10th International Workshop on HIV & Aging

10 - 11 October 2019, New York, NY, USA

Abstracts
Blunted increase in muscle mass after exercise training in people aging with HIV

Jankowski C1, Wilson M2, Brown T3, MaWhinney S2, Erlandson K4
1University Of Colorado College of Nursing, Aurora, United States, 2Department of Biostatistics, School of Public Health, University of Colorado, Aurora, United States, 3Division of Endocrinology, Diabetes, and Metabolism, Department of Medicine, Johns Hopkins University, Baltimore, United States, 4Division of Infectious Diseases, Department of Medicine, University of Colorado, Aurora, United States

Background: Newer antiretroviral therapies (ART) with less toxicity have prolonged the lives of people living with HIV (PLWH). Muscle wasting and lipoatrophy are now rare. Instead, older PLWH are facing age-related sarcopenia and increasing adiposity. Interventions to reverse these changes are needed. We previously found that older PLWH had similar improvements in physical function as uninfected controls (NEG) following an exercise intervention. Here, we compared adaptations in body composition.

Material & Methods: Sedentary PLWH (on ART >2 years) and NEG, ages 50-75 years, completed a 24-week, moderate-to high-intensity supervised cardiovascular and resistance exercise intervention. Total body lean mass (LEAN), appendicular lean mass adjusted for height (ALM/m²), total body fat mass (FAT), and visceral fat area (VFA) were measured pre/post intervention using dual energy x-ray absorptiometry. Comorbidity burden (Veterans Aging Cohort Risk Index; VACS) and use of testosterone and statins were collected at baseline. Participant characteristics are reported as the median (IQR) or mean (95% CI). Multivariable regression analyses were adjusted for age or VACS and exercise adherence.

Results: The majority of participants (27 PLWH, 28 NEG) were male (93%), white (80%) and non-Hispanic (86%). PLWH and NEG were of similar age [56 years (52, 61); 60 years (54, 64), respectively; P>0.05]. PLWH were diagnosed with HIV 23 years (16, 28) prior, ART duration was 17 (8, 19) years, had a CD4 count of 548 cells/μl (416, 772), and all had plasma HIV-1 RNA <50 copies/mL. Testosterone use was more prevalent in PLWH than NEG (18% vs. 7%; P < .05) but statin use was similar (41%). More PLWH had a VACS score > 20 [56.2% vs. 24.3%; P < .05].

Before training, PLWH had significantly less FAT than NEG [20.6 kg (17.7, 23.6) vs. 27.2 (24.0, 30.4); P < 0.01] but similar (P > 0.05) VFA [PLWH 184 cm² (151, 217); NEG 211 cm² (184, 237)], LEAN [PLWH 57.7 kg (61.1, 54.2); NEG 60.0 (56.4, 63.6)] and ALM/m² [PLWH 8.6 kg (8.1, 9.1); NEG 8.9 (8.5, 9.3)]. After training, LEAN increased significantly in NEG [0.8 kg (0.0, 1.6); P = 0.04] but not in PLWH [0.6 kg (-0.2, 1.4); P =0.12]. ALM/m² increased (P=0.06) in both groups [PLWH 0.14 kg/m² (-0.01, 0.29); NEG 0.15 kg/m² (0.0, 0.29)]. FAT decreased significantly in PLWH [-2.0 kg (-2.9, -1.1); P < 0.001] and NEG [-0.9 kg (-1.8, 0.0); P = 0.04]. VFA also decreased significantly in PLWH [-17.7 cm² (-8.2, -27.1); P < 0.001] and NEG [-10.3 cm² (-1.0, -19.6); P = 0.03]. Exercise adherence was a significant (P < .05) covariate of the decreases in FAT and VFA; VACS was not.

Conclusion: A supervised exercise intervention without dietary intervention led to modest total and visceral fat loss, with preservation of lean mass. The changes in response to exercise were not HIV-specific, except that the increase in lean mass (a surrogate for muscle mass), was blunted in PLWH and not explained by their greater comorbidity. During exercise, older PLWH may need more resistance exercise than NEG to stimulate muscle hypertrophy and increase lean mass.
Food insecurity and frailty among women in the US

Tan J1, Weiser S2
1University of California San Francisco, Center for AIDS Prevention Studies, San Francisco, United States, 2Division of HIV, ID and Global Medicine, University of California, San Francisco (UCSF), San Francisco, United States

Background: Frailty is frequently observed among older people living with HIV, and food insecurity is associated with frailty in the general population. Little is known about the associations between food insecurity and frailty among HIV-infected women, who may be particularly vulnerable to the impact of food insecurity with increased age. The goal of this study was to assess associations between food insecurity and frailty among women with or at risk of HIV-infection.

Methods: From 2017-2018, 1324 (900 HIV-seropositive, 424 HIV-seronegative) participants from the Women’s Interagency HIV Study participated in the five measures comprising the Fried Frailty Index. Women were subsequently categorized as not frail, pre-frail, or frail. Participants also completed a measure of food insecurity (U.S. Household Food Security Survey Module). Multinomial logistic regression models were conducted to examine cross-sectional associations between food insecurity and frailty after adjusting for socio-demographic, behavioral, and HIV status.

Results: Over one-third (36%) of women were food-insecure, of whom 68% were women living with HIV. In the fully adjusted model including HIV-status, the relative risk (RR) of frailty for women with very low food security was 3.37 times higher than for women with food security (95% CI [1.38 - 8.24], p<0.01), and the corresponding relative risk of pre-frailty was 3.63 (95% CI [1.76 - 7.51], p<0.01). Higher income was associated with lower relative risks of frailty or pre-frailty (p<0.01). Similarly, older age was associated with higher relative risk of frailty (RR=1.06, 95% CI [1.03 - 1.09], p<0.001). Women living with HIV were not more or less at risk for frailty compared to HIV-negative women.

Conclusions: Very low food security was associated with higher risks of being frail or pre-frail among HIV-infected and at-risk women. HIV status was not an issue for frailty. Longitudinal research is needed to investigate directionality and potential mediators, such as stress and poor nutritional status.
Impact of testosterone use on grip strength in men aging with HIV

Masters M1, Yang J1, Erlandson K3, Lake J1, Abraham A5, Kingsley L6, Brown T1, Palella F1

1Northwestern Memorial Hospital, Chicago, United States, 2Hospital for Special Surgery, New York, United States, 3University of Colorado, Aurora, United States, 4University of Texas Health Science Center Houston, Houston, United States, 5Johns Hopkins University, Baltimore, United States, 6University of Pittsburgh, Pittsburgh, United States

Background: Grip strength declines more rapidly in persons with HIV (PWH) compared to persons without HIV. Testosterone increases muscle mass and has been associated with increased strength in some studies. Testosterone supplementation in older men with HIV is very common, but its impact on their muscle strength and physical function is unclear.

Methods: The Multicenter AIDS Cohort Study (MACS) is a prospective study of men with or at risk for HIV. MACS participants undergo semi-annual assessments, including measures of grip strength. We used multivariate linear mixed models to assess associations between grip strength measured between 2006 and 2018 and covariates at baseline including testosterone use, demographic factors, HIV serostatus, BMI, glycemic status, substance abuse history, renal disease, liver disease, hypertension, arthritis, Center for Epidemiologic Studies Depression Scale score, Short Form 36 questionnaire scores, and hepatitis B or C virus infection.

Results: Of 2,575 participants, 54% were PWH. Mean age at study baseline was 45.0 years (SD 10.3) among PWH and 49.2 years (SD 11.9) among men without HIV. Of PWH, 69.6% had suppressed plasma HIV-1 RNA at baseline. Testosterone use at baseline was more common in PWH (16.5%) than in men without HIV (5.6%; p<0.001). Testosterone use was significantly associated with higher grip strength in univariate (coefficient 0.75, 95% CI=0.25, 1.24, p=0.003), but not multivariate models (coefficient 0.39, 95% CI=-0.22, 1.00, p=0.21). Without adjustment for testosterone use, HIV serostatus was associated with higher grip strength in univariate (coefficient 0.61, 95% CI=0.08, 1.15, p=0.025) and multivariate analyses (coefficient 0.81, 95% CI=0.20, 1.42, p=0.009). Virologic suppression did not have a significant effect in a multivariate model restricted to PWH. With inclusion of testosterone in the multivariate model, the effect of HIV serostatus on grip strength was no longer statistically significant (coefficient 0.58, 95% CI=-0.17, 1.33, p=0.13).

Discussion: Use of supplemental testosterone was higher among men aging with HIV in the MACS compared to men without HIV. While testosterone use alone did not independently predict grip strength, it did contribute significantly to differences in grip strength noted between men with and without HIV. These data suggest that supplemental testosterone use should be taken into account when evaluating physical function among PWH. Further investigation is needed to clarify whether testosterone use benefits physical function in PWH.
Epigenetic age acceleration and non-AIDS defining cancers among HIV infected adults

Achenbach C1, Zheng Y1, Joyce B1, Wang J1, Nannini D1, Martin J1, Matthews C1, Moore R1, Rodriguez B1, Mayer K1, Eron J1, Kitahata M1, Saag M1, Hou L1

1Northwestern University, Chicago, United States, 2University of California San Francisco, San Francisco, United States, 3University of California - San Diego, San Diego, United States, 4Johns Hopkins University, Baltimore, United States, 5Case Western Reserve University, Cleveland, United States, 6Fenway Health, Boston, United States, 7University of North Carolina - Chapel Hill, Chapel Hill, United States, 8University of Washington, Seattle, United States, 9University of Alabama - Birmingham, Birmingham, United States

Background: Individuals with HIV on effective antiretroviral therapy (ART) are at greater risk for numerous age-related diseases, such as cancer. Higher incidence of cancer in this population is multifactorial and an understudied mechanism is accelerated immunologic aging. DNA methylation is a biomarker for measuring biological age and used to evaluate age acceleration. While HIV infection has been shown to accelerate epigenetic aging, the association between accelerated epigenetic aging and non-AIDS defining cancer is unknown. Therefore, we investigated the association between epigenetic age acceleration, lung and anal cancer among HIV infected adults.

Material & Methods: We performed two matched case-control studies within the 8-site CFAR Network of Integrated Clinical Systems (CNICS). Cases were HIV infected adults with either incident lung cancer (n=25) or incident anal cancer (n=25). Controls were HIV infected adults without lung or anal cancer, respectively, at the time of the index case diagnosis who were selected via incidence density sampling from the CNICS primary study base. Controls were also matched by age, sex, smoking status, and availability of a stored PBMC sample within 1 to 4 years prior to the index case diagnosis. Epigenomic profiling was performed on DNA extracted from total PBMCs using the Illumina MethylationEPIC Beadchip (~850,000 sites). Four measures of epigenetic age acceleration were calculated: intrinsic epigenetic age acceleration (IEAA), extrinsic epigenetic age acceleration (EEAA), PhenoAge acceleration, and GrimAge acceleration. Conditional logistic regression, adjusting for race and CD4 count, was performed to assess the association between the epigenetic measures and incident cancer.

