicolas Feamster(1), Laura Finch(4), Marc Richardson(1), Nikita Thomas(1), Kelly Wagman(1) Wen Wan(1), Jocelyn Wilder(4), Louise Hawkley(4) *((1) University of Chicago, Chicago, IL, USA; (2) Rush University, Chicago, IL, USA; (3) Center for Jewish Elderly, Chicago, IL, USA; (4) NORC at the University of Chicago, Chicago, IL, USA)*

Background: Physical activity is essential for all age groups, across all comorbidities and geriatric syndromes; it has been described as the 'ideal' intervention for aging. Multimorbidity is more severe and more prevalent among African-Americans (AA) over their lifespan and they experience more accelerated aging than any other race in the US. Multimorbid OAs face increasing challenges to maintaining activity over time: disrupted physiology; required assistance to leave the home; reliance on care partners (CPs) with limited training; and restricted reimbursement for in-home exercise services. Increasing activity among homebound, multimorbid, AA OAs requires a shift in interventions to target the older adult-care partner (OA-CP) dyad and to test innovative vehicles for remote intervention delivery. EngAGE was co-developed through iterative participatory design and previously piloted. **Objective:** Our objective is to conduct a randomized efficacy trial of EngAGE in multimorbid, AA, homebound OAs and their CPs. **Methods:** The EngAGE trial

is a multisite randomized controlled trial designed to compare an exercise and social engagement intervention delivered over a voice-activated device (EngAGE) or on paper in n=124 AA, multimorbid OA-CP dyads in northeast Illinois. The intervention phase will last 6 months. Older adults are eligible if they score 3-8/12 on the Short Physical Performance Battery (SPPB). WiFi hotspots are provided when needed. Primary outcomes include lower and upper extremity strength and frequency of social contact. Secondary outcomes include the SPPB score, frailty phenotype, disability and relationship quality. We will assess individual, interpersonal and community-level moderators and will ascertain perceived barriers and facilitators to intervention use. **Results:** Recruitment began in October 2022; n=10 dyads have been enrolled and randomized as of January 2023. Most OAs are women (n=9); the mean age is 76.4 years. All 10 OAs scored a 0 or 1/4 on the SPPB chair subscale (mean performance time 23.5 seconds). Mean maximum grip strength among OAs is 23.5 kg. All CPs (n=10) are also African-American with a mean age of 61.6 years; 5 are women. **Conclusion:** This trial will evaluate whether EngAGE represents an effective, user-friendly, scalable approach to improving long-term exercise and social engagement for vulnerable AA OA-CP dyads. **Trial registration:** ClinicalTrials.gov NCT05337514

OC12- EFFECTS OF A 12-WEEK VIVIFRAIL EXERCISE PROGRAM ON INTRINSIC CAPACITY AMONG FRAIL COGNITIVELY IMPAIRED COMMUNITY-DWELLING OLDER ADULTS: SECONDARY ANALYSIS OF A MULTICENTER RANDOMIZED CLINICAL TRIAL. Juan Luis Sánchez-Sánchez(1,2,3), Philipe de Souto Barreto(1,4), Iván Antón-Rodrigo(5,6), Fernanda Ramón- Espinoza(7), Itxaso Marín Epelde(7), Marina Sánchez-Latorre(7), Debora Moral Cuesta (7) Álvaro Casas-Herrero(7,8,9) *((1) Gérontopôle de Toulouse, Institut du Vieillissement, Centre Hospitalier Universitaire de Toulouse, Toulouse, France; (2) MOVE-IT Research Group, Department of Physical Education, Faculty of Education Sciences, University of Cadiz, Cadiz, Spain; (3) Universidad Pública de Navarra (UPNA), Pamplona, Spain; (4) CERPOP, Inserm 1295, Université de Toulouse, UPS, Toulouse, France; (5) Hospital of Eibar, OSI Debabarrena. Osakidetza. Gipuzkoa, Spain; (6) Grupo de Investigación en Atención Primaria. Biodonostia Institute of Health Research. San Sebastián. Gipuzkoa. Spain; (7) Geriatric Department, Hospital Universitario de Navarra (HUN), Pamplona, Spain; (8) Navarrabiomed, Hospital Universitario de Navarra (HUN), Universidad Pública de Navarra (UPNA), IdiSNA, Pamplona; (9) CIBER of Frailty and Healthy Aging (CIBERFES), Instituto de Salud Carlos III, Madrid, Spain)*

Introduction: The World Health Organization (WHO) recently defined the construct of intrinsic capacity (IC), a function-based marker of older adult's health encompassing all mental and physical capacities of the individual. Multicomponent physical exercise (MCE) is a potential intervention capable to maintain/increase IC at older age; however, evidence is scarce on the effects of MCE on IC in cognitively impaired pre-frail/frail older adults. **Methods:** Secondary analyses of a randomized clinical trial. 188 older outpatients (age=84.06±4.77, 70.2% women) presenting with pre-frailty/frailty (according to Fried Criteria) and mild-cognitive impairment/mild-dementia were recruited in the Geriatric clinics of 3 tertiary hospitals in Spain. Subjects were randomized to participate in the 12-week home-based individualized Vivifrail MCE or usual care. An IC index was created based on the z-score of the locomotion (Short Physical Performance Battery), cognitive (Montreal Cognitive Assessment), psychology (15-item GDS Yesavage) and vitality (handgrip strength) domains. **Results:** After the 3-month intervention, linear mixed models showed significant between-group differences in the evolution of the IC composite score (β=0.48; 95% CI=0.24, 0.74; p<0.001), IC Locomotion (β=0.42; 95% CI=0.10, 0.74; p<0.001), IC Cognition (β=0.45; 95% CI=0.03, 0.87; p<0.05) and IC Vitality domains (β=0.50; 95% CI=0.25, 0.74 at 3-month) favoring the MCE group. **Conclusion:** The 12-week Vivifrail multicomponent exercise program is an effective strategy to enhance IC, especially in terms of locomotion, cognition, and vitality IC domains in community-dwelling older adults with pre-frailty/frailty and MCI/mild-dementia, compared to usual care.

OC13- BODY FAT MASS MEDIATES THE EFFECT OF INSULIN RESISTANCE ON FUNCTIONAL DECLINE BUT NOT ON MORTALITY IN A COMMUNITY-DWELLING OLDER ADULTS: RESULTS FROM TOLEDO STUDY OF HEALTHY AGING. Mariam El Assar(1,2), Javier Angulo(2,3), Jose A Carnicero-Carreño(1,2), Patricia Sosa(1), Alejandro Álvarez-Bustos(2), Francisco J García-García(2,4), Leocadio Rodríguez-Mañas(2,5) *((1) Fundación de Investigación Biomédica, Hospital Universitario de Getafe, Getafe, España; (2) Centro de Investigación Biomédica en Red sobre Fragilidad y Envejecimiento Saludable (CIBERFES), Instituto de Salud Carlos III, Madrid, España; (3) Servicio de Histología-Investigación, Unidad de Investigación Traslacional en Cardiología (IRYCIS-UFV), Hospital Universitario Ramón y Cajal, Madrid, Spain; (4) Servicio de Geriatría, Hospital Virgen del Valle, Toledo, España; (5) Servicio de Geriatría, Hospital Universitario de Getafe, Getafe, España)*

Background: Recent evidence suggests that insulin resistance (IR) is a risk factor for functional decline meanwhile it protects from mortality in non-diabetic older adults. Both age-related outcomes seem to be associated with body composition. **Objectives:** We aim to assess the potential role of body composition in the association of IR with functional decline and with mortality risk in older subjects. **Methods:** 1,114 non-diabetic subjects from the Toledo Study of Healthy Ageing cohort were included (mean age 74.56±5.73; 56.10% female). IR was determined by the homeostasis model assessment index (HOMA-IR) at baseline while frailty was assessed by the Frailty Trait Scale-5 (FTS5) at baseline and after a median follow-up period of 2.99 years. The functional decline during

follow-up was determined as the worsening in 2.5 points for the FTS5 score. Deaths were also registered (6.31 years median follow-up). Body compositions were determined using Dual-Energy X-ray absorptiometry. Multivariate regression models were used to analyze the effects of HOMA-IR on outcomes. Age, gender, and Charlson index were included in basic adjustment model while fat and lean mass were included as potential confounding variables. **Results:** HOMA-IR increased the risk of functional decline in FTS5 after basic adjustment (OR 1.44 [1.11-1.86], p=0.0056). This significant association was lost when further adjusted by total fat mass (OR 1.15 [0.88-1.52], p= 0.3046). Meanwhile, when controlling for lean mass, HOMA-IR was still able to predict incident worsening in FTS5 (OR 1.40 [1.07, 1.82], p= 0.01416). By contrast, HOMA-IR was inversely associated with mortality risk after basic adjustment (HR 0.67 [0.50-0.88], p=0.0043). Adjustment by total fat mass or by total lean mass did not modify the association (HR 0.72 [0.53-0.97], p= 0.0324; HR 0.67 [0.50-0.89], p= 0.0059 for fat mass and lean mass respectively). **Conclusion:** Fat mass but not lean mass mediates the associations of IR with functional decline but not with mortality in non-diabetic older adults. The present work was funded by grants from the Spanish Ministry of Economy, Industry and Competitiveness, cofinanced by the FEDER Funds (Instituto de Salud Carlos III, PI20/00977) and CIBERFES (CB16/10/00464), and el Proyecto MITOFUN, Fundación Francisco Soria Melguizo.

OC14- COGNITIVE STATUS AS A PREDICTOR OF BODY COMPOSITION PROFILES: A LATENT CLASS ANALYSIS. John A. Batsis(1,2,3), David H. Lynch(1), Annie Green Howard(2,3), Hsiao-Chuan Tien(3), Hillary Spangler, Shufa Du(3,4), Bing Zhang(5), Huijun Wang(5), Penny Gordon Larsen(3,4) *((1) Division of Geriatric Medicine and Center for Aging and Health, School of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA; (2) Department of Nutrition, Gillings School of Global Public Health, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA; (3) Carolina Population Center, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA; (4) National Institute for Nutrition and Health Chinese Center for Disease Control and Prevention, China)*

Background: Aging biology results in changes in body composition that are associated with adverse outcomes. Evidence suggests that cognitive status may lead to different phenotypes of body composition in older age. **Objectives:** We sought to evaluate whether cognition in late mid-life is associated with different clusters of body composition phenotypes. **Methods:** We included participants aged 60+ in 2015 from the China Health and Nutrition Survey, a nationally representative survey, with complete bioelectrical impedance analysis, body composition, and anthropometry measures in 2015 and cognitive data collected 9 to 11 years prior to 2015. Cognition was estimated based on a subset of the modified Telephone Interview for Cognitive Status (TICS, 0—27). Latent class analysis was done to identify different body composition patterns. Our primary analysis identified classes based on percent body fat, total skeletal muscle/height^2, and BMI adjusted for age and sex. In sensitivity analysis we ran the same models replacing appendicular mass for total skeletal muscle. We combined latent classes to improve study power and align with the Fried frailty phenotype (robust, pre-frail, frail). **Results:** Of the 1,424 adults (55% female, age 72.0$\pm$5.9 in 2015), mean BMI was 23.8$\pm$3.6, and TICS at the visit prior to 2015 was 13.5$\pm$6.2. Five classes were found to have the best fit: Class I (n=29, moderate BMI, lowest body fat, highest muscle); Class II: (n=211, lowest BMI, % body fat, and muscle); Class 3 (n=65, high BMI, body fat, muscle); Class 4 (n=602, low BMI, low body fat, low muscle); and Class 5 (n=517, moderate BMI, body fat, muscle). In our 5-class model, higher cognition roughly 10 years prior was associated with lower odds of being in Class 2 (low BMI, low % body fat, and low muscle mass) as compared to Class 5 (moderate BMI, body fat, muscle) with an odds ratio of 0.91 [0.82,1.00]). Presence of mild cognitive impairment or dementia in 2006 was suggestive of frailty at follow-up. **Conclusion:** Cognitive impairment reflected by the TICS may be a marker for future frailty phenotypes over time. Future, adequately powered studies are needed to confirm a statistically significant relationship.

OC15- CT-DERIVED BODY COMPOSITION IS ASSOCIATED WITH GRIP STRENGTH AND GAIT SPEED IN MROS STUDY. Peggy M. Cawthon(1), Katey Webber(1), Eric S. Orwoll(2), Kristine E. Ensrud(3) Jane A. Cauley(4), Leon Lenchik(5) *((1) California Pacific Medical Center, Research Institute, San Francisco, CA USA; (2) Oregon Health and Sciences University, Portland, OR, USA; (3) University of Minnesota, Minneapolis, MN, USA; (4) University of Pittsburgh, Pittsburgh, PA, USA; (5) Wake Forest University, Winston-Salem, NC, USA)*

Background: Automated analysis of biomarkers of body composition on CT images may improve prediction of physical function decline in older adults. **Objective:** In 2,644 men (mean age 74.0) in MrOS, determine if body composition biomarkers derived from abdominal CT images are associated with grip strength and walking speed. **Methods:** On CT images at L3 level, our fully-automated machine learning algorithm determined total abdominal skeletal muscle area (SMA) - biomarker of sarcopenia, skeletal muscle density (SMD) - biomarker of intramuscular myosteatosis, intermuscular adipose tissue area (IMAT) - biomarker of intermuscular myosteatosis, visceral adipose tissue area (VAT), and subcutaneous adipose tissue area (SAT). Association of CT metrics with grip strength and walking speed was determined using linear regression models adjusted for CT parameters (scanner model, slice thickness, tube current) and participant age and height. **Results:** For grip strength, Muscle area, muscle density, VAT, and SAT (but not IMAT) were significantly associated with grip strength in fully adjusted models. [standardized βs per 1 SD increment for grip: SMA (β = 2.16, CI = 1.78, 2.55); SMD (β = 0.56, CI = 0.16, 0.97); VAT (β = -0.65, CI = -1.04, -0.26); SAT (β = -0.41, CI = -0.75, -0.06); IMAT (β = -0.02, CI = -0.66,

0.62] For gait speed, only IMAT and VAT were associated with gait speed in fully adjusted models. [standardized βs, 1 SD increment in IMAT (β = -0.04, CI = -0.06, -0.02) and VAT (β = -0.01, CI = -0.02, -0.00); other non-significant β not shown]. **Conclusion:** In older men, CT-derived biomarkers of sarcopenia, intramuscular myosteatosis, and adiposity, but not the biomarker of intermuscular myosteatosis, are associated with lower grip strength. CT-derived biomarker of intermuscular myosteatosis and VAT are associated with slower gait speed.

OC16- COMBINED PHYSICAL AND COGNITIVE STIMULATION IN AN INNOVATIVE DUAL-TASK IN MICE AND APPLICATION IN AGING. Elpidio Attoh-Mensah, Antoine Huret, Camille Laurent, Marianne Léger, Gilles Loggia, Daniel Zuba, Chantal Chavoix, Pascale Schumann-Bard, Thomas Fréret *(Normandie Université, UNICAEN, INSERM, COMETE, CYCERON, CHU de Caen, Caen, France)*

Background: Physical activity (PA) is a recommended non-pharmacological intervention to prevent age-related frailty (for review see Smith et al., 2010). PA interventions have been associated with functional improvement particularly, through enhancement of gait and cognitive performance in older adults. Recent studies argued that PA would convey a stronger impact when combined with cognitive challenges within a single dual-task (DT) (Lipardo et al.,2018). Having an animal model of dual-tasking would therefore be useful to better understand underlying mechanisms of these benefits. **Objectives:** In this study, we sought to develop an innovative model of dual-task – combining physical activity and cognitive challenge – in adult mice. The effects of DT practice on motor and cognitive performance in young mice and subsequent effects at an older age were also examined. **Methods:** C57BL/6J mice of 3 months of age were trained to visual discrimination task and then to its reversal, in touchscreen chambers. During cognitive training sessions, mice were randomly split into 3 groups (n=10/group), either without PA (control), or with PA administrated apart from (single task, ST) or simultaneously with (DT), the cognitive task. PA was given through a home-made treadmill, specifically designed to fit in the touchscreen chambers. The speed was set at 9 m/min. Besides, mice were retested 15 months later, i.e. at 19 months, to assess long-lasting effect of single and dual tasks (versus control) on aged mice performance. **Results:** First, we have shown that this dual-task model was feasible in mice. Besides, young mice in DT group displayed better procedural ($p<0.001$) and cognitive flexibility ($p<0.01$) performance, than either ST or control groups. Furthermore, these positive impacts still remained 15 months later in aged mice, that displayed both better cognitive ($p<0,001$) and motor ($p<0,009$) performance in the DT versus ST and control groups. **Conclusion:** We developed for the first time a dual stimulation task in mice. This innovative task could help to unravel physiological and neurobiological correlates of the benefits of dual-tasking on cognitive and motor performance in various normal and pathological conditions.

OC17- PLASMA INFLAMMATORY MARKERS PREDICT LONGITUDINAL TRAJECTORIES OF INTRINSIC CAPACITY IN OLDER ADULTS. Wan-Hsuan Lu(1,2), Bruno Vellas(1,2), Philipe de Souto Barreto(1,2) *((1) Gerontopole of Toulouse, Institute of Ageing, Toulouse University Hospital (CHU Toulouse), Toulouse, France; (2) Maintain Aging Research team, Centre d'Epidémiologie et de Recherche en santé des POPulations (CERPOP), Inserm, Université Paul Sabatier, Toulouse, France)*

Background: Intrinsic capacity (IC), the composite of physical and mental capacities, declines with age at different rates and patterns between individuals. Whether aging biomarkers can predict different IC trajectories remains unclear. **Objectives:** This study had two objectives: (1) to identify IC multi-trajectories among older adults; (2) to investigate the association of trajectory groups with plasma biomarkers related to inflammation and mitochondrial dysfunction. **Methods:** This is a secondary analysis of the Multidomain Alzheimer Preventive Trial (MAPT). We included 1,271 community-dwelling older adults aged ≥70 with IC data over four years. IC was operationalized as a 0-to-100 score consisting of cognition (assessed by Mini-Mental State Examination [MMSE]), locomotion (evaluated by Short Physical Performance Battery [SPPB]), psychology (measured by Geriatric Depression Scale [GDS]), and vitality (assessed by handgrip strength). We performed group-based multi-trajectory modeling to identify participants who followed similar longitudinal patterns across four IC domains. Associations between the multi-trajectory groups and plasma biomarker levels were examined by multinomial logistic regression. **Results:** Five IC multi-trajectory groups were determined: low in all domains (8%), low locomotion (25%), low psychological domain (17%), robust (28%), and robust with high vitality (22%). The "low in all domains" group had the oldest age, the highest percentages of low educational levels, and the highest number of chronic diseases (all $p<0.01$). Compared to the best trajectory group (i.e., robust with high vitality), elevated levels of plasma interleukin-6 (IL-6), tumor necrosis factor receptor-1 (TNFR-1), and growth differentiation factor-15 (GDF-15) were associated with a higher risk of belonging to the "low in all domains" group (IL-6: relative risk ratio (RRR) [95% CI] = 1.42 [1.07 – 1.88]; TNFR-1: RRR = 1.46 [1.09 – 1.96]; GDF-15: RRR = 1.99 [1.45 – 2.73]). Higher GDF-15 was associated with an increased risk of being in the "low locomotion" group (RRR = 1.48 [1.17 – 1.89]) and "low psychological domain" group (RRR = 1.29 [1.01 – 1.64]). **Conclusion:** Plasma biomarkers reflecting inflammation distinguished older people with multi-impaired IC trajectories from those with high-stable IC trends.

OC18- THE PATHOGENESIS OF SARCOPENIA IS DIFFERENT IN THE GROUP OF MALE COPD AND NON-COPD SUBJECTS. Chih-Ming Lin(1), Jhih-Jhen Wu(2), Huan-Ting Lin(3), Shih-Wei Huang(4) *((1) Division of Internal Medicine, Taipei Chang Gung Memorial Hospital, Taipei, Taiwan; (2) Chang Gung Medical College, Taipei, Taiwan; (3) Mackey Medical College, Taipei, Taiwan; (4) Department of Internal Medicine, Linko Chang Gung Memo rial Hospital, Taipei, Taiwan)*

Background: The incidence and prevalence of sarcopenia is strongly age, sex, and diseases dependent. Men are more likely to develop sarcopenia according to previous study. The purpose of this study was to identify possible pathogenesis of sarcopenia for the male older adults with and without chronic obstructive pulmonary disease (COPD) using plasma metabolites. **Objective:** Cross-section study. **Methods:** Our participants are a group of healthy older people who live in retirement homes and can take care of their daily lives without nursing assistance. There were 305 enrolled and the average age was 81.8 years old with 43.3% being male. The incidence of COPD was 12.5% according to the 2017 GOLD guidelines. There were 38 in group of COPD subjects and 267 in the group of non-COPD subjects. There were 20 had sarcopenia in 25 COPD of 132 male subjects and 5 had sarcopenia in 13 COPD of 173 female subjects according to Asian Working Group for Sarcopenia (AWGS) 2019 criteria. Mass spectrometry-based profiling of metabolites in plasma of all participants were measured and then the results were calculated the difference between the group of male COPD and non-COPD subjects with/without sarcopenia. **Results:** Metabolite patterns of male COPD and non-COPD subjects with/without sarcopenia were explored in our study. Plasma acylcarnitines (C2, C4, C5, C9 and C14) were identified with higher concentrations with significant difference in the group of male non-COPD subjects with sarcopenia. Plasma amino acid (BCAA, essential AA, Ile, Leu, Lys, Orn, Thr, and Val) were identified with lower concentrations with significant difference in the group of male non-COPD subjects with sarcopenia. The concentration of plasma acylcarnitines and amino acid in the group of male COPD subjects with sarcopenia did not have difference with significant difference compared with the group of male COPD subjects without sarcopenia. **Conclusion:** The pathogenesis of sarcopenia in the group of male COPD and non-COPD subjects may be different by the metabolomic study.

OC19- HEALTH-RELATED QUALITY OF LIFE IN SARCOPENIA: A SYSTEMATIC REVIEW AND META-ANALYSIS. Charlotte Beaudart(1), Céline Demonceau(1), Jean-Yves Reginster(1), Médéa Locquet(1), Matteo Cesari(2,3), Alfonso J. Cruz Jentoft(4), Olivier Bruyère(1) *((1) WHO Collaborating Center for Public Health aspects of musculo-skeletal health and ageing, Division of Public Health, Epidemiology and Health Economics, University of Liège, Belgium; (2) Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy; (3) Geriatric Unit, IRCCS Istituti Clinici Scientifici Maugeri, Milan, Italy; (4) Servicio de Geriatría, Hospital Universitario Ramón y Cajal (IRYCIS). Madrid, Spain)*

Background: The decrease of physical abilities and functional decline that can be caused by musculoskeletal disorders as sarcopenia, can lead to a higher level of dependence and disabilities. Therefore, it may influence patient reported outcome measures (PROM), such as the health-related quality of life (HRQoL). The purpose of this systematic review and meta-analysis is to provide an exhaustive view on the relationship between sarcopenia and HRQoL. **Methods:** Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) were followed through the whole process of this work. A protocol was previously published on PROSPERO. The electronic databases MEDLINE, Scopus, Allied and Complementary Medicine (AMED), EMB Review – ACP Journal Club, EBM Review- Cochrane Central of Register of Controlled Trials and APA PsychInfo were searched up to October 2022 for observational studies reporting a HRQoL assessment in both sarcopenic and non-sarcopenic individuals. Study selection and data extraction were carried out by two independent researchers. Meta-analysis was performed with a random effect model giving an overall standardized mean difference (SMD) and its 95% confidence interval (CI) between sarcopenic and non-sarcopenic. Quality of individual studies was measured using the Newcastle Ottawa Scale and strength of evidence was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) tool. **Results:** The search strategy identified 3,725 references from which 43 observational studies were eligible and included in this meta-synthesis study. A significant lower HRQoL was observed for sarcopenic individuals compared to non-sarcopenic (SMD -0.76; 95%CI -0.95; -0.57). Significant heterogeneity was associated with the model (I^2=93%, Q test <0.01). Subgroups analysis showed that the specific questionnaire SarQoL discriminates better sarcopenia in regards of HRQoL (SMD -1.09; 95%CI -1.44; -0.74 versus -0.49; 95%CI -0.63; -0.36 with generic tools; p-value for interaction <0.01). A higher difference of HRQoL between sarcopenic and non-sarcopenic was found for individuals residing in living home cares compared to community-dwelling individuals (p-value for interaction <0.001). No differences between age, diagnostic techniques, and continents/regions were found. Level of evidence was rated as moderate using GRADE assessment. **Conclusion:** This systematic review and meta-analysis combining 43 observational studies demonstrates that HRQoL

is significantly reduced in sarcopenic patients. Using disease-specific HRQoL instruments may better discriminate sarcopenic patients in regards of their quality of life.