Results: For lung and anal cancer, comparable age, sex, and race demographics were observed between cases and controls. Cases exhibited lower CD4 count than controls for both lung (415 and 670 cells/μl) and anal cancer (388 and 629 cells/μl), while viral load was similar. GrimAge acceleration was significantly associated with lung cancer, with 316% greater odds per 5-year increase in age acceleration (OR = 3.16 [95% CI: 1.06, 9.45]; P = 0.04). IEAA (OR = 1.00 [95% CI: 0.64, 1.55]; P = 0.99), EEAA (OR = 1.13 [95% CI: 0.71, 1.80]; P = 0.60), and PhenoAge acceleration (OR = 1.05 [95% CI: 0.71, 1.57]; P = 0.80) were not associated with lung cancer. IEAA (OR = 0.58 [95% CI: 0.19, 1.77]; P = 0.33), EEAA (OR = 0.89 [95% CI: 0.58, 1.37]; P = 0.60), PhenoAge acceleration (OR = 0.71 [95% CI: 0.44, 1.16]; P = 0.17), and GrimAge acceleration (OR = 1.30 [95% CI: 0.66, 2.55]; P = 0.45) were not associated with anal cancer.

Conclusions: We identified a significant association between GrimAge acceleration and lung cancer among HIV infected adults. GrimAge captures epigenetic markers associated with oxidative stress and thus, may suggest that accumulation of molecular damage is associated with lung cancer among individuals with HIV independent of immune suppression. The causal role of DNA methylation patterns in the development of lung cancer is unclear, but they may be important predictive biomarkers for those aging with HIV.
Lipidome abnormalities and altered macrophage phenotype may contribute to cardiovascular disease risk in the aging HIV population

Bowman E1, Kulkarni M1, Gabriel J1, Kettelhut A1, Cichon M1, Riedl K1, Koletar S1, Richardson B2, Cameron C2, Cameron M2, Funderburg N1

1The Ohio State University, Columbus, United States, 2Case Western Reserve University, Cleveland, United States

Background: The number of people with HIV (PWH) over the age of 50 is increasing worldwide. Even with suppressive antiretroviral therapy (ART), chronic inflammation persists in PWH, which may complicate the aging process and accelerate the development of comorbidities. Both HIV infection and ART are associated with dyslipidemia and increased cardiovascular disease (CVD) risk. Macrophages accumulate in blood vessel walls and produce factors that contribute to vascular inflammation. The relationships among lipids and macrophage phenotype in PWH are not well understood.

Methods: Coronary artery calcification (CAC) in people with (n=40) and without (n=15) HIV was quantified by computed tomography scanning. PBMCs from people with (n=20) and without (n=20) HIV were cultured for 5 days in medium containing 20% autologous serum to generate monocyte-derived macrophages (MDMs). Concentrations and fatty acid composition of serum lipids were measured by mass spectrometry. MDM transcriptomes and differential gene expression (DGE) were analyzed using our R Bioconductor pipeline. Foam cell formation was assessed by Bodipy staining and DiI-OxLDL uptake. Immune activation and ROS production was assessed by flow cytometry.

Results: PWH (ages 27-67) had significantly increased CAC scores compared to people without HIV (ages 25-70) (CAC=367 v 25, p=0.01). Traditional risk assessments categorize individuals with CAC scores <100 at low risk, and >400 at high risk for CVD events. Older (over 55) PWH (n=17) had an average CAC score of 423, compared to a score of 71 in older people without HIV (n=7). PWH had significant alterations in lipidome composition, including increased serum levels of free fatty acids (FFAs), with enrichment of saturated fatty acids (SaFAs) and reduced polyunsaturated fatty acids (PUFAs). In older PWH, serum concentrations of triacylglycerols, diacylglycerols, ceramides (CERs), and FFAs tended to be increased compared to younger PWH. Saturated CERs, previously linked to CVD in the general population, were directly associated with sCD14 levels in older PWH (r=0.857, p=0.02), but not in younger PWH. DGE analysis of MDMs from participants with and without HIV identified broad alterations in innate immune signaling, cell cycle regulation, DNA damage repair, replication complexes, mitochondrial dysfunction, and lipid processing pathways. Levels of individual SaFA and PUFA lipid species correlated with unique DGE signatures and altered metabolic pathway activation in MDMs. Bodipy staining indicated greater lipid accumulation, and DiI-OxLDL exposure resulted in significantly increased OxLDL uptake by MDMs from PWH. MDMs from PWH also produced more TNFα, IL-6, and ROS, and had increased HLADR surface expression. SaFA levels were directly related, whereas PUFAs were inversely related to HLADR surface expression. Additionally, MDMs from people without HIV exposed to HIV+ pooled serum displayed greater intracellular lipid accumulation and DGE than did cells exposed to HIV- pooled serum.

Conclusions: Lipid abnormalities in HIV infection may contribute to a pro-atherogenic MDM phenotype. MDMs from PWH readily form foam cells, have altered transcriptional profiles, and produce mediators of vascular inflammation, which may enhance CVD risk. Identifying mechanisms of immune dysregulation in PWH will likely be of particular importance for management of comorbidities in the aging HIV population.
Elevated cardiac risk score by ASCVD calculation is associated with albuminuria in older people living with HIV

**Johnston C**, Ifeagwu K, Siegler E, Burchett C, Rice M, Choi M, Glesby M

*NYP-Weill Cornell Medical Center, New York, United States*

**Background:** Chronic non-communicable diseases such as kidney dysfunction and cardiac disease are associated with greater morbidity and mortality in older persons living with HIV (OPH), and can be assessed by estimated glomerular filtration rate (eGFR), measurement of albuminuria, and calculation of the 10-year ASCVD Risk Score. Here we describe eGFR and albuminuria in OPH, and assess for a relationship with ASCVD risk score. We hypothesize that the presence of albuminuria is related to elevated ASCVD risk scores, and that OPH with elevated cardiac risk may be undertreated with statin medications.

**Materials and Methods:** A cross-sectional analysis of OPH participating in the Research on Older Adults with HIV (ROAH) 2.0 Survey was undertaken at a single urban medical center. Potential ROAH participants were randomly selected from the outpatient HIV clinical practice and invited to complete a detailed questionnaire focusing on health status, quality of life and psychosocial factors. Participants over age 55 who completed the questionnaire were then invited to participate in a substudy consisting of additional laboratory testing and aging-related assessments.

**Results:** There were 164 participants who participated in this cross-sectional analysis. Median age was 60 years (IQR 57-64) and 55 (34%) were female (including one transgender woman). Median eGFR was 75 mL/min per 1.73 m² (IQR 60-91). By CKD classification 5 (3%) were G5, 3 (2%) G4, 33 (20%) G3, 79 (48%) G2, and 43 (26%) G1. Albuminuria was categorized as 0-15, 15.1-30, 30.1–300, and >300 mg urine albumin/g urine creatinine, respectively. Twenty-eight (18%) participants had moderately increased albuminuria (“microalbuminuria” as defined by 30-300 mg albumin/g urine creatinine), and 8 (5%) participants had > 300 mg albumin/g urine creatinine (“macroalbuminuria”). Albuminuria was inversely correlated with eGFR (r = -0.19, p=0.021), but not significantly with age (r= 0.13, p=0.11) by Spearman rank correlation. There was no significant relationship between presence of moderate-severe elevation of albuminuria and use of tenofovir disoproxil fumarate (TDF) (p=0.24) or tenofovir alafenamide (TAF) (p=0.26) by Fisher’s Exact test. There was no relationship between moderate-severe elevation of albuminuria and use of ACE/ARB medications (p=0.32) by Fisher’s Exact test.

The median ASVCD score was 9.8% (IQR 6.4-15.2). ASCVD score was correlated with albuminuria by Spearman rank correlation (r= 0.25, p=0.005). There was a significant relationship between presence of diabetes and moderate-severe elevation of albuminuria (p=0.019) by Kruskal-Wallis rank test. Among participants with ASCVD score >7.5%, 52% were on statin and 19% on abacavir.

**Conclusions:** Nearly a quarter (23%) of OPH in our study had moderate-severely elevated albuminuria. Moreover, PLWH had a remarkably elevated risk of cardiovascular disease using the ASCVD calculator, with a median 10-year risk score of 9.8%. Elevated cardiac risk was correlated with moderate-severely elevated albuminuria, suggesting common metabolic and inflammatory pathophysiologic mechanisms. Nearly half (48%) of participants with ASCVD 10-year risk score >7.5% were not on statin therapy, and despite evidence of increased risk of cardiac events with abacavir use, 19% were on antiretroviral regimens that included this drug. Our data suggest that there is room to optimize cardiovascular disease prevention in OPH.
The association between mitochondrial DNA copy number and longitudinal lung function decline among people with or at risk of HIV

Sun J1, Piggott D1, 2, Astemborski J1, Brown R1, 2, Arking D2, Kirk G1, 2

1Johns Hopkins University Bloomberg School of Public Health, Baltimore, United States, 2Johns Hopkins University School of Medicine, Baltimore, United States

Background: People living with HIV (PLWH) experience accelerated lung function decline and higher incidence of chronic obstructive pulmonary disease (COPD) compared to their HIV uninfected counterparts, yet the causal mechanism is unclear. Mitochondrial DNA copy number (mtDNA CN) reflects mitochondrial biogenesis and is related to mitochondrial function and oxidative stress. mtDNA CN might be associated with COPD and lung cancer, but previous studies had contradictory results and few studies have examined mtDNA CN and lung function in a high-risk HIV population.

Material & Methods: mtDNA CN was measured using the qPCR of DNA isolated from buffy coats of participants of the Study of HIV Infection in the Etiology of Lung Disease (SHIELD), which is nested within a cohort of people who inject drugs (PWID). We used the difference of cycle threshold value of a nuclear genome and a mitochondrial gene as the measurement, and standardized by cell composition. Pre-bronchodilator spirometry forced expiratory volume in one second (FEV1) and forced vital capacity (FVC) were performed during each visit and ratios<70% were considered COPD. Logistic regression models were used to determine the association between mtDNA CN and COPD at baseline. Mixed effect linear regression models were used to determine the association of mtDNA CN on adjusted annual changes in FEV1/FVC. Analysis controlled for demographics, smoking (pack-year and current status), and current injection drug use. Models specific among PLWH additionally controlled for CD4+ count and exposure to thymidine analogues (D4T and AZT).

Results: Of 501 participants with median follow-up time of 4.5 years, most were older than 50 years, male, black, and 34% infected with HIV and 25% were considered COPD. High mtDNA CN was associated with a 2-fold (95% CI: 1.2-3.3) increased odds of COPD at baseline. FEV1 and FVC ratio (FEV1/FVC) started to decline after age 50 in participants with or without HIV. FEV1/FVC declined faster among PLWH than people without HIV. Among people without HIV, the decline of FEV1/FVC was significantly faster among those who had higher mtDNA CN compared to those who had lower CN (0.21% per-year decrease vs. 0.16% per-year decrease in FEV1/FVC ratio, adjusted interaction between time and mtDNA CN groups p-value=0.02). There was no observed difference in decrease of FEV1/FVC by mtDNA CN groups among PLWH.

Conclusions: In a cohort of PWID infected with or at risk of HIV, we observed high mtDNA CN associated with increased risk of COPD. Lung function declined faster among people with higher rather than lower mtDNA CN after age 50 among people without HIV. This finding provided some evidence for the hypothesis that mtDNA CN might compensatively increase among COPD patients to adjust for oxidative stress, especially among people without HIV. Among PLWH, HIV infection still appears to be the major driver for lung function decline over time.
The aging of HIV epidemic in Ukraine: new HIV diagnoses from 2015-2018 and related mortality among adults ≥50 years

Rozanova J1, Zeziulin O2, Sosidko T3, Rich K4, Kiriazova T4, Zaviriukha I2, Altice F1, Justice A1, Shenoi S1

1Yale University School Of Medicine, New Haven, United States, 2Ukrainian Institute on Public Health Policy, Kyiv, Ukraine, 3100-Life All-Ukrainian Network for People Living with HIV, Kyiv, Ukraine, 4Harvard Medical School, Cambridge, United States

Background: Ukraine is home to Europe’s most volatile HIV epidemic, with over 240,000 estimated people with HIV (PWH). Like other European countries, Ukraine’s government has focused its HIV treatment and prevention programs on youth (15-24 years), yet adults ≥50 years constitute 37% of the population. We examined new HIV diagnoses from 2015-2018 and related mortality among older adults (≥50 years) in Ukraine.

Material & Methods: Using the data from the Ukrainian Center for Public Health (UCPH), we analyzed the trends of new HIV diagnoses for three age groups of PWH from 2015-2018: 15-24 years; 25-49 years; and ≥50 years. As UCPH started collecting CD4 counts and mortality data only in 2019, we used aggregate subnational data from the largest clinical dataset in Ukraine to analyze mortality trends from 2016-2018 for three age groups of PWH: 15-24 years; 25-49 years; and ≥50 years. As the clinical dataset comprised from 41% (2015) to 76% (2018) of all newly diagnosed HIV cases in Ukraine registered in the UCPH data, we assessed possible gender and age differences between the clinical and UCPH datasets with a chi-square goodness of fit test. AIDS was defined as CD4<200cl/mm3. Mortality was defined as deaths per 1000 patients newly diagnosed with HIV during that calendar year. Standardized mortality ratios (SMRs) were calculated for 2016, 2017, and 2018, and compared respectively to age-matched general population death rates.

Results: In 2015, Ukraine registered 15,869 new HIV infections; in 2018, there were 18,099 new HIV infections. From 2015-2018, the proportion of new HIV cases reported annually increased significantly (p<.01) among those ≥50 (11.2% to 14.9%) while declining among those 25-49 (from 81.7% to 80.2%) and among 15-24 year-old group (7% to 4.9%). Those ≥50 years were also significantly (p<0.01) more likely to have AIDS at diagnosis (43.8%) relative to 25-49 (30%) and 15-24 (13.5%) year-olds. In 2016, 2017, and 2018 mortality among newly diagnosed PWH ≥50 years ranged from 3-11 times higher than the matched Ukrainian general population and was significantly (p<0.01) higher for all 5-year age strata between 50 and 65 years; except for PWH ≥65-70 years. There were no significant gender differences in new HIV diagnoses or mortality in any age group.

Conclusion: The proportion of PLW in Ukraine who are ≥50 years is significantly increasing. Older adults with HIV in Ukraine are more likely to be diagnosed with AIDS, and experience higher age-adjusted mortality. Improved detection linked to immediate antiretroviral therapy (ART) is urgently needed.
Frailty phenotype in older virologically suppressed PLWHIV is strongly correlated with specific comorbidities and tobacco use

Psomas C1, Petit N2, Ravaux I2,3, Philibert P1, Tollinchi F6, Allegre T10, Cohen-Valensi R1, de Jaureguiberry J8, Pichancourt G12, Pelissier L1, Chadapaud S9, Breggeon S1, Darque A2, Retornaz F1,4, Enel P2,4

1European Hospital Marseille, Department of Infectious Diseases and Internal Medicine, Marseille, France, 2Assistance Publique, Hôpitaux de Marseille, University Hospital, Marseille, France, 3Institut Hospitalo-Universitaire Méditerranée Infection, Marseille, France, 4Department of Public Health, Self-Perceived Health Assessment Research Unit EA3279, Aix-Marseille University, Marseille, France, 5Institut Hospitalo-Universitaire Méditerranée Infection, Marseille, France, 6Department of Dermatology, Saint-Joseph Foundation Hospital, Marseille, France, 7Department of Internal Medicine, Martigues Hospital Center, Martigues, France, 8Department of Internal Medicine and Oncology, Sainte-Anne Military hospital, Toulon, France, 9Department of Internal Medicine, Hyères-les-Palmiers Hospital Center, Hyères-les-Palmiers, France, 10Department of Internal Medicine and Hemato-Oncology, Aix-en-Provence Hospital Center, Aix-en-Provence, France, 11Department of Internal Medicine, Gap Hospital Center, Gap, France, 12Department of Clinical Hematology and Medical Oncology, Avignon Hospital Center, Avignon, France

People living with HIV (PLWHIV) are mostly virologically suppressed and efficiently followed up, growing older and older and accumulating health problems related to ageing. This ageing state is characterised by a decreased capacity to manage adverse outcomes (disease, hospitalization, disability, falls, trauma) which defines the frailty phenotype.

Our aim was to assess factors related to frailty according to Fried phenotype in a French cohort of older PLWHIV.

This cross-sectional multicenter study was carried out between November 2012 and April 2014 in 12 HIV-dedicated Hospital Units of the South of France including PLWHIV of at least 50 years-old. We evaluated demographic factors, HIV-related parameters (duration of HIV diagnosis, history of AIDS diagnosis, ART duration, CD4 T cell count, CD4 T cell nadir count, viral suppression), as well as general health parameters (BMI for Body Mass Index, associated comorbidities, pain scale, social deprivation). Phenotype of Frailty according to Fried is based on the assessment of 5 criteria: shrinking (unintentional weight loss), weakness (grip strength), poor endurance (exhaustion), slowness (walking speed) and physical activity. Frailty phenotype corresponded at the presence of at least 3 criteria of the above mentioned.

Our study involved 509 PLWHIV, 72.8% were male, of a mean age of 58.4 ± 7 years, mostly (87.9%) virologically suppressed. Mean duration of infection since HIV diagnosis was 18.3 ± 7.4 years. Prevalence of frailty in our cohort concerned 8.2% between them. Univariate analysis evidenced no association (at p <0.05) of frailty with age, sex, level of studies, tobacco/alcohol or drug use, or HIV-related parameters. On the contrary, significant associations at p <0.05 were found between frailty and BMI, pain scale, social deprivation, professional activity, psychiatric history, falls, rheumatologic history, and having at least 2 comorbidities.

Multivariate analysis of variables selected at p <0.20 in the univariate model confirmed associations of frailty state with BMI (OR = 1.34 [1.12-1.22], p = 0.00), pain scale (OR = 1.46 [1.07-1.25], p = 0.004), psychiatric (OR = 7.62 [1.03-2.80], p = 0.044) and rheumatologic history (OR = 7.84 [1.05-2.86], p = 0.040), falls (OR = 8.33 [1.09-3.01], p = 0.034), while revealing associations of frailty with cancer history (OR = 15.03 [1.61-4.92], p = 0.005), tobacco use (OR = 11.52 [1.37-3.97], p = 0.011) and CD4 T cell nadir count less than 200/mm3 (OR = 0.74 [0.11-0.29], p = 0.010).

Our study strongly suggests that comorbidities are the main factors that convey the embrittlement state of older virologically suppressed PLWHIV. This embrittlement state precedes polyopathy or disabilities and undermines one's capacity to fight against physical or mental assaults. Efficient medical follow-up focusing on preventing comorbidities especially in individuals with cancer history, could delay frailty as well as its associated adverse outcomes.
Cellular and molecular assessment of muscle function as a predictor of ageing phenotype in older PLWH

Hunt M1, McNiff M1, Sabin C2, Winston A3, Payne B1
1Newcastle University, Newcastle upon Tyne, United Kingdom, 2UCL, London, United Kingdom, 3Imperial College London, London, United Kingdom

Background: Despite successful viral suppression by ART, some people living with HIV (PLWH) exhibit phenotypes of accelerated aging. This can be characterised by reduced physical function and an increased prevalence of frailty and age-related comorbidities. The underlying pathological mechanisms remain poorly understood, although mitochondrial dysfunction is suspected to play a role. We therefore performed a range of exploratory analyses on skeletal muscle from older HIV positive and negative individuals, in combination with assessments of physical function and frailty, with the aim of developing pathologically defined subgroups for future stratified interventional trials.

Methods: A cohort of 45 age-matched males ≥50 years old (30 HIV+, 15 HIV-) was established. All HIV+ subjects were on cART. Tibialis anterior (TA) biopsies were obtained as well as general and HIV-related medical history.

Subjects underwent standardised functional testing and had DXA scans performed in order to assess their physical capabilities and body composition.

Multiplex fluorescence immunohistochemistry was performed on 10µm skeletal muscle cryo-sections with automated quantification of the abundance of mitochondrial respiratory chain complexes I and IV (CI, CIV) and mitochondrial mass within individual myofibres.

Results: Compared with the HIV- group, HIV+ subjects had a significantly higher proportion of myofibres with CI defects (z-score ≤ -3) (p=0.05) and CIV defects (p=0.0011).

Apart from age (r=0.311; p=0.038), there were no associations between mitochondrial defects and HIV-related clinical characteristics (current or nadir CD4 count, viral load, months on cART, months with untreated HIV, exposure to historical NRTIs) or body composition (BMI, percentage lean mass, percentage fat mass). There was also no association between mitochondrial defects and possible cofounders such as smoking status or alcohol consumption, although ex-drinkers did have a significantly higher proportion of myofibres with CI defects compared to the current drinkers (p=0.017) and subjects who had never drank (p=0.017). Both age and HIV status were independently associated with mitochondrial defects.

In the HIV+ group, 13% were classified as frail and 50% as pre-frail. None of the HIV- group were classified as frail and 53% as pre-frail. 3% of the HIV+ group had a ‘low’ physical performance capability and 34% had ‘intermediate’, whereas none of the HIV- group had a ‘low’ capability and 27% ‘intermediate’. 17% of the HIV+ group were characterised as sarcopenic, and 20% as pre-sarcopenic, whereas 100% of the HIV- group were characterised as having normal muscle function. There was a significant association between CI defects and ‘low’ physical capability (p=0.011) as well as frailty (p=0.028).