OC21- FISH INTAKE AND PRE-FRAILTY IN NORWEGIAN OLDER ADULTS. A PROSPECTIVE COHORT STUDY: THE TROMSØ STUDY 1994–2016. Dina Moxness Konglevoll(1), Lene Frost Andersen(1), Laila Arnesdatter Hopstock(2), Bjørn Heine Strand(3,4,5), Magne Thoresen(6), Torunn Holm Totland(5), Anette Hjartåker(1), Monica Hauger Carlsen(1) *((1) Department of Nutrition, Institute of Basic Medical Sciences, University of Oslo, Oslo, Norway; (2) Department of Health and Care Sciences, UiT The Arctic University of Norway, Tromsø, Norway; (3) The Norwegian National Centre for Ageing and Health, Vestfold Hospital Trust, Tønsberg, Norway; (4) Department of Geriatric Medicine, Oslo University Hospital, Oslo, Norway; (5) Department of Physical Health and Ageing, Norwegian Institute of Public Health, Oslo, Norway; (6) Department of Biostatistics, Institute of Basic Medical Sciences, University of Oslo, Oslo, Norway)*

Background: Fish are suggested as being part of a healthy diet and a dietary factor in the prevention of frailty. However, the influence of a lifelong habitual fish intake on pre-frailty is unknown. **Objective:** To investigate the longitudinal association between the frequency of fish intake and pre-frailty in Norwegian older adults. **Methods:** This prospective cohort study used data from the fourth (1994–1995), sixth (2007–2008) and seventh (2015–2016) survey of the large, population-based Tromsø Study in Tromsø, Norway. We included 4350 men and women aged ≥65 years with data on frailty (modified Fried's frailty phenotype: weight loss, exhaustion, and low physical activity, grip strength and walking speed) in Tromsø7 and self-reported frequency of fish intake (low (0–3 times/month), medium (1–3 times/week) and high (≥4 times/week)) in Tromsø4, Tromsø6 and Tromsø7, respectively. We used multivariable logistic regression to study the association between (1) frequency of intake of lean, fatty and total fish in Tromsø6 and pre-frailty in Tromsø7, and (2) stable patterns of total fish intake across Tromsø4, Tromsø6 and Tromsø7 (21 years) and pre-frailty in Tromsø7. **Results:** The prevalence of pre-frailty was 28% (n = 1124). A medium and high intake of fatty fish in Tromsø6 was associated with 18% (odds ratio (OR) = 0.82, 95% confidence interval (CI) = 0.69, 0.98) and 37% (OR = 0.63, 95% CI = 0.43, 0.91) lower odds of pre-frailty after 8 years, compared with a low intake. For lean and total fish, a high intake was associated with 28% (OR = 0.72, 95% CI = 0.53, 0.97) and 31% (OR = 0.69, 95% CI = 0.52, 0.91) lower odds of pre-frailty after 8 years, respectively, compared with a low intake. There was no association between patterns of total fish intake over 21 years and pre-frailty. **Conclusion:** A higher frequency of intake of lean, fatty and total fish was associated with lower odds of pre-frailty after 8 years in older community-dwelling Norwegian adults. This underlines the importance of promoting frequent fish intake as part of a healthy diet to facilitate healthy ageing.

OC23- DESCRIPTIVE STUDY OF THE ICOPE PATHWAY FROM STEP 1 TO 3 IN THE INSPIRE-T COHORT. Catherine Takeda(1), Christelle Cantet(1), Emeline Muller(1), Sophie Guyonnet(2), Bruno Vellas (1,2) for the INSPIRE Plateform group *((1) Gérontopôle, Geriatric Department, CHU of Toulouse, Toulouse, France; (2) CERPOP Inserm UMR 1295, Toulouse, France; University of Toulouse III, Toulouse, France)*

Background: The World Health Organization (WHO) has been leading international action plans under the United Nations 2021–2030 Decade of Healthy Ageing. In 2017–2019 WHO published guidelines on the implementation of an Integrated Care for Older People (ICOPE) framework targeting intrinsic capacity through mobility, cognition, psychological, vitality, hearing and vision. The INSPIRE study is implementing this program in the INSPIRE-T cohort (1014 participants; aged 20-102 years at baseline; with 10 years follow-up). **Objectives:** The primary objective of this study was to describe the intrinsic capacity characteristics in the INSPIRE-T cohort and identify abnormalities in intrinsic capacity during step 1 with the screening tool, step 2 with a full assessment of each capacity and describe the different step 3 (care plan). **Methods:** In this prospective study, we analyzed the ICOPE step 1 to 3 for the participants aged 60 years and older from the INSPIRE-T cohort at base line. All individuals were screened using the step 1 screening tool. In-depth assessments (step 2) was systematically performed regarding the results of the screening test and a personalized care plan was proposed according to the ICOPE guidelines. **Results:** Between October 2019, and March 2022, 603 participants, 60 years and older, (mean age 74·7, SD 8·8 years; 357 [59.2%] of whom were women) were included in the INSPIRE-T cohort. 595 (98·8%) participants had a positive intrinsic capacity result during screening at baseline. Step 2 findings: mean MMSE 28.2, SD 2.2; mean MNA 27.4, SD 2.3; mean PHQ-9 3.3, SD 3.8; mean SPPB 11.2 SD 1.8 and 213 (36.2%) had visual impairment. Among the subjects 338 (56.5%) were robust, 206 (34.4%) were pre-frail and 54 (9%) were frail. A step 3 (care plan) was proposed to 602 participants. **Conclusion:** The very high prevalence of positive screening for impaired intrinsic capacity during step 1, were confirmed deficits in intrinsic capacity during step 2. The 10 year follow-up of the INSPIRE-T cohort will allow a longitudinal prospective study to helps us confirm that the ICOPE program is able to target individuals with increased risk for functional loss, frailty, age related disease and disability.

OC24- MUSCLE COMPOSITION CHANGES IN TYPE 2 DIABETES AND CORONARY HEART DISEASE – RESULTS FROM THE LONGITUDINAL UK BIOBANK IMAGING STUDY. J. Linge(1,2), O. Dahlqvist Leinhard(1,2,3) for the INSPIRE Plateform group *((1) AMRA Medical, Linköping, Sweden; (2) Department of Health, Medicine and Caring Sciences, Linköping University, Sweden; (3) Center for Medical Image Science and Visualization (CMIV), Linköping University, Sweden)*

Background: Previous studies have indicated people with metabolic disorders may experience more rapid muscle wasting with aging. **Objective:** To determine change in fat-free muscle volume (FFMV) and muscle fat infiltration (MFI) of the thighs and spinal erectors in participants with type 2 diabetes (T2D) and coronary heart disease (CHD) from the longitudinal UK Biobank imaging study. **Methods:** 2,942 participants were scanned twice approximately 2.2 years apart using magnetic resonance imaging. Muscle composition was quantified using AMRA Researcher. Sex-, height- and weight-invariant thigh FFMV z-scores were calculated using N≥150 matched controls. Changes in muscle composition comparing controls (participants without T2D, CHD) to T2D (without CHD), and CHD (without T2D) respectively were tested using t-test and linear regression adjusted for sex, baseline BMI, age, and muscle composition, and change in weight. **Results:** Controls showed significant change in thigh FFMV (mean (SD) -0.16 (0.34) L, p=0.032), FFMV z-score (-0.15 (0.25) SD, p<0.001), and MFI (+0.26 (0.37) pp, p<0.001), as well as spinal erectors FFMV (-0.17 (0.31) dL, p<0.001) and MFI (+0.58 (0.82) pp, p<0.001). For T2D, significant differences compared to controls were observed for change in thigh FFMV (T2D=-0.25 (0.44) L; p=0.005, padjusted=0.018 vs controls) and FFMV z-score (-0.21 (0.29) SD; p=0.020, padjusted=0.011 vs controls) as well as spinal erectors FFMV (T2D=-0.23 (0.33) dL; p=0.029, padjusted=0.080 vs controls). No significant differences were observed comparing CHD to controls. **Conclusion:** Significant changes in muscle composition were observed following 2.2 years of aging. People with T2D experienced a more rapid loss in muscle volume of the thighs and spinal erectors compared to controls.

OC25- A NEW SEX-SPECIFIC SARCOPENIC OBESITY Z-SCORE FOR THE APPRAISAL OF THE RISK OF MORTALITY: A POPULATION-BASED STUDY. E. Benz(1,2), A. Pinel(1), C. Guillet(1), F. Capel(1), B. Pereira(3), M. de Ridder(4), M. Pouget(5), T. Voortman(2), J. Schoufour(6), P. Weijs(7,8), Y. Boirie(1,5) and JPI SO-NUTS consortium *((1) Human Nutrition Unit, Université Clermont Auvergne, Clermont Ferrand, France; (2) Department of Epidemiology, Erasmus University Medical Center, Rotterdam, Netherlands; (3) Biostatistics Unit, Université Clermont Auvergne, Clermont Ferrand, France; (4) Department of Medical Informatics, Erasmus University Medical Center, Rotterdam, The Netherlands;C (5) Clinical Nutrition , Université Clermont Auvergne, Clermont Ferrand, France; (6) Faculty of Sports and Nutrition, Centre of Expertise Urban Vitality, Amsterdam University of Applied Sciences; (7) Department of Nutrition and Dietetics, Amsterdam University Medical Centers, Amsterdam; (8) Public Health Institute, VU University, Amsterdam, Netherlands)*

Background: Sarcopenic obesity (SO) has been recently defined as a combination of low muscle function/mass and high-fat mass, both of which are independently associated with adverse outcomes such as mortality among older people. Nevertheless, there is limited evidence regarding SO prevalence and its association to overall mortality. **Objectives:** to determine the prevalence of SO using the recent definition of SO, and to assess its association with all-cause mortality by using a sex-specific SO z-score. **Methodology:** Baseline characteristics of 5,888 (mean age 69.5±9.1, BMI 27.5±4.3, 56.8% female) participants from the Rotterdam Study were collected and they were followed for mortality for a median of 9.9 years [interquartile range:8.7-11.1]. SO was defined using muscle strength measured by handgrip (HGS), muscle mass (ALM/weight) and body fat percentage (BF%) by dual-energy X-ray absorptiometry (DXA) as recommended by the ESPEN/EASO consensus. In addition, we calculated a new SO z-score as a combination of sex-specific z-scores of HGS and ALM/weight minus z-score of BF%. Cox regression models were adjusted for age, comorbidities and smoking status. Differences of SO z-score among SO categories were tested by using ANOVA. **Results:** By applying the ESPEN/EASO consensus, which screens obese subjects as the first step (n=2938, age 69.6±8.9, BMI 30.8±3.3, 55.7% female) 12% [95% CI: 10.9; 13.3] had low handgrip strength (probable SO), and in the second step 1.2% [95% CI: 0.8; 1.5] had low handgrip strength plus high BF% and low ALM/weight (confirmed SO). Significant differences were found in the SO z-score among probable SO (SO z-score; mean -2.93±1.30, p-value <0.001), confirmed SO (z-score:-5.46±1.23, p-value <0.001) and no SO subjects (z-score: -0.58±1.74). Probable SO (HR:1.97 [95%CI: 1.66; 2.33]) and confirmed SO (HR: 2.80 [95%: 1.86; 4.21]) had a worse survival probability than obese people without SO; whereas each unit increase in z-score reduced the risk of death in the whole population (HR:0.88 [95% CI: 0.86; 0.91] and in subjects with obesity (HR:0.84 [95% CI: 0.81; 0.88]). **Conclusion:** The ESPEN/EASO consensus and its cut-

offs allows to determine the prevalence of SO. However, the SO score is able to determine the risk of all-cause mortality, allowing a preventive approach of SO-associated risk of outcomes.