Conclusion: Older PLWH had a higher proportion of myofibres with mitochondrial defects compared to well-matched HIV- individuals. These mitochondrial defects are independently associated with both age and HIV status, but surprisingly these mitochondrial defects were not explained by prior exposure to historical “mitochondrially toxic” NRTIs. Mitochondrial defects were associated with ‘low’ physical performance capability and frailty, suggesting a potential causal link with aging phenotypes.
HIV infection does not increase the frequency of phosphorylated tau and beta amyloid in brain in late middle age

Morgello S1, Cortes E1, Jacobs M1, Meloni G1, Murray J1, Crary J1
1Icahn School of Medicine at Mount Sinai, New York, United States

Background: Viral infection and neuroinflammation have been implicated in the genesis of Alzheimer's Disease (AD), but whether HIV predisposes to early incidence of AD neuropathologic change is unclear.

Materials & Methods: We assessed 120 brains (82 from autopsies of individuals with HIV, 38 from demographically similar controls) with immunohistochemistry to detect abnormal hyperphosphorylated tau (pTau) and amyloid-beta peptide (Aβ) deposition in medial temporal lobe/rostral-caudal hippocampus and prefrontal neocortex. Each region was scored for the presence or absence of pTau neuropil threads, pTau containing neurons, intra- and extra-neuronal Aβ deposition, cerebral congophilic angiopathy (CAA), and aging-related tau astrogliopathy (ARTAG).

Results: The mean age of death for the sample was 58.4 (11.5) years (57.6 HIV+, 60.3 HIV-); among them, 42% were women (39% HIV+, 47% HIV-), 79% were minorities (21% non-Hispanic white in both groups), and 29% had an ApoE ε4 allele (30% HIV+, 27% HIV-). For the entire sample, the frequency of abnormal protein deposition was: 91% temporal pTau neuropil threads; 75% pTau-containing medial temporal neurons; 43% prefrontal pTau neuropil threads; 14% pTau-containing frontal neurons; 36% ARTAG; 36% extra-neuronal Aβ deposition; 83% intra-neuronal Aβ deposition; and 7% CAA. There was no evidence for increased prevalence of any of the pTau or Aβ pathologies in brains from HIV+; in fact, a greater prevalence (p<0.05) of ARTAG, and temporal and prefrontal pTau neuropil threads was seen in HIV-. Age was the strongest predictor of all pTau and Aβ pathologies, and ARTAG was not seen in any individual under the age of 50. When analyses were limited to individuals dying at ages 50 and older, the frequency of temporal pTau neuropil threads did not significantly differ between the two groups, but frontal pTau neuropil threads and ARTAG remained more frequent in HIV-.

Conclusion: In this sample, HIV is not associated with a greater frequency of pathologic pTau and Aβ accumulation when contrasted to demographically similar individuals who died with diverse medical disorders. Age is the strongest predictor of neurodegenerative pathology. While this analysis is likely confounded by biases inherent in autopsy samples, our findings are consistent with published observations in PET imaging studies performed in late middle age HIV-infected populations.
Predictors of longitudinal neuropathic pain in older patients with HIV-associated distal sensory polyneuropathy

Diaz M1, Keltner J1, Franklin D1, Moore R1, Collier A1, Marra C1, Clifford D1, Gelman B1, Sacktor N1, Morgello S1, McCutchan J1, Letendre S1, Heaton R1, Ellis R1

1University Of California, San Diego; HIV Neurobehavioral Research Program, San Diego, United States, 2University of Washington, Seattle, USA, 3Washington University, St. Louis, St. Louis, USA, 4University of Texas Medical Branch, Galveston, Galveston, USA, 5Johns Hopkins University, Baltimore, USA, 6Icahn School of Medicine at Mount Sinai, New York, USA

Background: Distal sensory polyneuropathy (DSP) is a common cause of disability in persons living with HIV (PLWH), leading to worse quality of life and more frequent falls in older age[1, 2]. Pain is a prevalent symptomatic feature of DSP[3, 4], however the prevalence of paresthesias in HIV-associated DSP and their longitudinal effects on development of future neuropathic pain is unknown. We investigated the effect of paresthesias (with and without neuropathic pain at baseline) on neuropathic pain at 12-year follow-up.

Material & Methods: This was a prospective longitudinal study of data from 264 PLWH enrolled in the CNS HIV Antiretroviral Therapy Effects Research (CHARTER) study who had presence or absence of neuropathy signs and symptoms at baseline and at 12-year follow-up. We used univariate and multivariable logistic regression analyses to determine the specific effects of paresthesias at baseline (PAR1) on the development of distal neuropathic pain (DNP2) at 12-year follow-up, unadjusted and adjusted for demographics and common HIV disease co-variates (nadir CD4, absolute current CD4, plasma viral load, antiretroviral use). We also analyzed the univariate effect of demographics, HIV characteristics and past use of peripherally-neurotoxic antiretroviral therapy (ART) on longitudinal symptoms at follow-up using logistic regression analyses.

Results: Our cohort included PLWH with mean age 56±8 years, 21% female and 45% black. HIV characteristics included median nadir CD4 170 (IQR 29, 278), median absolute current CD4 568 (IQR 342, 785) at follow-up time. Nearly the entire cohort (96%) was on ART and 81% had suppressed plasma viral loads at follow-up. About 60% reported past use of antiretroviral therapy commonly associated with peripheral neurotoxicity. Of those with DNP2, 23% had PAR1 (p<.0001, compared to those without DNP2). The presence of PAR1 (with or without DNP1) increased the risk of DNP2 overall (OR 2.23; 95% CI 1.19, 4.37). In particular, the combination of both PAR1 and DNP1 predicted a higher frequency of DNP2 (OR 5.80; 1.68, 23.6). For those without DNP1, this relationship was not significant (OR 1.58; 0.70, 3.43). DNP1 (with and without PAR1) predicted worse severity of DNP2 among all participants (OR 5.64; 3.20, 9.94). Age was a significant univariate predictor of DNP2, but was not significant in the multivariable model including both PAR1 and DNP1. DNP2 was not related to sex, current or nadir CD4, plasma viral load, or past use of peripherally neurotoxic ART. Past use of peripherally neurotoxic ART did not predict DNP2 (with [OR 1.29; 0.54, 3.07] and without PAR1 [OR 1.18; 0.57, 2.44]).

Conclusions: These findings support the importance of neuropathic paresthesias as a clinically significant predictor of distal neuropathic pain, especially with neuropathic pain at baseline, among aging PLWH with DSP. Neuropathic paresthesias at baseline may help identify a person who is at-risk for developing neuropathic pain years later, subsequently worsening quality of life and disability, among aging PLWH with DSP.
The utility of olfactory function in distinguishing early stage Alzheimer's disease from HIV-associated neurocognitive disorder: a pilot study

Sundermann E1
1University Of California, San Diego, La Jolla, United States

Background: Given the rising rate of older people living with HIV (PLWH), it becomes important to differentiate Alzheimer’s disease (AD) and its precursor, amnestic mild cognitive impairment (aMCI) from HIV-Associated Neurocognitive Disorders (HAND). Identifying aMCI among PLWH is challenging given the overlap in neurocognitive profiles between aMCI and HAND. There are, however, differences between aMCI/AD and HAND that may allow us to distinguish between the conditions. In this preliminary study, we examined whether olfactory function could contribute to distinguishing between aMCI/AD and HAND since olfactory dysfunction represents one of the earliest signs of AD and tends to be specific to AD versus other age-associated dementias.

Materials & Methods: We assessed 51 HIV-seropositive participants (mean age=62.4, [SD=10.1], mean education=14.4yrs [SD=2.7], 80% male, 67% White) from the California NeuroAIDS Tissue Network that were administered the University of Pennsylvania Smell Identification Test (UPSIT; higher scores=better smell identification) and the Story Recall Test. In the Story Recall Test, participants learned a 20-unit story to 90% criterion (i.e., 18 out of 20 units) and then completed free recall and recognition trials at 30-minute (in-person) and 1-week (via telephone) delays. In addition, participants completed a standard, comprehensive seven-domain neuropsychological battery and a neuromedical evaluation. Participants were classified as HAND+ versus HAND- according to Frascati criteria. Participants were also classified as aMCI/AD+ versus aMCI/AD- based on an adapted diagnostic schema for aMCI (Jak/Bondi), which requires impairment (>1.0 SD below demographically-corrected normative mean) on two tests of memory recall and/or recognition (at least one recognition impairment required) from the Hopkins Verbal Learning Test-Revised (HVLT-R) and the Brief Visuospatial Memory Test-Revised (BVMT-R).

Results: Sixty-eight percent of participants were classified as HAND+ (n=34) and 37% were classified as aMCI/AD+ (n=19; 95% HAND). UPSIT scores were significantly lower in the aMCI/AD+ versus the aMCI/AD- group (F[1,48]=5.7, p=.02, Cohen’s d=0.7), but did not differ between HAND groups (p=.99). Among the Story Recall Test outcomes, UPSIT scores showed a moderate correlation with lower 1-week recognition scores (R=0.48, p<.001).

Conclusions: The aMCI/AD+ group showed olfactory deficits relative to the aMCI/AD- group, which further supports that these PLWH may be on an AD-like cognitive trajectory. Olfactory function correlated with 1-week story recognition and differed between aMCI/AD groups, but not HAND groups. Results suggest that olfactory assessments may help in detecting early aMCI/AD that exists among PLWH, and may allow for more targeted and appropriate interventions in early disease stages.
The structure and correlates of loneliness and social isolation among PLWH over 55 with mild neurocognitive disorder

Dobbins S1, Merrilees J1, Moskowitz J2, Javand S2, Sharma B2, Valcour V2
1UCSF School of Nursing, San Francisco, United States, 2UCSF Memory and Aging Center, San Francisco, United States, 3Medical Social Sciences, Northwestern University, Chicago, USA

Social isolation and loneliness are tightly linked to outcomes in geriatric medicine, though they are different conceptual constructs. Despite the lack of definitional consensus for social isolation and loneliness, studies show that measures of social connectedness are associated with poor cognitive trajectories in HIV-seronegative populations. There is little research on this topic among aging people living with HIV (PLWH). We aimed to describe the structure and correlates of social isolation and loneliness of 171 PLWH over 55 years who have mild cognitive impairment.

Methods: This study is a secondary analysis of a cohort recruited for a mindfulness based stress reduction trial. Social isolation was measured with the Norbeck Social Support scale and loneliness was measured with the UCLA-20 item loneliness scale. Neither scale has validated cutoff scores. Other scales included the Geriatric Depression Scale (GDS) scale, State and Trait Anxiety Scales, and Perceived Stress Scale. ZIP-code level income data from the American Community Survey 2017 census data for ZIP code was used (people below poverty line, median income, and median housing costs). Sociodemographic and clinical characteristics were obtained.

We described our sample and examined correlates of social isolation and loneliness using t-tests, ranksum tests, and correlations. Alpha was set to 0.10 for the purposes of this exploratory, secondary data analysis.

Results: Our sample was 92% male, 72.5% White, mean 64.3 years of age (SD 5.3), mean 26 years living with HIV (SD 6.8). All had confirmed Mild Neurocognitive Disorder. 49% had past substance use, 52% had a past depressive episode, and 28% had past anxiety disorder.