OC26- FRAILTY INDEX AND ITS ASSOCIATION WITH THE ONSET OF POSTOPERATIVE DELIRIUM IN OLDER ADULTS UNDERGOING ELECTIVE SURGERY. Janina Steenblock(1,2,3,4), Ulrike Braisch(1,2,5), Simone Brefka(1,2,3), Christine Thomas(6,7,8), Gerhard W. Eschweiler(9), Michael Rapp(10), Brigitte Metz(11), Christoph Maurer(12), Christine A. F. von Arnim(13), Matthias. L. Herrmann(7,9), Sören Wagner(8,14), Michael Denkinger(1,2,3,4), Dhayana Dallmeier(1,2,4,15) *((1) Agaplesion Bethesda Clinic, Ulm, Germany; (2) Geriatric Center Ulm/Alb-Donau, Ulm, Germany; (3) Institute for Geriatric Research, University Clinic Ulm, Ulm, Germany; (4) Medical Faculty, Ulm University, Ulm, Germany; (5) Institute of Epidemiology and Medical Biometry, Ulm University, Ulm, Germany; (6) Department of Old Age Psychiatry and Psychotherapy, Klinikum Stuttgart, Stuttgart, Germany; (7) Department of Neurology and Neurophysiology, Medical Center-University of Freiburg, Freiburg, Germany; (8) Department of Anesthesia, Critical Care and Pain Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA; (9) Geriatric Center, University Hospital Tuebingen, Tuebingen, Germany; (10) Department of Social and Preventive Medicine, University of Potsdam, Potsdam, Germany; (11) Geriatric Center Karlsruhe, ViDia Christian Clinics Karlsruhe, Karlsruhe, Germany; (12) Center for Geriatric Medicine and Gerontology, University of Freiburg, Germany; (13) Department of Geriatrics, University Medical Center Göttingen, Göttingen, Germany; (14) Department of Anaesthesiology, Klinikum Stuttgart, Stuttgart, Germany; (15) Department of Epidemiology, Boston University School of Public Health, Boston, MA, USA)*

Background: The association of frailty based on the accumulation of deficits with postoperative delirium (POD) in older adults has been poorly examined. **Objective:** We aimed to analyze this association in older patients undergoing elective surgery. **Methods:** Preoperative data was used to build a 30-item frailty index (FI) for participants of the PAWEL-study. Delirium was defined by a combination of I-CAM and chart review. Using logistic regressions models we analysed the association between frailty and POD adjusting for age, sex, smoking, alcohol consumption, education and type of surgery. **Results:** Among 701 participants (mean age 77.1, 52.4% male) median FI was 0.27 (Q1 0.20| Q3 0.34), with 528 (75.3%) frail participants (FI≥0.2). Higher median FI were seen in orthopedic than cardiac surgery patients (0.28 versus 0.23), and in women (0.28 versus 0.25 in men). Frail participants showed a higher POD incidence proportion (25.4% versus 17.9% in non-frail). An increased odds for POD was observed in frail versus non-frail participants (OR 2.14 [95% CI 1.33, 3.44], c-statistic 0.71). A 0.1 increment of FI was associated with OR 1.57 [95% CI 1.30, 1.90] (c-statistic 0.72) for POD. No interaction with sex or type of surgery was detected. Adding timed-up-and-go-test and handgrip strength to the FI did not improve discrimination. **Conclusion:** Our data showed a significant association between frailty defined through a 30-item FI and POD among older adults undergoing elective surgery. Adding functional measures to the FI did not improve discrimination. Hence, our preoperative 30-item FI can help to identify patients with increased odds for POD.

OC27- ASSOCIATION OF HEALTHY LIFESTYLE AND SOCIAL ENVIRONMENT WITH MORTALITY AMONG THE FRAIL: FINDINGS FROM THE UK BIOBANK. Junhan Tang(1), Jie Chen(2), Jirong Yue(3), Chenkai W(1) *((1) Global Health Research Center, Duke Kunshan University, Kunshan, Jiangsu, China; (2) Center for Global Health, Zhejiang University School of Medicine, Hangzhou, Zhejiang, China; (3) Department of Geriatrics and National Clinical Research Center for Geriatrics, West China Hospital, Sichuan University, Chengdu, Sichuan, China)*

Background: Physical frailty is a prevalent aging-related geriatric syndrome associated with various adverse health outcomes. Among the frail, adherence to a healthy lifestyle may provide an opportunity to decrease the risk of adverse health outcomes, including mortality and disability. In addition, the health benefits of adhering to a healthy lifestyle may be heterogenous across different social environments. **Objectives:** To examine whether adherence to a healthy lifestyle was associated with lower all-cause mortality among the frail; to evaluate the associations between lifestyle factors and all-cause mortality by the desirability of social environment; to measure the joint association of healthy lifestyle and social environment with all-cause mortality. **Methods:** Data were from the UK Biobank; 15,594 frail adults without missing lifestyle information were included. Frailty was assessed by five criteria: slowness, weakness, exhaustion, inactivity, and shrinking. We created a composite healthy lifestyle score using four lifestyle factors: smoking, alcohol consumption, physical activity, and diet. We used 17 social factors to construct a polysocial score. We classified the lifestyle score into unhealthy and healthy levels, and the polysocial score into low, intermediate, and high level. We used the Cox regression to measure the association of each lifestyle factor and the binary lifestyle score with all-cause mortality, respectively. We also measured the associations within low, intermediate, and high polysocial score categories, respectively. We evaluated the joint association of the binary lifestyle score and the categorical polysocial score with all-cause mortality. **Results:** After multivariable adjustment, frail participants with a healthy level of smoking, physical activity, diet, and lifestyle score had a 40%, 33%, 15%, and 34% lower hazard of all-cause mortality than those with an unhealthy level, respectively. We found significant associations between smoking and lifestyle score with all-cause mortality across polysocial score categories. We revealed the joint effect of a healthy lifestyle and social environment on all-cause mortality. **Conclusion:** A healthy lifestyle may offer an effective solution

to decrease the risk of adverse health outcomes among the frail, especially among those living in an unfavorable social environment.

OC28- EFFECT OF A ONE-YEAR PERSONALIZED INTENSIVE DIETARY INTERVENTION ON BODY COMPOSITION IN COLORECTAL CANCER PATIENTS: A RANDOMIZED CONTROLLED TRIAL. Dena Helene Alavi(1), Hege Berg Henriksen(1), Manuela Zucknick(2), Peter Mæhre Lauritzen(3), Rune Blomhoff(1,4) *((1) Department of Nutrition, Institute of Basic Medical Sciences, University of Oslo, Oslo, Norway; (2) Oslo Centre for Biostatistics and Epidemiology, Institute of Basic Medical Sciences, University of Oslo, Norway; (3) Division of Radiology and Nuclear Medicine, Oslo University Hospital, Oslo Norway and Faculty of Health Sciences, Oslo Metropolitan University, Oslo Norway; (4) Norway and Department of Clinical Service, Division of Cancer Medicine, Oslo University Hospital, Oslo, Norway)*

Background: Given the last years' decrease in mortality rates for colorectal cancer (CRC) patients, there is a growing number of elderly CRC survivors. These may experience larger changes in body composition, such as declines in fat-free mass (FFM) or increases in fat masses (FM). The suggested treatment for low muscle mass or high FM mass is diet and physical activity. There is little evidence on how a personalized dietary intervention influences body composition alone. **Objectives:** Investigate the effect of a dietary intervention on total body weight and body composition after 6 and 12 months of follow-up in patients with CRC stage I-III. **Methods:** Patients from the randomized controlled trial CRC-NORDIET study were included. Body composition was measured using Lunar iDXA at baseline, 6 months and 12 months. The intervention group received an intensive dietary intervention. The control group underwent similar measurements, but no dietary intervention. **Results:** Both groups increased significantly in weight, but the intervention group increased 0.74 kg less than the control group at 6 months (p=0.020). For total FM, the intervention group increased 0.59kg less at 6 months (p=0.019). For FM%, the intervention group had a 0.50% and 0.69% lower increase at 6 months (p=0.012) and 12 months (p=0.011) compared to the control group, respectively. The intervention group gained 63g less visceral adipose tissue (VAT) than the control group at 6 months (p=0.031). No difference between groups was found for FFM and subcutaneous adipose tissue (SAT) at any time point. The control group had a higher increase in FM/FFM ratio after both 6 (p=0.011) and 12 months (p=0.021) compared to the intervention group. **Conclusion:** The dietary intervention mostly affected the fat masses, but not SAT and FFM. Despite the small changes, the dietary intervention may have resulted in an overall more favourable body composition development in the intervention group.

OC29- THE IMPACT OF FRAILTY ON THE OUTCOMES AFTER CARDIAC SURGERY. Jaewon Chang *(St George Hospital, department of cardiothoracic surgery, Sydney, NSW, Australia)*

Background: Frailty is an increasingly recognized marker of poor surgical outcomes in cardiac surgery. Frailty first was described in the seminal «Fried» paper, which constitutes the longest-standing and most well-recognized definition. **Objectives:** This study aimed to assess the impact of the Fried and modified Fried frailty classifications on patient outcomes following cardiac surgery. **Methods:** The PUBMED, MEDLINE, and EMBASE databases were searched from January 2000 until August 2021 for studies evaluating postoperative outcomes using the Fried or modified Fried frailty indexes in open cardiac surgical procedures. Primary outcomes were one-year survival and postoperative quality of life. Secondary outcomes included postoperative complications, intensive care unit (ICU) length of stay (LOS), total hospital LOS, and institutional discharge. **Results:** Eight eligible studies were identified. Meta-analysis identified that frailty was associated with an increased risk of one-year mortality (Risk Ratio [RR]:2.23;95% confidence interval [CI]1.17 -4.23), postoperative complications (RR 1.78;95% CI 1.27 - 2.50), ICU LOS (Mean difference [MD] 21.2 hours;95% CI 8.42 - 33.94), hospital LOS (MD 3.29 days; 95% CI 2.19 - 4.94), and institutional discharge (RR 3.29;95% CI 2.19 - 4.94). A narrative review of quality of life suggested an improvement following surgery, with frail patients demonstrating a greater improvement from baseline over non-frail patients. **Conclusion:** Frailty is associated with a higher degree of surgical morbidity, and frail patients are twice as likely to experience mortality within one-year post-operatively. Despite this, quality of life also improves dramatically in frail patients. In the age of increasing life expectancy and patient complexity owing to advancement in interventional cardiology, patient selection, thus recognising frailty, is more important than ever in cardiac surgery.