33% had above-normal depressive symptoms on the GDS (median 8, IQR 0-24), the mean stress score was 14.2 (SD 6.3), and the median anxiety state and trait scores were 33 (IQR 20-60) and 37 (IQR 30-60), respectively.

Loneliness scale had a mean score of 44.4 (SD 11.7). A median of 7 people were listed in social networks (IQR 4 – 24) on the Norbeck scale. 3% of the sample listed nobody, 33% listed a partner or spouse, 78% listed friends (mean 4.8), 72% listed family (mean 2.9), 47% listed healthcare providers (mean 1.2), and 23% listed counselors/therapists (mean 1.4). 32% reported losing an important relationship in the past year. 22% reported that “quite a bit” or “a great deal of support” was provided by someone lost to them. Loneliness and social network were significantly correlated (r=-.35, p=0.000).

Loneliness was significantly associated with age (r=0.30, p=0.074), history of depression diagnosis (t=-3.24, p=0.001), above-normal depressive symptoms (t=-5.52, p=0.000), perceived stress (r=0.37, p=0.000), history of anxiety disorder (t=-1.75 p=0.081), and state and trait anxiety (r=0.26, p=0.001 and r=0.50, p=0.000, respectively).

Social isolation (measured as total network) was associated with years of education (r= 0.28, p=0.000, past history of substance use (z=2.55, p=0.011), years living with HIV (r=-0.14, p= p=0.082), hepatitis C history (z=1.783, p=0.074), and ZIP-code level income measures (proportion of people living in poverty [r= -0.2140, p= 0.008] and ratio of median monthly costs to median monthly income above 0.3 [z=2.38, p=0.017]).

Our data suggests that among PLWH age 55 and over who have Mild Neurocognitive Disorder, loneliness is a construct linked to mental health while social isolation is linked with certain social determinants of health. Further research on social connections in aging with HIV may reveal modifiable risk factors for HIV-associated cognitive impairment.
What is the lived experience of loneliness in older men living with HIV? A qualitative analysis to guide service development

Austin-Keiller A1, Lessard D2, Harris M1, Fellows L4, Park M2, Mayo N5, Brouillette M1

1Department of Psychiatry, McGill University, Montreal, Canada, 2Department of Family Medicine, McGill University, Montreal, Canada, 3BC Centre for Excellence in HIV/AIDS, University of British Columbia, Vancouver, Canada, 4Montreal Neurological Institute, Montreal, Canada, 5Centre for Outcomes Research and Evaluation, Research Institute of the McGill University Health Centre, Montreal, Canada

Background: Loneliness, a known predictor of poor health and early mortality, is found at higher rates among older people living with HIV. While there are many services available to people living with HIV, services to help overcome loneliness is reported to be the greatest area of unmet need for this population. Loneliness is a complex issue experienced differently across gender, cultural, and age groups. However, to develop focused and effective services, we need to discover the experience of loneliness in older people living with HIV and understand the associated problems from their perspective. Caucasian men are a major component of the HIV community; therefore, this study aims to understand the lived experience of loneliness in older Caucasian men living with HIV in the Montreal area.

Methods: We followed a qualitative design to access and compare distinct lived experiences of loneliness among older men living with HIV. First, participants were selected using a theoretical sampling method, which aims to recruit individuals based on theoretical relevance, rather than representativeness of a given population. Thus, for comparison purposes, from the Canadian Positive Brain Health Now study Montreal participant pool, we selected men who answered, ‘quite often’ (n=6) and ‘almost never’ (n=4) to the question “do you find yourself feeling lonely, quite often, sometimes or almost never?” Then, the first author conducted one-to-one, face-to-face, semi-structured, audio-recorded interviews with participants until theoretical saturation was reached (total=10), meaning no novel information was obtained in the final interview. Audio-recordings were transcribed verbatim and we conducted an inductive thematic analysis using MaxQDA to identify major emerging themes.

Results: The participants defined their loneliness as an overall lack of intimacy due to the absence of a romantic or platonic friend. Their experiences were generally centered on three main interacting themes: 1) participants often referred to ‘a missing other’: they usually attributed the absence of an intimate other to the loss of someone who had previously filled this role; death or stigma surrounding HIV were frequently the underlying causes for the loss; 2) they also mentioned ‘a deceiving search for intimacy’: participants tried to find friends or partners using online dating or dating apps, but more often than not, they found “hook-ups” which did not remedy their loneliness; and 3) they also spoke about ‘a fear of rejection’: participants expressed concerns about the possibility of being rejected by a potential friend or partner, due to their HIV status, age or their physical appearance, especially if they have lipodystrophy.

Conclusion: Our qualitative study identified three main themes indicating that participants are concerned about an absence of intimacy, as well as the difficulties and fear they experience when trying to restore intimacy in their lives. Service development should focus interventions on the barriers and facilitators associated with creating meaningful relationships with partners and/or friends. This may include social and networking events, coaching on HIV status disclosure and relationship building, as well as strategies to cope with past trauma and overcome fears.
Intrinsic capacity but not frailty predicts functional status in PLWH: a multi-centre prospective study

Guaraldi G1, Orsini M2, Caselgrandi A1, Malagoli A1, D’Imprima F3, Milic J1, Chinelli P1, Martoglia R1, Mandreoli F1, Ferran D7, Liu G6, Bloch M7

1Modena HIV Metabolic Clinic, University Of Modena And Reggio Emilia, Modena, Italia, 2DataRiver Srl, Modena, Italia, 3University of Modena and Reggio Emilia, Modena, Italia, 4Clinical and Experimental Medicine PhD Program, University of Modena and Reggio Emilia, Modena, Italia, 5Department of Mathematics, University of Modena and Reggio Emilia, Italy, 6Department of Mathematics, University of Modena and Reggio Emilia, Italy, 7Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong, Hong Kong, 8Holdsworth House Medical Practice, Sydney, NSW, Australia, Sydney, Australia

Objective
My Smart Age with HIV (MySAwH) is a multi-centre prospective ongoing study with the intention of empowering people living with HIV (PLWH) 50+ years to develop healthy lifestyles. MySAwH is based on collection of physical function data and patient-related outcomes through a dedicated smart-phone app (MySAwH App). Our objective was to describe health changes assessed with frailty index (FI), collected by health professionals, and with a self-generated health measure called intrinsic capacity (IC) index which explores 5 different health domains: locomotion, vitality, sensory, cognition and psychosocial factors. FI and IC were used to predict physical performance at follow up.

Methods
We included 220 PLWH who were recruited from Italy (106), Australia (83) and Hong Kong (31). Two scheduled visits were performed, at baseline and follow-up (9 months). Frailty index was measured with a 36-item FI which objectively detect the presence of health deficits, while 27-item IC index was self-assessed with fitness tracking wearable devices and a MySAwH app. Outcome variables was reduced physical performance assessed with the Short Physical Performance Battery (SPPB) (SPPB score ≤10).

Results
Mean age was 57.6 years; 87.4% patients were men. Median CD4 was 676 c/µL (492-808 IQR) and 98.7% of patients had undetectable HIV viral load. Mean FI at baseline and follow-up were 0.22 (±0.1 SD) and 0.20 (±0.1 SD) respectively, p<0.01. Mean IC at baseline and follow-up were 0.69 (±0.1SD) and 0.71 (±0.1 SD), p=0.27. At baseline, PLWH showed higher prevalence of multi-morbidity (24.6% vs. 12.1%; p=0.04), higher mean FI (0.25 vs. 0.21; p=0.02) and lower mean IC (0.64 vs. 0.7; p=0.002). At the follow up, 42 individuals with impaired SPPB and 130 with normal SPPB remained stable, while 36 (16.3%) with impaired SPPB at baseline obtained normal value and 12 (5.4%) with normal SPPB at baseline were impaired at follow up. In the multivariate logistic regression model for reduced physical performance at follow-up, lower IC at baseline predicted lower SPPB (OR=0.54, CI=0.34-0.85; p=0.01), but not FI (OR=1.3, CI=0.77-2.18; p=0.33), nor age (OR=1.05, CI=0.97-1.14; p=0.26).

Conclusion
FI and IC are performative tools that can be used in research and clinical setting to describe respectively disease and health status in PLWH. IC score contrary to FI displayed ability to predict reduced physical performance in PLWH. This suggests that this patient-generated health outcome, obtained by smartphone MySAwH App and fitness tracking wearable devices, can be used to identify patients who need dedicated care programs.
Traditional risk factors and darunavir use associated with muscle and fat quality and quantity in adults with HIV on antiretroviral therapy

Lake J1, Erlandson K2, Feng H1, Adrian S1, Scherzinger A1, Malagoli A1, Milic J3, Miao H1, Guaraldi G3

1UTHealth, Houston, United States, 2University of Colorado Anschutz Medical Center, Aurora, United States, 3University of Modena and Reggio Emilia, Modena, Italy

Background: Changes in muscle and fat quality and quantity occur in people with HIV (PWH) on antiretroviral therapy (ART), but the implications for these changes on clinical outcomes such as physical function are less well understood, as are the contributions of specific ART agents.

Materials and Methods: In a retrospective analysis of PWH in care at the Modena HIV Metabolic Clinic, persons on atazanavir (ATV)-, darunavir (DRV)- or raltegravir (RAL)-based ART with ≥1 abdominal CT scan available for muscle and fat area and density quantification were included (n=295). Mixed effect model combined with interrupted time series accounted for traditional and HIV-/ART-specific covariates associated with body composition and physical function.

Results: Median age at time of first CT scan was 48 years, body mass index (BMI) 24 kg/m2, duration of HIV infection 17 years; about 32% were female. Median baseline visceral fat (VAT) area was greatest in the DRV group (DRV 166 cm2 vs RAL 142 vs ATV 119, p=0.001), whereas VAT density, subcutaneous fat (SAT) and muscle (psoas, paraspinous, lateral and rectus) area and density were similar by ART. Of note, DRV-treated persons were also significantly older (DRV 51 years vs RAL 49 vs ATV 46, p=0.0009) and had longer duration of HIV infection (DRV 20 years vs RAL 18 vs ATV 16, p=0.01). In multivariate models, greater VAT area was independently associated with DRV use, greater BMI and older age, with an interaction observed between DRV use and increasing BMI. Poorer VAT quality (lower density) was associated with older age and greater BMI. Greater SAT area was associated with female sex, higher BMI, and younger age, but not ART type. Lower SAT density was associated with female sex and higher BMI, with trends toward lower SAT density with DRV use (p=0.058) and a female sex-by-DRV use interaction (p=0.05) observed. Smaller lateral muscle area was associated with RAL (p=0.02) and greater area with DRV (p=0.04); DRV was also associated with lower lateral muscle density (p=0.02); other muscle areas and densities were associated with traditional risk factors but not ART type.

Independent of ART use, greater strength correlated with greater muscle density (higher quality muscle, especially for men). Trends were also observed between poorer performance on the short physical performance battery (SPPB) and ATV use (p=0.058), and higher grip strength with RAL use (p=0.079). DRV treatment was associated with greater grip strength among women only (p=0.045), but trended towards poorer SPPB performance (p=0.08).