OC30- FRAILTY INDEX AND MEXICAN AMERICANS LIVING ON THE US-MEXICO BORDER. Eron G Manusov, Vincent Diego *(University of Texas Rio Grande Valley Rio Grande City, Brownsville, TX, USA))*

Background: Frailty results from overwhelmed resilience related to biopsychosocial and cultural determinants of well-being. The Frailty Index (FI) comprises a ratio of suffered health deficits and total deficits. The FI can identify contributors to health and well-being targeted in healthcare delivery and research across the lifespan. **Objective:** The purpose of our community case study is to describe a Frailty Index calculated from data in a predominantly Mexican American Community residing on the Texas-Mexico border. **Methods:** We used Logistic regression and factor component analysis to identify potential associations between clinical variables, candidate predictor variables, seven physiological health variables, and two survey instruments. We analyzed data obtained from

participants (894) that live in two Colonias located on the Texas-Mexico border. We calculated the FI for 19 health deficits (seven physiological variables, the PHQ-9 score, and the 11 domain-specific Duke Profile scores). **Results:** FI against age in males (n = 272) and females (n = 622) was regressed. Females had a significantly higher starting frailty, and males had a substantially greater change rate with age. FI against age for Cameron Park Colonia and Indian Hills Colonia was regressed. We calculated a significantly higher starting FI in Indian Hills and a considerably greater change rate in Cameron Park residents. Men score higher in the Health-Related Quality of Life (HrQoL), and women higher in anxiety, depression, anxiety/depression, and pain. **Conclusion:** Contributors to Frailty are complex, especially in neighborhoods of poverty, immigration, low education level, and high chronic disease prevalence. We report characteristics of Frailty in a vulnerable population. The methods and the Frailty Index used in this study effectively identify Frailty. Our discussion explores possible explanations.

OC31- MITOCHONDRIAL CALCIUM IMPORT DECLINES DURING SARCOPENIA AND IS STIMULATED BY THE POLYPHENOL OLEUROPEIN TO BOOST ENERGY METABOLISM AND SKELETAL MUSCLE PERFORMANCE. Gaia Gherardi(1), Anna Weiser(2), Flavien Bermont(2), Benjamin Brinon(2), Guillaume E. Jacot(2), Aurélie Hermant(2), Eugenia Migliavacca(2), Mattia Sturlese(3), Leonardo Nogara(1), Denis Barron(2), Stefano Moro(3), Bert Blaauw(1), Rosario Rizzuto(1), Cristina Mammucari(1), Astrid Horstman(2), Umberto De Marchi(2), Jerome N. Feige(2) *((1) Department of Biomedical Sciences, University of Padova, Padova, Italy; (2) Nestlé Institute of Health Sciences, Nestlé Research, EPFL Innovation Park, Lausanne, Switzerland; (3) Department of Pharmaceutical and Pharmacological Sciences, University of Padova, Padova, Italy)*

Background: Mitochondrial decline during aging is a hallmark of sarcopenia. Mitochondrial calcium (mtCa2+) import via the Mitochondrial Calcium Uniporter (MCU) couples the regulation of cellular calcium homeostasis to energy production across organs. In skeletal muscle, MCU-mediated mtCa2+ import is rate-limiting for mitochondrial activation during contraction, but how MCU is affected during physiopathology and whether it can be stimulated therapeutically remains largely uncharacterized. **Objectives:** We aimed to understand the preclinical and clinical association of mitochondrial calcium import with skeletal muscle aging and sarcopenia and to discover a novel MCU-targeted nutritional intervention for skeletal muscle health. **Methods:** We analyzed biomarkers and functional measures of mitochondrial calcium in muscle biopsies and primary myoblasts from older people with or without sarcopenia, and their association with muscle mass and performance. We developed a high-throughput screen of 5000 natural bioactives present in food, that specifically increase Ca2+mt and determined the efficacy and molecular mechanism of Oleuropein as the best nutritional activator of mitochondrial calcium import with a history of safe human use. **Results:** We identified the natural polyphenol Oleuropein and its major metabolites as direct activators of MCU via binding to MICU1. Oleuropein stimulates mtCa2+, mitochondrial respiration and ATP production in an MCU- and MICU1-dependent fashion. Oral administration of Oleuropein acutely stimulates mtCa2+, pyruvate dehydrogenase (PDH) and muscle energy metabolism to increase physical performance and limit muscle fatigue in young, aged but not MCU muscle-specific KO mice. The design of an ongoing clinical trial will be presented where Oleuropein in an olive leave extract is being tested in older people to improve muscle energy and decrease physical fatigue. **Conclusion:** Our work demonstrates that mitochondrial Ca2+ is a direct regulator of mitochondrial decline during aging, and establishes Oleuropein as a novel nutrient that specifically targets MCU to stimulate mitochondrial bioenergetics and muscle performance in healthy and aged individuals.

OC32- DYNAPENIA, MUSCLE QUALITY AND HEPATIC STEATOSIS IN PATIENTS WITH OBESITY AND SARCOPENIC OBESITY. Francesco Frigerio(1), Marina De Marinis(1), Francesca Camardella(1), Vito Cantisani(2), Alessandro Pinto(1), Marco Bernardi(3), Carla Lubrano(1), Lucio Gnessi(1), Massimo Federici(4), Lorenzo Maria Donini(1), Eleonora Poggiogalle(1) *((1) Department of Experimental Medicine, Sapienza University, Rome, Italy; (2) Department of Radiological, Oncological and Pathobiological Sciences, Sapienza University, Rome, Italy; (3) Department of Clinical, Internal Medicine, Anesthesiology and Cardiovascular Sciences, Sapienza University, Rome, Italy; (4) Department of Systems Medicine, University of Rome Tor Vergata, Rome, Italy; Center for Atherosclerosis, Policlinico Tor Vergata, Rome, Italy)*

Background: Accumulating evidence supports a connection between sarcopenic obesity (SO) and NAFLD. To which extent fatty liver contributes to impaired muscle contractility is not well established yet. **Objectives:** The aim of our study was to investigate the effect of NAFLD on dynapenia in patients with SO. **Methods:** Study participants were recruited among patients referring to the High Specialization Center for the Care of Obesity, Policlinico "Umberto I" Hospital, Sapienza University, Rome, Italy. Inclusion criteria were: age > 18 and < 75 years, body mass index >= 30 kg/m^2, Caucasian ethnicity. Obesity was defined as BMI >=30 kg/m^2. Sarcopenic obesity was defined in accordance with the 2022 EASO-ESPEN consensus statement. Muscle strength and quality were assessed through the Handgrip strength (HGS) test using a digital dynamometer (DynEx, Akern, Pontassieve, FI, Italy). The arithmetic mean of three consecutive measurements was calculated for each arm. Hepatic ultrasonography was performed and hepatic steatosis was evaluated based on a semiquantitative method, i.e. the computerized calculation of the hepatorenal index (HRI >=1.28). **Results:** In this study 71 non-diabetic subjects [age 55 (7.8) years, BMI 35.2 kg/m^2 (32.6-38.8)] were classified as having SO and non-sarcopenic obese (NSO). SO patients

displayed worse serum lipid profile, higher body fat and lower skeletal muscle mass (both total and appendicular) than NSO patients, despite no significant difference in body weight, glycometabolic parameters and hepatic steatosis prevalence. A positive correlation between disposition index and muscle quality index (MQI) (r=0.393, p=0.013) emerged after controlling for menopause and body fat percentage. Based on multiple linear regression analysis, MQI was significantly positively associated with the disposition Index (β: 0.059, SE: 0.002, p=0.006) after adjustment for menopause, body fat percentage and the presence of hepatic steatosis according to Hepato-Renal Index (HRI). Similar findings emerged when including liver enzyme levels in place of hepatic steatosis. **Conclusion:** Muscle quality is positively associated with β-cell function corrected for insulin resistance among patients with obesity and sarcopenic obesity, irrespective of fatty liver disease presence.

OC33- INTRINSIC CAPACITY TRAJECTORIES IN THE INSPIRE ICOPE CARE COHORT. Emmanuel Gonzalez-Bautista(1,2), Philipe de Souto Barreto(1,2), Maria Eugenia Soto Marin(1,2), Caroline Berbon(1), Neda Tavassoli(1) *((1) Gerontopole, W.H.O Collaborative Center for Frailty, Clinical Research and Geriatric Training, Toulouse University Hospital, 31059 Toulouse, France; (2) Maintain Aging Research team, CERPOP, Université de Toulouse, Inserm, Université Paul Sabatier, Toulouse, France)*

Background: Intrinsic capacity (IC) is the aggregate of physical and mental capacities people can draw upon as they age. Five domains operationalize IC: cognition, locomotion, nutrition, vision, hearing and psychological with clinical pathways in the WHO's Integrated Care for Older People (ICOPE). The INSPIRE ICOPE Care cohort has assessed IC among 21,000 people aged 60 and over in France. **Objectives:** To characterize the transition patterns between two consecutive IC assessments; and the cross-sectional and longitudinal trajectories of the IC domains in the INSPIRE ICOPE Care cohort participants. Also, to explore the interrelation among the IC domains. **Methods:** We explored INSPIRE ICOPE care data from professional assessments of ICOPE Steps 1 and 2. We used descriptive techniques to obtain the cross-sectional trajectories of IC domains by age and sex. We got the transition patterns between two consecutive assessments. We applied group-based trajectory modelling and mixed-effects methods to explore the longitudinal IC trajectories. **Results:** There were 2,246 people with at least 3 IC screenings and about 150 adults with at least three IC in-depth assessments. The following pairs of domains showed similar transition patterns: cognition-locomotion, psychological-nutritional and hearing-vision. More than half of the participants with positive malnutrition screening reversed to negative at 5.5 months follow-up. All the domains showed screening reversion ≥20% except for hearing. Trajectories of deteriorated cognition and nutrition were associated with functional declines for ADLs. Locomotion trajectories showed capacity recoveries (SPPB). **Conclusion:** In this exploratory analysis, we found that the IC domains exhibit differential patterns in older adults seeking health care in the French Occitania region, notably positive screening reversion and capacity recovery. Further research is needed to understand the natural history of the IC domains and their interrelation.

OC35- MOVING TOWARDS THE ICOPE APPROACH: EVALUATION OF COMMUNITY-BASED INTERVENTION ACTIVITIES ON IMPROVING INTRINSIC CAPACITY. Ruby Yu(1,2), Derek Lai(1), Grace Leung(1), Jean Woo(1,2) *((1) CUHK Jockey Club Institute of Ageing, The Chinese University of Hong Kong, Hong Kong, China; (2) Department of Medicine & Therapeutics, The Chinese University of Hong Kong, Hong Kong, China)*

Background: Community-based intervention activities can be effective in improving the intrinsic capacity (IC) of older people. However, it is less well-known whether different types of activities may have differential effects. **Objectives:** Following the ICOPE framework, this study aims to guide community service providers in Hong Kong to adopt a people-centred approach for maximizing the benefits of their intervention activities. To this end, the study attempts to (1) identify subgroups of older people based on their IC, (2) examine whether and how the effects of different types of activities vary across these subgroups, and (3) assess whether the activity par-ticipation patterns of older people align with their actual needs. **Methods:** Participants were community-dwelling older people aged 60 years or above. They were screened for impairments in IC domains at baseline, and their participation records of different types of intervention activities were collected for one year. Cluster analysis was used to group participants based on their IC impairment patterns. Mixed-effects regression was used to examine whether and how the effects of activity partici-pations on IC vary across the identified subgroups. Activity participation patterns were compared across subgroups using a profile analysis. **Results:** Four clusters were identified, including those who were robust (cluster 1), those who had cognitive decline (cluster 2), those who had impaired mobility and vitali-ty (cluster 3), and those with poor psychological well-being (cluster 4). Using cluster 1 as the reference, the effects of cognitive, exercise, and mental activities were respec-tively higher for cluster 2 ($\beta = 0.031$, 95% CI [0.013, 0.049]), cluster 3 ($\beta = 0.044$, 95% CI [0.018, 0.069]), and cluster 4 ($\beta = 0.044$, 95% CI [0.009, 0.080]). However, the profiles of activity participations of the four clusters were parallel (Wilk's $\Lambda = 0.997$, $F = 1.735$, $p = .053$) and coincident (Wilk's $\Lambda = 1.000$, $F = 0.236$, $p = .872$), indicating that the activi-ties might not have targeted the populations based on their needs. **Conclusion:** Given that intervention activities are most beneficial to those with impair-ments in the corresponding IC domains, a people-centred and targeted approach should be adopted to maximize the overall benefits.

OC36- FRAILTY IN THE CHRONIC RESPIRATORY PATIENT: ASSOCIATION WITH MORTALITY AND CLINICAL FEATURES IN OBSTRUCTIVE, RESTRICTIVE AND MIXED SPIROMETRIC PATTERNS. Simone Scarlata(1), Sonia Zotti(1), Panaiotis Finamore(1), Matteo Cesari(2,3), Christian R. Osadnik(4,5), Raffaele Antonelli Incalzi(1), Pedone Claudio(1) *((1) Unit of Internal Medicine and Geriatrics; Fondazione Policlinico Campus Bio-Medico University Hospital, Rome- Italy; (2) Geriatric Unit, Fondazione IRCCS Istituti Clinici Scientifici Maugeri, Milan, Italy; (3) Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy; (4) Department of Physiotherapy, Monash University, Melbourne, Australia; (5) Monash Lung and Sleep, Monash Health, Melbourne, Australia)*

Background: Frailty showed to be strongly associated with respiratory impairment and likely accounts for additional mortality in subjects with poor lung function. However, little is known on whether differences exist in frailty determinants according to the different respiratory patterns. We hypothesized that qualitative parameters composing the Frailty Index (FI) may vary according to different spirometry-related dysfunction. **Objectives:** The aim of the present study was therefore to evaluate the mortality risk between frail and not-frail subjects with chronic lung impairment, and identify if factors leading to frailty present differently according to spirometric groups. **Methods:** Data from the Salute Respiratoria nell'Anziano – Respiratory Health in the Older Persons (SARA) study were retrospectively analyzed, including 1,339 participants (aged 73.7, SD 6.3 years). Hazard ratios (HR) for 5-year mortality were calculated using Cox regression models. The accuracy of the FI, computed on 21 health domains, in predicting mortality was estimated using Receiving Operator Curves and calculation of the Area Under the Curve (AUC). The association between spirometric groups and frailty parameters was quantified using Odds Ratios (OR). **Results:** After adjustment for age and sex, a two-fold increased mortality risk was found in all spirometric groups with frailty versus the not frail comparators (HR 2.25, 95%CI 1.37-2.84, p<0.001 overall cohort; HR=2.08, 95%CI 1.37-3.18, p=0.001 obstructive; HR=2.27, 95%CI 1.04-1.17, p=0.04 restrictive; HR=2.21, 95%CI 1.20-3.08, p=0.03 mixed). The overall ROC-AUC of FI in predicting mortality was 0.68, ranging from 0.641 in obstructive to 0.741 in restrictive patterns. A strong association in having reduced walking distance capability, smoking history, and dyspnea was found in all spirometric groups (p<0.05). History of myocardial infarction presented significatively with obstructive pattern (OR: 1.6, 95% CI: 1.04 – 2.66), cognitive impairment and chronic heart failure with restrictive (OR: 3.6, 95% CI: 1.9 – 6.8; OR: 3.8, 95% CI: 1.5 – 9.3, respectively) and type 2 diabetes mellitus with mixed one (OR: 1.7, 95% CI: 1.07 – 3). **Conclusion:** Fragile patients affected by chronic respiratory disease, have an increased risk of mortality, independently of age and sex. Differences in FI parameters across respiratory patterns, may help clinicians to treat reversible frailty aspects and prevent associated worse outcomes in chronic respiratory disease.

OC37- ASSOCIATION BETWEEN INTRINSIC CAPACITY AND FRAILTY IN THE PRIMARY CARE POPULATION WITH MULTIMORBIDITY. X Ng(1), SZ Sim(1), SY Tan(1), GTY Ding(1), ES Lee(1,2) *((1) National Healthcare Group Polyclinics, Singapore, Singapore; (2) Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore, Singapore)*

Background: Multimorbidity is prevalent in primary care and is associated with declines in intrinsic capacity (IC), frailty and subsequent disability. Although IC is a distinct concept from frailty, there is overlap between them and it is important to understand their relationship, to enable implementation of appropriate and timely interventions in individuals with multimorbidity. **Objectives:** We aimed to determine the association between IC and frailty with respect to disease burden, demographic, social and lifestyle factors in an elderly primary care population with multimorbidity. **Method:** A cross-sectional survey was conducted in three primary care centres in Singapore from August to October 2022. Participants were aged 60 to 100 years who could walk independently and had at least the most common multimorbidity triad in Singapore- hypertension, hyperlipidaemia, and diabetes mellitus. Data collected included socio-demographic variables, social factors including social isolation (Lubben Social Network Scale-6), loneliness (three-item UCLA loneliness scale) and social participation (social role domain of the Late-Life Function and Disability Instrument); smoking, level of multimorbidity, IC (WHO Integrated Care for Older People (ICOPE) Screening Tool), and frailty (modified Fried). The association between IC (number of intact domains) and frailty status (robust and pre-frailty/frailty) was determined using Mann-Whitney U test and then adjusted for the other factors using multiple regression analysis. **Results:** The study included 412 participants (mean age 69.9$\pm$6.0 years). Robust participants had a median of four intact IC domains (IQR 3-4) while pre-frail/frail participants had a median of three intact domains (IQR 2-4). Mann-Whitney U showed significant association between IC and frailty (p<0.001) but that was lost in multiple regression analysis (p-value=0.147) which instead showed significant associations between IC and age (older participants had lower IC, p-value<0.01), gender (females had lower IC, p-value=0.036), ethnicity (non-Chinese had lower IC than Chinese, p-value=0.001), loneliness (those who were somewhat lonely or lonely had lower IC, p-value=0.002) and social participation (those with increased participation had higher IC, p-value=0.005). **Conclusion:** Social factors may influence the association between IC and frailty in the primary care population with multimorbidity. More longitudinal studies are required to understand their role in the development of declines in IC and frailty.

OC38- CIRCULATING REJUVENATING FACTORS AND DECLINE OF GRIP STRENGTH IN OLDER ADULTS: THE BALTIMORE LONGITUDINAL STUDY OF AGING. Yuko Yamaguchi(1,2), Pingbo Zhang(1), Min Zhu(3), Ruin Moaddel(3), Elango Palchamy(3), Luigi Ferrucci(3), Richard D. Semba(1,4) *((1) Wilmer Eye Institute, Johns Hopkins University School of Medicine, Baltimore, MD, USA; (2) Graduate School of Health Sciences, Kobe University, Kobe, Hyogo, Japan; (3) National Institutes on Aging, National Institutes of Health, Baltimore, MD, USA; (4) Center for a Livable Future, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD USA)*

Background: Although growth/differentiation factor 11 (GDF11), growth/differentiation factor 8 (GDF8), and their circulating antagonists, which include GDF11 and GDF8 propeptides, follistatin (FST), WFIKKN1, and WFIKKN2, have been shown to influence skeletal muscle and aging in mice, the relationship of these circulating "rejuvenating factors" with human phenotypes is less clear. Objectives: To characterize the relationship between plasma GDF8, GDF11, FST, WFIKKN1, and WFIKKN2 concentrations with the decline of grip strength in adults, ≥65 years, who participated in the Baltimore Longitudinal Study of Aging and had grip strength measured over time. **Methods:** Plasma GDF8 and GDF11 mature proteins, GDF8 and GDF11 propeptides, FST (isoform FST315 and cleaved form FST303), WFIKKN1, and WFIKKN2 concentrations were measured using selected reaction monitoring-tandem mass spectrometry at baseline. Grip strength was measured at baseline and at follow-up visits (median follow-up 8.87 months). **Results:** Mean (standard deviation) grip strength declined in men and women by -0.84 (2.45) and -0.60 (1.32) kg/year, respectively. Plasma GDF8 and GDF11 mature proteins, GDF8 and GDF11 propeptides, FST315, FST303, WFIKKN1, and WFIKKN2 concentrations were not independently predictive of the decline of grip strength in men or women in multivariable linear regression analyses that adjusted for potential confounders. Rejuvenating factors and their antagonists and interaction terms between proteins were not associated with decline of grip strength in men or women in alternative analyses in which all proteins were entered together in the models. **Conclusion:** Circulating GDF8, GDF11 and their antagonists do not appear to influence the decline of grip strength in older men or women. Studies in humans have largely been unable to replicate the findings regarding "rejuvenating factors" from aging studies in mice.

OC39- PREOPERATIVE FRAILTY AND MORTALITY IN MEDICARE BENEFICIARIES UNDERGOING MAJOR AND MINOR SURGICAL PROCEDURES. Chan Mi Park(1), Jessica J. Lie(2), Laiji Yang(1), Natalia Gouskova, Dae Hyun Kim(1) *((1) Hebrew SeniorLife, Boston, MA, USA; (2) Division of General Surgery, University of British Columbia, Vancouver, BC, Canada)*

Background: The number of older adults receiving surgical procedures is increasing owing to advancements in surgical and anesthetic techniques. Previous studies showed that preoperative frailty is associated with postoperative mortality and poor surgical outcomes even after low-risk procedures. Whether the association is consistent across major and minor surgical procedures of different surgical stress has not been well studied. **Methods:** This retrospective study used the 2014-2019 5% random sample of Medicare fee-for-service beneficiaries who underwent surgical procedures (N=1,129,055). Surgical procedures were categorized by the Operative Stress Score (OSS) (range: 1 [e.g., knee arthroscopy] to 5 [e.g., removal of lung]). Preoperative frailty was measured by a claims-based frailty index (range: 0 to 1; non-frail <0.15, pre-frail 0.15-0.24, mildly frail 0.25-0.34, and moderate to severely frail ≥0.35). We estimated the age and sex-adjusted risk ratio (RR) of mortality at 30 days, 6 months, and 1 year associated with frailty category stratified by OSS category. **Results:** We identified 1,885,652 surgical procedures (OSS category 1 to 5: 30.1%, 47.7%, 20.2%, 1.9%, and 0.2%). The mean age was 76.3, 48.5% were female, and 90.3% were white. Overall, postoperative mortality was 1.6% at 30 days, 5.1% at 6 months, and 7.8% at 1 year. Frailty was associated with increased 30-day, 6-month, and 1-year postoperative mortality across OSS categories. At 1 year, patients with moderate-to-severe frailty had significantly elevated mortality after OSS category 1 minor procedures (27.4% vs 3.2%; adjusted RR [95% CI], 7.9 [7.6-8.1]) as well as after OSS category 5 major procedures (33.3% vs 15.8%; adjusted RR [95% CI], 2.1 [1.4-3.1]) compared to non-frail patients. **Conclusion:** Frailty is associated with increased 30-day, 6-month, and 1-year mortality after major and minor procedures. These national data can be useful for risk stratification and shared decision-making before surgery with older patients.