Conclusions: Female sex, greater BMI and older age were the strongest predictors of muscle and fat area and density. DRV use was associated with greater VAT and lateral muscle area and lower lateral muscle density, suggesting excess ectopic fat deposition. However, despite poorer muscle quality, no deficit in physical function was observed. No other consistent ART effects on body composition were observed. Further study is needed to understand the contributions of ART-associated changes in body composition with clinical outcomes.
 Persistent low-level HIV-1 transcription associated with systemic inflammation and age related comorbidities

Olson A1, Asundi A1, Belkina A2,3, Cappione J2,4, Lina N1
1Section of Infectious Diseases, Boston Medical Center, , United States, 2Flow Cytometry Core Facility, Boston University School of Medicine, , United States, 3Department of Pathology and Laboratory Medicine, Boston University School of Medicine, , United States, 4Department of Microbiology, Boston University School of Medicine, Boston, United States

Background: Despite use of effective antiretroviral therapy (ART) people infected with HIV are at greater risk for developing age-associated comorbidities, such as cardiovascular disease, neurocognitive disorders, and malignancies. Prior studies have identified persistent inflammation that is in part due to excessive cell exhaustion as a possible contributor to this phenomenon, however, the role and association of HIV persistence and reservoir in this immune dysfunction among treated HIV-infected individuals is unknown. To identify possible mechanisms driving the accelerated aging phenotype we aim to understand the relationship between the low-level HIV replication, inflammation and their cumulative effects on immune function.

Methods: Uninfected controls and HIV-infected patients on suppressive antiretroviral therapy between the ages of 18-35 and ≥50 years old were enrolled from Boston area hospitals. Measures of HIV reservoir and low level viremia (total HIV cell associated (ca)-DNA and ca-RNA, respectively) were measured from peripheral blood mononuclear cells using a sensitive quantitative PCR assay. A panel of inflammatory markers was measured in paired plasma samples by multiplex assay. CD4+ and CD8+ T cell exhaustion markers (PD1, TIGIT, CD160, LAG3, and TIM3) were measured by flow cytometry. Correlations between inflammatory markers, degree of immune exhaustion, and number of cardiac risk factors were made against HIV viral measures.

Results: Older HIV-infected participants (≥ 50 yo) had nearly two-fold greater HIV ca-RNA (p=0.006) and a trend to greater HIV ca-DNA (p=0.08) compared to younger age group (≤35 yo) matched by duration of viral suppression. Furthermore, among older individuals with two or more reported cardiovascular comorbidities or risk factors (e.g. coronary artery disease, high cholesterol, diabetes, and hypertension) had significantly higher HIV ca-DNA level compared to those who had either one or no risk factors (p=0.02). Regardless of age, level of ca-RNA correlated with increased inflammatory marker d-dimer (r=0.64, p<0.0001). Older age and HIV infection synergistically increased percentage of CD8+ T-cells expressing multiple markers of exhaustion, at much higher levels than age-matched uninfected counterparts.

Conclusions: HIV persistence and low-level replication are increased with older age, and associated with greater CVD risk factors and level of systemic inflammation. Greater T cell exhaustion in suppressed older HIV+ individuals suggest a possible a mechanistic interaction of HIV persistence in premature aging among persons living with HIV.
Frailty, physical function impairment, comorbidity burden, and falls are predictive of mortality among middle-aged adults with HIV

Abdo M1, MaWhinney S1, Pelloquin R1, Jankowski C1, Erlandson K1

1 University of Colorado Denver, Aurora, United States

Background: Higher than expected rates of frailty and functional impairment are described among people with HIV (PWH). Whether these impairments, particularly among middle-aged persons, are predictive of poor outcomes including death are not well established. The objective of this study was to determine if frailty and physical function impairments are associated with long-term mortality among middle-aged adults with suppressed HIV.

Material & Methods: PWH ages 45-65 with ART-suppressed HIV-1 RNA for a minimum of 6 months were evaluated in 2010-2011 (baseline) using the Fried Frailty Phenotype (composite score and grip strength alone), Short Physical Performance Battery ([SPPB] composite and chair rise alone), 400-m walk, Veterans Aging Cohort Study (VACS) Index, and any fall in the prior year. Medical records were reviewed in 2018 to determine vital status. Participants who were not able to complete the 400-m walk or the chair rise were assigned a pace of zero. Hazard ratios were used to estimate survival by baseline frailty, function, comorbidity burden, or falls, stratified by age ≥/<50 years. Patients without a confirmed date of death were censored at last follow-up visit. Time-dependent area under the ROC (ROC-AUC) curves were estimated to compare the predictive accuracy of mortality between each physical function measure, where values of 0.5 and 1.0 represent random chance or no predictability and perfect predictability, respectively.

Results: Of 351 participants, 299 (85%) identified as male, 52 (15%) as female, 16% were Black and 19% Hispanic. At baseline, the mean (SD) age was 51.9 (5.2) years and the majority (58%) had a CD4 count of >500 cells/µL; all had an HIV-1 RNA <200 copies/mL. Twenty-three (7%) were frail and 164 (47%) pre-frail, 103 (29%) had ≥1 fall in the prior year, 74 (21%) had an SPPB score of ≤10, 33 (9%) had weak grip strength. The mean (SD) 400-m walk pace (m/sec) was 1.4 (0.4) and the mean (SD) chair rise pace (rises/sec) was 0.5 (0.2). The mean (SD) follow-up time was 6.7 (2.4) years. All physical function measures except grip strength were associated with mortality. 8-year overall survival differed significantly between participants who were pre-frail/frail compared to participants who were non-frail (HR=3.2 [95% CI=1.4,7.3], p-value=0.008) as well as between participants who had more than one fall compared to participants who had no falls (HR=2.8 [95% CI=1.4,5.7], p-value=0.004) and between participants who had a SPPB score ≤10 compared to participants who had a SPPB score >10 (HR=4.3 [95% CI=2.1,8.6], p-value<0.0001). VACS score was associated with increased hazard of death (10-unit increment, HR=1.6 [95% CI=1.3,1.9], p-value<0.0001). Individually, the 400-m walk was the best predictor of mortality with time-dependent ROC-AUC=0.82, followed by VACS index: 0.80, SPPB: 0.70, chair rise pace: 0.67, frailty 0.63, falls: 0.61 and average grip: 0.49.

Conclusions: In middle-aged adults with suppressed HIV, physical function, comorbidity burden (VACS Index), and falls are associated with long-term mortality. These simple clinical measures can be useful tools to guide clinical decisions by aiding in the identification of participants with higher mortality risk.
Increased frailty symptoms relate to poorer self-reported sleep quality among older people living with HIV

**Balon E1, Sun-Suslow N2, Montoya J3, Saloner R3, Campbell L3, Serrano V4, Ellis R2, Moore D2**

1University of Cincinnati College Of Medicine, Cincinnati, United States, 2University of California, San Diego, La Jolla, United States, 3San Diego State University/University of California, San Diego Joint Doctoral Program in Clinical Psychology, San Diego, United States, 4San Diego State University, San Diego, United States

**Background:** Older people living with HIV (PLWH) experience heightened risk for the acquisition of cumulative, multisystem decline, i.e., frailty syndrome. Frailty relates to poorer sleep quality in the general older adult population; however, the association between frailty and sleep quality has yet to be explored among PLWH.

**Material & Methods:** A cross-sectional analysis of 288 PLWH 50 years and older (mean age 60.5 ± 7.0) examined the relationship between frailty and self-reported sleep quality. The Pittsburgh Sleep Quality Index (PSQI) was used to measure subjective quality, latency, duration, and efficiency of sleep, as well as sleep disturbances, use of medications intended for sleep, and daytime dysfunction. Global PSQI scores range from 0 to 21, with higher scores indicating poorer sleep quality. Frailty was measured with the Fried Frailty Index, which evaluates the following frailty phenotype components: unintentional weight loss, weakness, exhaustion, slowness, and decreased activity. Individuals were categorized into three frailty levels: non-frail (no symptoms), pre-frail (1 or - 2 symptoms), and frail (3 or more symptoms). All participants completed a comprehensive medical history evaluation assessing for medical comorbidities and HIV specific disease characteristics. Participant demographics, measures of health status (e.g., medical comorbidities), and sleep quality were compared by frailty status using one-way analysis of variance or chi-squared analyses. Multivariable linear regression modelled global PSQI as a function of the number of frailty symptoms, including relevant covariates (age, sex, race/ethnicity, education, current depression measured by the Beck Depression Inventory-II, and current substance use disorder diagnosis) determined by a backward stepwise selection method using minimum Akaike Information Criterion (AIC) as the stopping rule.

**Results:** Global PSQI differed by frailty status, such that pre-fragile and frail individuals reported poorer sleep quality than those who were non-frail. The non-frail group consisted of more individuals who identified as white than those in the pre-frail or frail groups (p<.001) and had greater years of education than those in the frail group (p=.04). The frail group reported greater current depression (p<.001), however the groups did not differ by age, sex, medical comorbidities, or HIV disease characteristics (AIDS status, viral load, current and nadir CD4 T cell count, estimated duration of infection, and proportion on antiretroviral therapy). Number of frailty symptoms contributed to variance in global PSQI scores in the optimal AIC-based multivariable model (B=.122; p=.042) after accounting for covariates; F(4,279)=13.28, p<.001; R2=.160. Other factors significantly associated with greater global PSQI scores included age (B=-.154, p=.007), female sex (B=1.14, p=.009), and current depression (B=.252, p<.001).

**Conclusions:** Older PLWH with increased frailty symptoms report poorer sleep quality, even after accounting for covariates. Frailty and poor sleep individually have adverse effects on health and everyday functioning; thus, understanding the association between the two may inform clinical care. Given the cross-sectional nature of our study, causality between components of frailty and poorer sleep quality cannot be determined. Future research is warranted to elucidate the temporal association between frailty and sleep quality.
Vitamin D deficiency and frailty phenotype in HIV-infected men

1Johns Hopkins Bloomberg School of Public Health, Baltimore, USA, 2University of Michigan, Ann Arbor, USA, 3Northwestern University Feinberg School of Medicine, Chicago, USA, 4Johns Hopkins University School of Medicine, Baltimore, USA, 5Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center, Torrance, USA, 6University of Washington, Seattle, USA

Introduction & objective: Frailty is a geriatric syndrome characterized as a state of diminished reserve and increased vulnerability to stressors due to dysregulation in multiple physiological systems, conferring higher risk for adverse health outcomes such as falls, hospitalization, disability, and death. More HIV-infected persons are experiencing aging related diseases, including frailty, with the introduction of highly active antiretroviral therapy (HAART). Vitamin D deficiency, which has been linked to increased comorbidities such as osteoporosis, metabolic syndrome, and decreased cognitive function, may interfere with immune restoration following HAART and accelerate the onset of frailty in HIV-infected population. We examined the association between vitamin D and frailty among HIV-infected men from the Multicenter AIDS Cohort Study.

Methods: Levels of the standard (25-hydroxyvitamin D or 25[OH]D) and active (1,25-dihydroxyvitamin D or 1,25[OH]₂D) vitamin D metabolites were measured once in serum from 625 HIV-infected men, collected 1.9 median years (IQR: 1.4-2.1 years) post-HAART between 1999 and 2008. Vitamin D deficiency was defined as 25[OH]D <20 ng/ml. 1,25[OH]₂D was analyzed as tertiles due to absence of a clinically relevant cut-off. Frailty was assessed at 6-month intervals between 1994 and 2018 using the Fried frailty phenotypic criteria with those meeting ≥3 of the 5 criteria considered frail and 1 or 2 criteria prefrail. Discrete-time multistate models examined factors associated with transitioning from non-frail to prefrail to frail. Models adjusted for baseline (race, season, HCV co-infection, enrollment after 2001, enrollment center, education, AIDS diagnosis) and time updated covariates (age, body mass index (BMI), depression, kidney function, cumulative pack-years smoking, diabetes, CD4+ T-lymphocyte/mm³, HIV RNA, and cumulative HAART use).

Results: HIV-infected men had a median of 24 frailty measures (IQR: 18-32) and median follow-up of 14.9 years (IQR: 11.8-18.6 years). At baseline, Vitamin D deficiency prevalence was 41%, 60% of men were non-frail, 27% prefrail, and 5% frail. Across follow-up, 6% (824) of visits were characterized as frail, 30% (4,219) prefrail, and 51% (7,050) non-frail. Among non-frail and prefrail men, vitamin D deficiency had no effect on the probability of transitioning to frail. However, non-frail men with 1,25[OH]₂D values in the first tertile (median: 32.9 ng/ml, IQR: 28.0-36.2 ng/ml) had 2.74 (95% CI: 1.10-6.84) times the risk of becoming frail compared to men with 1,25[OH]₂D values in the third tertile (median: 60.3 ng/ml, IQR: 55.5-67.6 ng/ml). For both vitamin D metabolites, there was an elevated risk of transitioning into a higher frail state (prefrail or frail) with older age, depression, and diabetes among non-frail men. AIDS diagnosis and low kidney function in particular were associated with increased risk of becoming frail, regardless of non-frail or prefrail state. CD4 ≥200 cells/mm³ was the only risk factor to confer protection against becoming frail among non-frail men (RRR for 25[OH]D: 0.13, 95% CI: 0.04-0.46, and RRR for 1,25[OH]₂D: 0.14, 95% CI: 0.04-0.48), while BMI (25-29.9 kg/m²), college education, and HIV RNA <50 copies/ml decreased the risk of becoming prefrail.

Conclusion: Among HIV-infected men, vitamin D deficiency was not associated with transitions to frailty, while the active vitamin D metabolite, 1,25(OH)₂D, captured an increased risk of becoming frail among non-frail men. Risk factors contributed in varying degrees to increase or decrease the risk of transitions into frailty, consistent with prior work.
Frailty predicts recurrent falls among older women with and without HIV

Sharma A1, Hoover D2, Shi Q1, Gustafson D3, Plankey M4, Tien P5, Weber K6, Vance D6, Floris-Moore M7, Bolivar H8, Golub E9, Holstad M10, Yin M11

1Albert Einstein College Of Medicine, Bronx, USA, 2Rutgers University, Piscataway, USA, 3New York Medical College, Valhalla, USA, 4State University of New York Downstate Health Sciences, Brooklyn, United States, 5Georgetown University Medical Center, Washington DC, USA, 6University of California San Francisco, San Francisco, USA, 7Cook County Health and Hospitals System/Hektoen Institute of Medicine, Chicago, USA, 8The University of Alabama at Birmingham, Birmingham, USA, 9University of North Carolina School of Medicine, Chapel Hill, USA, 10University of Miami Health System, Miami, USA, 11Johns Hopkins Bloomberg School of Public Health, Baltimore, USA, 12Emory School of Nursing , Atlanta, USA, 13College of Physicians and Surgeons, Columbia University Medical Center, New York, NY, USA, New York, USA

Background: Frailty is common with aging and may occur prematurely among HIV+ populations. We evaluated associations of frailty status with self-reported single and recurrent falls in the prior 12 months in the Women’s Interagency HIV Study (WIHS).

Methods: The Fried Frailty Index (FFI) defined frailty as ≥3/5 of: impaired mobility, reduced grip strength, exhaustion, unintentional weight loss, and low physical activity, and was assessed among 897 HIV+ and 392 HIV- women. Adjusting for HIV status and study site, stepwise logistic regression models were fit to evaluate associations of FFI with single fall (1 vs. 0) and recurrent falls (≥2 vs. 0). Additional analyses evaluated associations of the individual FFI components with single and recurrent falls. Models restricted to HIV+ women evaluated the contribution of HIV disease-related variables on relationships between frailty and falls.

Results: Median age was 53 years. Among HIV+ women, 93% reported current ART use and 71% had undetectable HIV RNA viral load. HIV+ women were less likely than HIV- women to be frail (9% vs. 14% vs. p=0.009), and report current smoking (38% vs. 46%, p=0.006), cocaine or heroin use (7% vs. 13%, p=0.0001), heavy drinking (4% vs. 9%, p<0.0001) or current cannabis use (21% HIV+ vs. 25% HIV-, p=0.06). Single fall was reported in 13% of HIV+ and HIV- women, and recurrent falls in 13% of HIV+ vs. 16% of HIV- women (overall p=0.43). In multivariate analyses among all women, frailty was associated with increased risk of recurrent falls [adjusted odds ratio (AOR) 1.96, 95%CI: 1.15-3.32, p=0.013] but not with single fall (AOR 1.59, 95%CI: 0.92-2.76, p=0.09). Older age, current cannabis use, cognitive complaints, central nervous system active medications, and depressive symptomatology were associated with higher risk of recurrent falls. Of FFI components, reduced grip strength (AOR 1.75, 95% CI: 1.07-2.87, p=0.03), exhaustion (AOR 1.88, 95% CI: 1.19-2.97, p=0.007), and low physical activity (AOR 1.89, 95% CI: 1.19-2.99, p=0.007) were associated with higher risk of recurrent falls. HIV status was not associated with falls. In models restricted to HIV+ women, frailty was associated with higher risk of single fall (AOR 2.87, 95%CI: 1.25-6.60, p=0.013), but not recurrent falls (AOR 1.97, 95%CI: 0.78-4.98, p=0.15). Among HIV+ women, former cocaine or heroin (AOR 3.11, 95%CI: 1.53-6.32, p=0.002) and current cannabis use (AOR 2.76, 95% CI: 1.18-6.45, p=0.02) were associated with higher risk of single fall. Having a history of AIDS was associated with a higher risk of recurrent falls (AOR 1.82, 95%CI: 1.00-3.32, p=0.04) and current ART use was associated with lower risk of recurrent falls (AOR 0.30, 95%CI: 0.12-0.76, p=0.01).

Conclusions: Prevalent frailty and FFI components (reduced grip strength, exhaustion, and low physical activity) were independently associated with risk of recurrent falls in the prior 12 months among older women with or without HIV. Evaluating frailty as a risk factor for falls as women age with HIV and a history of advanced HIV disease is clinically warranted.
Comparison of 2 frailty scores in HIV infected people aged 50 and over: SOF index and FRIED phenotype


European Hospital Marseille, Marseille, France, 2Department of Clinical Research, State Geriatric Center, Marseille, France, 3Assistance Publique, Hôpitaux de Marseille, Public University Hospital, Marseille, France, 4Department of Dermatology, Saint-Joseph foundation hospital, Marseille, France, 5Department of Public Health, Self-Perceived Health Assessment Research Unit EA3279, Aix-Marseille University, Marseille, France, 6Institut Hospitalo-Universitaire Méditerranée Infection, Marseille, France, 7Department of Internal Medicine, Martigues Hospital Center, Martigues, France, 8Department of Internal Medicine and Oncology, Sainte-Anne Military hospital, Toulon, France, 9Department of Internal Medicine, Hyères-les-Palmiers Hospital Center, Hyères-les-Palmiers, France, 10Department of Internal Medicine and Hemato-Oncology, Aix-en-Provence Hospital Center, Aix-en-Provence, France, 11Department of Cardiology and Pneumology, Digne-les-Bains Hospital Center, Digne-les-Bains, France, 12Department of Internal Medicine, Gap Hospital Center, Gap, France, 13Department of Clinical Hematology and Medical Oncology, Avignon Hospital Center, Avignon, France, 14Aix Marseille Univ, INSERM, INRA, C2VN, Marseille, France

Background: The overall life expectancy of people living with HIV (PLWHIV) is increasing mainly due to access to highly active antiretroviral treatment and multidisciplinary care. The prevalence of frailty among PLWHIV is frequent and begins earlier compared to the general population. The measurement of frailty in PLWHIV is currently recommended but the best identification tool remains to be defined. The objective of this study was to compare the frailty criteria according to the FRIED phenotype and the SOF index (Study of Osteoporotic fractures) in PLWHIV.

Method: This multicentre, cross-sectional study included 509 PLWHIV aged 50 and over treated in 12 French hospitals. Demographic data, comorbidities, HIV data, geriatric parameters, Fried phenotype fragility markers and the SOF index were collected.

Results: Among the 509 PLWHIV (73% male, mean age 58.4 ± 7 years), according to the Fried phenotype 58.8% were pre-fragile and 8.2% were fragile; according to the SOF index, 37.1% were pre-fragile and 11.2% were fragile. The SOF index was weakly correlated to Fried’s phenotype, with a Kappa score = 0.267 ± 0.042 for patients classified as "fragile and pre-fragile" versus "robust" patients. In multivariate analysis, the presence of Fried’s phenotype fragility markers was associated with the risk of depression, falls and a history of cancer. Frailty according to the SOF index was significantly associated with precariousness, incapacity for activities of daily living, risk of depression and falls.

Conclusion: In PLWHIV over fifty years old the SOF index and Fried's phenotype are low correlated scores. The use of Fried’s phenotype identify more pre-fragile and fragile patients and therefore to be potentially more useful in identifying fragility in this population. Prospective studies assessing frailty and the risk of adverse change in morbidity and mortality are crucial in order to define relevant screening tools for this population.
Existing and future trials have potential to provide information on frailty

Inceer M1, Mayo N1
1Mcgill University, Montréal, Canada

Background: HIV has moved from a dire disease to a manageable one and life expectancy approaches that of the general population. However, of concern is that HIV is associated with accelerated aging which is hypothesized to affect the early onset of frailty. There is not an age cut-point for frailty but it is argued that the earlier it is identified the better the chances for reversal or postponement.