OC40- ASSOCIATIONS BETWEEN CIRCULATING MICRONUTRIENTS, CLINICAL BIOMARKERS AND SKELETAL MUSCLE MASS: PRELIMINARY RESULTS FROM A CROSS-SECTIONAL ANALYSIS OF DATA FROM THE BALTIMORE LONGITUDINAL STUDY OF AGING. Jamie Scott(1), Donnie Cameron(1,2), Max Yates(1), Toshiko Tanaka(3), Luigi Ferrucci(3), Ailsa Welch(1) *((1) Norwich Medical School, University of East Anglia, Norwich, UK; (2) Department of Radiology, C.J. Gorter MRI Center, Leiden University Medical Center, Leiden, Netherlands; (3) Translational Gerontology Branch, Intramural Research Program, National Institute on Aging, National Institutes of Health, Baltimore, MD, USA)*

Background: Over the next two decades the prevalence of sarcopenia is predicted to increase dramatically due to an ageing population, resulting in increased healthcare costs and challenges for public health (1). Loss of skeletal muscle mass (SMM) is a key component of sarcopenia (2): many micronutrients and routinely-measured clinical biomarkers influence muscle physiology, but relationships between these and SMM have not been extensively explored. Investigating these relationships may highlight micronutrients that are important for maintaining muscle mass during ageing, and

biomarkers that are useful for identifying individuals at risk of sarcopenia. Our prior preliminary work investigated micronutrients and clinical biomarkers and measures of muscle function. **Objectives:** To investigate associations between blood concentrations of micronutrients (vitamin B12, vitamin D, magnesium, potassium and iron), clinical biomarkers (albumin, haemoglobin, HbA1c, creatinine and homocysteine) and SMM. **Methods:** Cross-sectional data were provided for 1,761 adults aged between 22 and 103 years old from the Baltimore Longitudinal Study of Aging. DXA-measured appendicular SMM (ASM) was calculated as the sum of lean mass minus bone mass in the arms and legs, and was scaled for height (ASM/height2: ASMht). This preliminary analysis investigated associations between circulating micronutrients or clinical biomarkers and ASMht using univariate linear regression, and multiple linear regression, adjusted for age, BMI, smoking status and race. **Results:** After adjustment for age, BMI, smoking status and race, both haemoglobin (g/dL) (B = -0.056, p = 0.031) and albumin (g/dL) (B = -0.26, p = 0.001) were negatively associated with ASMht in women. In men, albumin (g/dL) (B = -0.20, p = 0.046) and homocysteine (μmol/L) (B = -0.031, p = 0.045) were negatively associated with ASMht. Additionally, in men, there was a trend toward significance for HbA1c (%) (B = -0.093, p = 0.063) and creatinine (mg/dL) (B = 0.25, p = 0.057). No significant associations were observed between any micronutrient and SMM. **Conclusion:** Further analysis will determine whether these associations are altered following adjustment for physical activity and micronutrient supplementation, however, these preliminary findings suggest that specific clinical biomarkers may be associated with SMM and, therefore, may be useful for identifying individuals at risk of sarcopenia. **References:** 1. Ethgen O, Beaudart C, Buckinx F, Bruyere O, Reginster JY. The Future Prevalence of Sarcopenia in Europe: A Claim for Public Health Action. Calcif Tissue Int. Mar 2017;100(3):229-234. doi:10.1007/s00223-016-0220-9; 2. Cruz-Jentoft AJ, Bahat G, Bauer J, et al. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing. Jan 1 2019;48(1):16-31. doi:10.1093/ageing/afy169

OC41- RADIOMIC FEATURES OF SKELETAL MUSCLE DERIVED FROM CT SCANS ARE ASSOCIATED WITH PHYSICAL FUNCTION IN THE MROS STUDY.

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Background: Radiomic analysis of CT images provides biomarkers of muscle heterogeneity (variation in patterns and texture on images) which may improve prediction of physical function in older adults. "Radiomic" refers to multiple parameters derived from images. **Objective:** To determine if radiomic features of skeletal muscle derived from abdominal CT images are associated with leg power, grip strength, and gait speed, independent of muscle size and density, in 2644 men (mean age 74.0) in the MrOS Study. **Methods:** On CT images at L3 level, our fully-automated machine learning algorithm determined total abdominal skeletal muscle area (SMA), skeletal muscle density (SMD), and 75 radiomic features of muscle texture. Factor analysis was used to reduce the number of radiomic features into latent variables that explain the underlying data. Association of these factors with leg power, grip strength, and gait speed was determined using linear regression models adjusted for SMA, SMD, intermuscular adipose tissue area (IMAT), CT parameters (scanner model, slice thickness, tube current), participant age, height, diabetes status, self-reported health, and number of medications. **Results:** In fully adjusted models with standardized βs, 1 SD increment in SMA (β = 25.10; CI = 15.19, 35.01) was independently associated with greater leg power. 1 SD increment in radiomic factor 2 (β = -13.68, CI = -18.77, -8.58) and radiomic factor 4 (β = -12.64, CI = -19.68, -5.60) were independently associated with lower leg power. Each 1-SD increment in SMA (β = 2.03; CI = 0.55, 3.50) was independently associated with greater grip strength, but no radiomic factors or other CT-derived metrics were associated with grip strength. Each 1-SD increment in IMAT (β = -0.03, CI = -0.05, -0.01) was associated with slower gait speed; no other CT-derived metrics were significantly associated with gait speed. **Conclusion:** In older men, CT-derived radiomic features indicating higher muscle heterogeneity are associated with lower grip strength and leg power independent of skeletal muscle size and density.

OC42- CIRCULATING SENESCENT AND ANGIOGENIC T LYMPHOCYTES IN AGEING AND FRAILTY.

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Background: Though typically characterised by a loss of physical function, there is also an under-researched vascular dimension to frailty. There is a need to identify vascular and geroscience-relevant markers and mediators that can physiologically link ageing to vascular disease. There is evidence of specific T cell subsets, all influenced by age, that exert positive and negative effects on vascular health. CD31+, termed angiogenic T cells, have been linked to vascular repair whereas CD28NULL, termed senescent T cells, display pro-inflammatory and cytotoxic effector functions. CD31+CD28NULL, described as senescent angiogenic T cells, are associated with endothelial dysfunction in hypertension. **Objective:** This study sought to determine

the combined influence of increasing age and frailty status on these circulating CD31+ and CD28NULL T cell subsets. **Methods:** This cross-sectional study recruited four different cohorts of men and women; young (20-30 years, n=23), older (65-75 years, n=17), robust non-frail (76+ years, n=17), and frail (76+ years, n=15) adults. Frailty was determined using the Fried Frailty method. T cell subsets were determined by whole blood flow cytometry based on the expression of CD3, CD4, CD8, CD31 and CD28. **Results:** Whether expressed as circulating counts or as a % of total T cells, there was a progressive decrease ($p<0.05$) in CD31+ angiogenic T cells with increasing age but paradoxically higher values ($p<0.05$) in the frail compared to the robust non-frail groups, a trend particularly evident in the CD4+ fraction. CD28NULL senescent T cells were considerably higher ($p<0.05$) in the CD8+ compared to the CD4+ fraction. Specific CD28NULL subsets were higher in the combined older non-frail compared to the young participants and higher in the frail compared to the robust non-frail participants. Percentage CD28 negativity was higher in the CD4+ (4% vs 9%, $p<0.05$) and CD8+ (34% vs 53%, $p<0.05$) fractions in the frail compared to the robust non-frail group respectively. CD8+CD31+CD28NULL were also higher in the frail compared to the robust non-frail participants ($p<0.05$). **Conclusion:** CD8+CD28NULL T cells are considerably elevated in frailty and may serve as a useful target for intervention. In contrast, CD31+ T cells may have a more complex association with ageing and disease.

OC43- ONLINE REMOTE PHYSICAL ACTIVITY INTERVENTION TO PREVENT PHYSICAL PERFORMANCES IN COMMUNITY-DWELLING OLDER ADULTS DURING ISOLATION PERIODS: ONLY ONE RECIPE? Mylene Aubertin-Leheudre(1,2), Jordan Granet(1,2), Eva Peyrusqué(1,2), Fabien Ruiz(1,2), Fanny Buckinx(1,2), Benjamin Pageaux(2,3) *((1) UQAM, Faculté des sciences, Département des sciences de l'exercice, GRAPA, Montréal; Québec-Canada; (2) Centre de recherche de l'institut Universitaire de Gériatrie de Montréal (CRIUGM), Montréal; Québec-Canada; (3) U de Montréal, Faculté de Médecine; École de kinésiologie et des sciences de l'activité physique, Montréal; Québec-Canada)*

Background: Periods of involuntary isolation (such as lockdown; heat or cold waves) increase the risk of physical inactivity, which can contribute to physical decline among older adults. Online technology could be an innovative solution to promote physical activity habits in this context. However, the effects of these adapted remote web-based interventions (live or video or combined) remain unclear in older adults. **Objectives:** 1) To examine the acceptability, feasibility and potential benefits of 2 modalities of web-based PA interventions (study-1); 2) To explore which recorded-live sessions ratio leads to the best implementation and benefits (study-2). **Methods:** Non-physically active community-dwelling older adults (>60yrs) were recruited during the 2 first COVID-19 lockdowns and randomized by block period to a 12-week web-based PA intervention [study-1: Live Group (LG; n=38) vs. Recorded Group (RG; n=45) /study-2: Live-Recorded-Live group (LRL; n=22) vs. Recorded-Live-Recorded group (RLR; n=24)]. Acceptability, feasibility as well as physical performance [muscle endurance (30sec STS); muscle power (10 STS); SPPB] quality of life (EQ-5D) and PA level/motivation were assessed pre- and post-intervention. **Results:** 1st study: Fewer dropouts in LG than RG (LG:16% vs. RG:46%) were found. Adherence rate (LG:89%; RG:81%), level of satisfaction (LG:77%; RG:64%) and enjoyment (LG:68%; RG:62%) were similar across groups. Physical performance and quality of life improved significantly in both groups. Only LG showed significant improvements in perceived health and PA levels. Finally, LG showed greater physical performance and quality of life improvements than RG. 2d study: Dropout rate (LRL:14% vs. RLR: 29%) and adherence (>85%) were similar between groups. Both groups reported similar levels of satisfaction (>70%), enjoyment (>75%) and perceived exertion (>60%). Both groups increased physical performances with greater improvements in muscle power ($p=0.010$) and endurance ($p<0.001$) in the LRL group. **Conclusion:** Web-based PA interventions using a decisional tree to prescribed adapted levels are safe, feasible, acceptable and beneficial for improving physical performance during isolation periods. However, PA programs which included full or more interactive web and live sessions (LLL or LRL) appear to be more effective for maintaining or improving physical health. Further research is needed as well as longitudinal follow-up (in process).

OC44- SINGAPORE CLINICAL PRACTICE GUIDELINES FOR SARCOPENIA: PROCESS, RESULTS AND LESSONS LEARNT. WS Lim(1,2), CY Cheong(3), J.P. Lim(1), MMY Tan(4), JQ Chia(1), NA Malik(5), L Tay(6) *((1) Institute of Geriatrics and Active Ageing, Tan Tock Seng Hospital, Singapore; (2) Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore; (3) Khoo Teck Puat Hospital, Singapore; (4) Ng Teng Fong Hospital, Singapore; (5) St Mary's Hospital, Portsmouth, United Kingdom; (6) Sengkang General Hospital, Singapore)*

Background: Singapore recently published the first country-specific Clinical Practice Guidelines (CPG) for sarcopenia. Building upon the seminal ICFSR 2018 CPG for sarcopenia, facilitators included: national interest in sarcopenia as a major risk factor of public health concern for frailty; upsurge in clinical and research interest; strong support from the local professional bodies; and need for contextualized evidence-based recommendations that facilitate adoption of the Asian Working Group for Sarcopenia (AWGS) 2019 consensus into current practice in Singapore. **Objectives:** To present the final recommendations of the Singapore CPG for Sarcopenia, and to distil lessons learnt from the process. **Methods:** The workgroup drew upon three main sources of evidence: AWGS'2019 consensus; updated literature review of Singapore studies till 31 Dec 2020; and recent systematic reviews. From 40 local studies included for data extraction, we constructed evidence tables organized as: definition and epidemiology; diagnosis and

evaluation; and treatment and intervention. We developed 20 recommendations covering case-finding, diagnosis, treatment, prevention, and research, which were graded for strength and quality using the GRADE approach. Consensus from an expert panel was achieved after two rounds of the modified Delphi process. **Results:** We conditionally recommend a case-finding approach in at-risk older adults using validated case-finding tools. For diagnosis, we conditionally recommend using the AWGS'2019 algorithm, with dual-energy X-ray absorptiometry performed only when necessary to determine low lean mass for confirmatory diagnosis. For treatment, we strongly recommend resistance-based exercises and conditionally recommend a quality diet with adequate protein/caloric intake, with Vitamin D supplementation for insufficiency (<30 micrograms/L). We strongly recommend regular physical activity and resistance-based exercise for sarcopenia prevention. We encourage more research to address local evidence gaps. **Conclusion:** The Singapore CPG represents a major step in translation of sarcopenia into clinical practice. Key takeaways include: 1) alignment with national agenda of local health authorities; 2) support from major stakeholders and professional bodies; 3) adequate representation in the workgroup and expert panels; 4) operational efficiency by leveraging upon prior work (such as ICFSR 2018 CPG and existing consensus criteria); 5) harnessing local body of evidence; and 6) adopting Pasteur's quadrant lenses to develop recommendations which balance rigor with relevance.

OC45- PREBIOTIC SUPPLEMENTATION IMPROVES COGNITION VERSUS PLACEBO IN HEALTHY OLDER TWINS: THE PROMOTE STUDY. Mary Ni Lochlainn, Ruth C.E. Bowyer, Paul Seed, Kevin Whelan, Claire J Steves *(King's College London, London, United Kingdom)*

Background: There is a growing body of evidence linking the microbiota in the human gut, to the brain and specifically to cognition. Animal and human studies have shown that inducing changes in the microbiota can alter cognitive behaviour, suggestive of causative pathways. **Objectives:** The PROMOTe trial aimed to test whether the gut microbiome mediates anabolic resistance to protein in older adults. A secondary objective was to test whether modulation of the gut mi-crobiome using a pre-biotic food supplement, improved cognition versus placebo. **Methods:** This is a placebo controlled double blinded randomised controlled trial using twin pairs, re-curited from the TwinsUK cohort. We recruited those aged >=60, with low protein intake at baseline, and access to a computer to take part (due to remote trial delivery). Each twin pair was randomised as a pair, so one twin received protein supplementation plus placebo and the other twin received protein supplementation plus a gut microbiome modulator (prebiotic). Intervention period was 12 weeks, with participants advised to take 1 sachet of supplement daily, and all were advised to undertake regular resistance exercises. The primary outcome was muscle strength as measured using chair-rise time. Cognition, as measured by CANTAB cognitive batter was a secondary outcome. A factor analysis score was used to combine the results of the five cognitive tests carried out. Linear mixed effects regres-sion models were used to compare intervention groups (arm 1 vs arm 2; blinded) on their change in cognition score at 12 weeks. Twin clustering was considered as random effects, both family identifier and zygosity, and treatment group as fixed effect. **Results:** Target sample size was 70 individuals. We screened 626 and randomised 72 participants (36 pairs). More adverse events occurred in the prebiotic group (n=8 versus n=2 in placebo group; p=0.041), but compliance remained high in both groups (% adherence based on sachet count at study end >78% in each group; p=0.37). There was no significant difference between arms for the primary outcome of chair rise time (coefficient 0.184; 95% CI -0.569-0.938; p=0.631). The prebiotic intervention arm had an improved cognition factor score versus the placebo group (coefficient 0.482; 95% CI 0.823-0.141; p=0.014). **Conclusion:** Prebiotic food supplementation improves cognition versus placebo in a cohort of healthy older twins.

OC46- KNEE OSTEOARTHRITIS AND MUSCLE ADIPOSITY INDEPENDENTLY PREDICT AN ACCELERATED ACCUMULATION OF FRAILTY DEFICITS DIFFERENTIALLY MEDIATED BY PHYSICAL FUNCTION: THE 6-YEAR LONGITUDINAL AMBERS COHORT STUDY. Andy Kin On Wong(1,2), Courtney Kennedy(3,4), Kenneth Tam(1,6), Siwen Liu(1), Shannon Reitsma(5), Hana Gillick(5), Alexandra Papaioannou(3,4), Jonathan D. Adachi(5) *((1) Joint Department of Medical Imaging; Schroeder's Arthritis Institute, University Health Network, Canada; (2) Dalla Lana School of Public Health, University of Toronto, Canada; (3) GERAS Centre for Aging Research, Hamilton Health Sciences, Canada; (4) Division of Geriatrics, McMaster University, Canada; (5) Division of Rheumatology, McMaster University – all Ontario, Canada; (6) Department of Physiology, University of California Davis, San Francisco, CA, USA)*

Background: Muscle quantity and weakness are associated with frailty and knee osteoarthritis (KOA). It is unclear how fat distribution within muscles contribute to frailty acceleration in the context of KOA. **Objectives:** To determine how inter- and intramuscular fat (IMF) of the calf relates to frailty trajectories – either within the causal pathway from KOA to accelerated frailty, or independently of KOA. **Methods:** Women 60-85 were recruited to the Appendicular Muscle and Bone Extension Research Study (AMBERS) and completed baseline fast spin echo MRI and peripheral QCT mid-calf scans (66% site) along with 30-sec chair stand and timed 'up-and-go' tests. Comorbidities, health utilities and activities of daily living questionnaires were administered annually for 5 subsequent years to formulate the CaMos Frailty Index (CFI, cumulative deficits approach). Muscle and IMF were segmented from MR images using a fully-automated algorithm we designed in Python. CT muscle was separated from fat by density thresholds. Statistics: Group-based trajectory modeling classified individuals into frailty trajectories with classes and trajectory polynomials guided by AIC/BIC, parsimony

and scientific rationale. Logistic regression determined how presence of KOA, muscle quantity, density or IMF% each predicted high-accelerating versus medium-moderately-changing or low-unchanging CFI trajectory classes. Path analysis evaluated IMF% or physical function as mediators in the relationship between KOA and frailty trajectories. **Results:** Among 280 women (mean age: 75.2±5.9yrs, BMI: 29.4±5.6kg/m^2), 8.2%(23) had KOA and 22.2%(70) had IMF% in the highest quartile. Each of IMF% (OR: 1.47(1.05,2.05)) and muscle mass (adjusting for muscle area, 3.08(1.43,6.65)) predicted accelerated frailty independently of KOA. Muscle density was no longer a predictor (OR: 1.66(1.15,2.39)) after accounting for IMF% (OR: 1.42(0.88,2.27)). Having KOA showed a 3.68(1.11-12.21)-fold odds for accelerated frailty even adjusting for IMF% or physical function. Neither IMF% nor physical function were significant mediators to the KOA-CFI trajectory relationship. Physical function was a mediator (39.3-40.5% indirect effect) in the IMF%-CFI trajectory relationship but IMF%'s direct effect (59.5-60.7%) on accelerated frailty remained marginally significant (p=0.085-0.096). **Conclusion:** KOA is a major predictor of accelerated accumulation of frailty-related deficits that is not explained by fat within muscle or weaker physical function. Having leaner muscles prevents accelerated frailty independently of KOA.

OC47- ASSOCIATION OF CIRCULATING MIRNAS WITH SARCOPENIA: THE SARCOPHAGE STUDY. Marjorie Millet(1,2), Maxime Auroux(1,5), Charlotte Beaudart(3), Jean-Yves Reginster(3), Olivier Bruyère(3,4), Roland Chapurlat(1,2,5), Jean-Charles Rousseau(1,2) *((1) INSERM 1033; (2) PMO, Lyon, France; (3) Department of Public Health, Epidemiology and Health Economics, University of Liège, Belgium; (4) Department of Sports Sciences, University of Liège, Belgium; (5) Hôpital E. Herriot, Hospices Civils de Lyon, France; University of Lyon, France)*

Background: Sarcopenia, the age-related decline in skeletal muscle mass and function, is a major health issue in geriatric medicine. With aging, skeletal muscle gene expression is significantly dysregulated suggesting that epigenetic alterations may play a crucial role in the skeletal muscle aging process. The small non-coding microRNAs (miRs) are endogenous regulators of gene expression. They bind to complementary sequence on target messenger RNA transcripts resulting in translational repression or target degradation. The remarkable miR stability in biofluids suggests they could become non-invasive disease biomarkers. **Objectives:** The objective of our study is to identify a microRNA signature associated to sarcopenia compared to a non-sarcopenic control population. **Methods:** The study group included Belgian subjects belonging to the population-based cohort SarcoPhage. Expression levels of serum miR were measured in 92 healthy subjects without sarcopenia (74.2 ± 10 years) and in 92 subjects with sarcopenia (75.3 ± 6.8 years). Both groups were matched for age and sex. We selected 8 miRs to measure their serum expressions based on results from our previous NGS study (Next Generation Sequencing, ICFSR 2018) and according to the literature. **Results:** Serum has-miR-133a-3p and has-miR-200a-3p were significantly decreased in the sarcopenic group vs controls. Has-miR-744-3p and has-miR-151a-3p were decreased and increased in the sarcopenic group respectively, but this barely reached significance. **Conclusion:** In sarcopenic subjects, miR-133a-3p and 200a-3p expression was downregulated, consistent with their potential targets inhibiting muscle cells proliferation and differentiation. In contrast, the variations of miR-744a-3p and miR-151a-3p may reflect the adaptation of metabolic activity of muscle cells to lower muscle mass in order to maintain the steady state of muscle quality. These variations of miR-744a-3p and miR-151a-3p are possibly inadequate to compensate for the muscle loss leading to sarcopenia.

OC48- EFFECT OF SIRT6 AND PHYSICAL EXERCISE ON PHYSIOLOGICAL AND METABOLIC PROCESSES IN SKELETAL MUSCLE IN AGING. M. Gonen, A. Katz, Z. Schwart, G. Jacobson, N. Touitou, R. Nagar, B. Lerrer, H.Y. Cohen *(Bar Ilan University, Ramat Gan, Israel)*

Background: Unfortunately, the increase in human life expectancy of the last century, is not consistent with parallel increase in healthspan. Hence, aging is correlates with age-related diseases like: neurodegenerative diseases, cardiovascular diseases, cancer, diabetes, and musculoskeletal disorders that have a great impact on the life quality. One of the common diseases whose prevalence increases with aging and affects healthy lifestyle is sarcopenia. Sarcopenia is characterized by loss of skeletal muscle mass, function and immobility. Physical activity is one of the most important determinants of health, playing a role in the prevention of age-related processes. Physical exercise can improve respiratory and metabolic function, body composition and frailty. Moreover, physical exercise is known to prevent the loss of skeletal muscle mass, and improve muscle function. However, the mechanism underlying the positive effects of physical exercise on aging is poorly understood. SIRT6, an NAD+ dependent deacetylase, is known to extend lifespan, and healthspan. SIRT6 overexpression mice showed improved glucose homeostasis, lipid metabolism and energy production. **Objectives:** Here, we examined the interphase between physical activity and SIRT6 to understand the role of SIRT6 in the regulating physical exercise. Which allows us to deal with sarcopenia and age-related diseases and improve active and healthy life. **Methods:** We performed forced physical exercise in young and old, WT and SIRT6 overexpression mice and metabolic and physiological parameters were examined. Transcriptome analysis of the skeletal muscle was performed to explore the mechanism of SIRT6 and physical exercise in skeletal muscle. **Results:** In comparison to WT mice, young and old SIRT6 mice run longer time. SIRT6 mice under physical exercise exhibit improved body composition, which establishes in reducing fat mass and increasing muscle mass. Moreover, WT and SIRT6 old mice under forced exercise showed an increase mtDNA number in skeletal muscle. Transcriptome analysis of the gastrocnemius muscle showed that forced exercise in old WT enhances the expression of genes that are known to be

downregulated by aging and old SIRT6 mice under physical exercise implicated this effect. **Conclusion:** These results emphasize the potential role of SIRT6 and physical exercise as an intervention to delay sarcopenia and improve healthier life in old age.