Identifying frailty requires using performance-based tests, commonly gait speed and hand grip strength. However, it is unlikely that these tests will be administered in busy clinical practices that likely lack the space and equipment required. Some studies have used self-report proxy items to replace the performance-based tests. Many of the proposed self-report items are included in health-related quality of life (HRQL) measures, available from most large cohort studies and in clinical trials. For example, Fried’s Frailty criteria includes exhaustion, physical activity, slowness, weakness, and unintentional weight loss. These five items have been shown to be on many of the HRQL measures. If frailty can be identified in clinical trials, there is an added advantage in that the interventions and the rich biological data could also be evaluated for their effect on frailty.

Objective: The global aim of this study was to identify sources of data that could be used to estimate the prevalence of frailty and its associated predictors and consequences. The specific objective was to estimate the extent to which HIV clinical trials use the HRQL measures that can identify frailty.

Methods: A systematic review of the PubMed database was undertaken using the search terms “HIV”, “quality of life” and “health related quality of life” with a clinical trial filter. Study characteristics and the specific measures used were extracted from the included studies. Studies that used one of the 12 measures that covered 3 or more of the 5 frailty criteria were considered a frailty estimable study.

Results: The search yielded a total 323 papers. The initial screen identified 55 clinical trials (46 completed and 9 protocols), published between 1992 and 2018. Of the completed trials (protocols), 26 (3) tested pharmaceuticals and 29 (6) were of other interventions. The completed studies yielded data on 25,005 participants (mean age from 33 to 55.4 years), 5,698 women and 19,023 men, two studies did not present gender distribution. The majority of the studies were conducted in the USA or Europe. Of the 46 completed studies, 29 used a HIV-specific measure, 16 used a generic measure, and 1 remained unclear. Overall, 46 completed clinical trials used a measure that could provide information on at least 3 of the 5 frailty criteria potentially providing data from 16,870 people with an additional 698 available from future trials. In addition, many studies measure BMI and BMI< 21 kg/m2 has been used to approximate weight change if unintentional weight loss in the last year is missing.

Conclusion: There is a wealth of existing data that could be tapped to conduct an in-depth study of frailty in people with HIV.
Physical activity in asymptomatic middle-aged men with and without HIV infection is associated with routine blood-based biomarkers

Montano M1,2, Pencina K1,2, Li Z2

1Harvard Medical School, Boston, United States, 2Brigham and Women’s Hospital, Boston, United States

Background: The use of circulating clinically routine biomarkers and volitional physical activity (PA) using wristband accelerometry in preclinical middle-aged adults may provide sensitive measures of physical function and predict sooner the onset of age- and HIV-related physical decline.

Methods: Nested cross-sectional cohort study of adult men 50-65 years old with HIV infection on potent antiretroviral therapy and uninfected control participants within the Boston metropolitan area. Gait speed derived from wristband accelerometry, gait speed derived from a standardized six-minute walk test (6-MWT), cellular immune biomarker levels (CD4 T cell, CD8 T cell) and serum anabolic biomarker levels (total and free testosterone, and sex-hormone binding globulin) were measured.

Results: Of the 5 measured biomarkers, 4 were significantly associated with volitional gait speed based on accelerometry, whereas only 1 was associated with gait speed based on the 6-MWT collected in a laboratory environment.

Conclusion: Levels of selected immune and anabolic biomarkers were associated with volitional PA in middle-aged individuals. Digital and circulating biomarkers may be useful in future studies designed to identify presymptomatic individuals at increased risk for age- and HIV-associated functional decline.
Long-term pre-HAART survivors of HIV: a specific group with specific needs

Brañas F1, Ramírez M2, Galindo M3, Torralba M4, Ryan P1, Dronda F5, Machuca F1, Busca C1, Antela A6, Vergas J7, Bustinduy M10, Cabello A11, Sánchez-Conde M8

1Hospital Universitario Infanta Leonor, Madrid, Spain, 2Hospital Universitario Gregorio Marañón, Madrid, Spain, 3Hospital Clínico Universitario de Valencia, Valencia, Spain, 4Hospital Universitario de Guadalajara, Guadalajara, Madrid, Spain, 5Hospital Universitaria Ramón y Cajal, Madrid, Spain, 6Hospital Universitario Reina Sofía, Córdoba, Spain, 7Hospital Universitario La Paz, Madrid, Spain, 8Complejo Hospitalario Universitario de Santiago, Santiago, Spain, 9Hospital Clínico San Carlos, Madrid, Spain, 10Hospital Universitario Donostia, San Sebastián, Spain, 11Fundación Jiménez Díaz, Madrid, Spain

Background: Nearly half of people living with HIV (PLWH) in Europe are 50 years old or older. Some of them were diagnosed before the modern era of effective HIV drugs known as “long-term pre-HAART survivors” (LTS), while others are newly diagnosed. Our objective was to evaluate differences between older PLWH LTS and non-LTS.

Methods: Prospective cohort study. Patients from the “HIV-FUNCFRAIL: Multicenter spanish cohort to study frailty and physical function in 50 years or older HIV-infected patients” were included and stratified by year of diagnosis: < 1996, 1997-2000, >2000. We recorded sociodemographic data, comorbidities, variables related to HIV infection, frailty, physical function, and the risk of 5-year all-cause mortality measured by VACS index.

Results: We evaluated 540 PLWH who were 50 years old or over, of which 272 (50.3%) were LTS. Differences were found regarding the proportion of older than 65 years [6.6% in the LTS, 18% in the 1997-2000 group and 22.3% in the >2000 group (p=0.0001)], the proportion of women [30% in the LTS, 23.6% in the 1997-2000 group and 19.7% in the >2000 group (p=0.04)] and in the risk practice for HIV infection (p=0.0001). No significant differences were found regarding median CD4+ T-cell count, median CD4/CD8 ratio and the proportion of patients with undetectable viral load. LTS suffered significantly more from: OCPD (p=0.001), depression (p=0.018), psychiatric disorders (p=0.0001) and osteoarticular pathology (p=0.03). No differences were found regarding: cardiovascular risk factors, ischaemic heart disease, cerebrovascular disease and chronic kidney failure. Polypharmacy was prevalent among LTS [25.5% in the LTS, 25% in the 1997-2000 group and 15.6% in the >2000 group (p=0.03)], and particularly the use of neuroleptics (p=0.003), benzodiazepines (0.007) and hypnotics (p=0.009). Differences were found regarding mean BMI [24.7 (SD 4.2) in the LTS, 26 (SD 4.2) in the 1997-2000 group and 26.7 (SD 4.3) in the >2000 group (p=0.01)], frailty [3.7% in the LTS, 10.1% in the 1997-2000 group and 6.4% in the >2000 group (p=0.01)], and in gait speed < 0.8m/s [3.7% in the LTS, 9% in the 1997-2000 group and 5.1% in the >2000 group (p=0.01)]. No differences were found regarding cognitive impairment (MOCA-test) and the risk of 5-year all-cause mortality measured by VACS index.

Conclusions: In our cohort, LTS represented half of the total older adults living with HIV. Despite the fact that LTS were not the oldest patients, they had more comorbidities and polypharmacy and the burden of depression and psychiatric disorders was higher among them. Frailty and slow gait speed were more prevalent among those diagnosed between 1997 and 2000.
Characterizing gender differences in Canadians living with HIV to improve management of comorbidities


1Maple Leaf Medical Clinic, Toronto, Canada, 2Church Wellesley Health Center, Toronto, Canada, 3Department of Medicine, University of Saskatchewan, Regina, Canada, 4Clinique Medicale l’Actuel, Montreal, Canada, 5Spectrum Health, Vancouver, Canada, 6University of Ottawa Health Services, Ottawa, Canada, 7Cool Aid Community Health Centre, Victoria, Canada, 8Clinique de Médecine Urbaine du Quartier Latin, Montreal, Canada, 9St. Clair Medical Associates, Toronto, Canada, 10Infectious Diseases Care Program, St. Joseph’s Hospital, London, Canada, 11Advisory Physicians Research Services Inc., Sooke, Canada, 12Gilead Sciences Canada Inc., Mississauga, Canada

Background: We compared gender differences in comorbidities and risks of developing cardiovascular disease (CVD) and chronic kidney disease (CKD) in people living with HIV (PLHIV) to improve management of the aging population.

Methods: This retrospective analysis characterized 2000 most recently seen PLHIV across 10 Canadian HIV clinics via chart review. Data on demographics, comorbidities and lab results were collected, and risks of developing CVD and CKD were calculated by D:A:D and Framingham. Gender association analyses and mean difference of younger (<50 years) and older (≥50 years) individuals were completed by Chi-square or Fisher’s exact and t-tests respectively.

Results: This cohort included mostly males (87%) on ART with well managed HIV (median CD4 count, 583 cells/µL and HIV RNA <400 copies/mL, 97%). Younger females (n=163) and males (n=702) were comparable in age (mean, 39 vs 38 respectively, P=0.33), as were older females (n=98) and males (n=1036; both 59, P=0.93). Younger females were more likely to have ≥2 comorbidities compared to young men (63% vs 52%, P=0.01) and most frequently reported comorbidities in this age group were neuropsychiatric (50% and 57%), obesity/overweight (44% and 34%), and liver-related comorbidities (44% and 29%). Among older individuals, comorbidity rates were high (>96% had ≥1 comorbidity for both) and similar (P=0.42). Most commonly reported comorbidities in older females and males were neuropsychiatric (66% vs 60%), dislipidemia (51% vs 35%) and obesity/overweight comorbidities (49% vs 50%). Where data was available, CVD (n=1672) and CKD risks (n=1150) were calculated. Regardless of age, more men scored high or intermediate using the Framingham 10-year CVD risk algorithm than women (both P<0.0001) and older males had a 3.8-fold increase in scoring high compared to females (17.7% vs 4.6%). Conversely, younger women frequently scored high or medium in CKD risk compared to their male counterparts (high, 31% vs 11%; p<0.0001), while there was a marginal increase in older females having greater CKD risk than males (high, 85% vs 71%; p=0.05).

Conclusions: Routine clinical practice should be optimized to consider gender-related differences to better prevent and manage age-associated comorbidities and risks in all PLHIV.
Physical health of older people living with HIV in Eswatini

Harris T1, Floren S1, Mantell J, Nkambule R1, Lukhele N1, Malinga B4, Chekenyere R1, Kidane A1
1ICAP at Columbia University, New York, United States, 2HIV Center for Clinical and Behavioral Studies, Department of Psychiatry, NYS Psychiatric Institute and Columbia University Irving Medical Center, New York, USA, 3Eswatini Ministry of Health, Mbabane, Eswatini, 4Mankayane Government Hospital, Eswatini Ministry of Health, Mankayane, Eswatini

Background: The number of older people living with HIV (OPLHIV) globally is growing and predicted to increase to 7.5 million by 2020. However, little is known about the intersection of HIV and aging, especially in sub-Saharan Africa, which accounted for 61% of the 6.7 million OPLHIV and 60% of the 120,000 OPLHIV newly diagnosed globally in 2017.

Materials and Methods: A cross-sectional pilot study on HIV and aging was conducted from October 2016-January 2017 among OPLHIV age ≥50 years receiving ART as outpatients at an Eswatini health facility. A convenience sample of 50 OPLHIV were enrolled in the study. Participants completed a survey that captured information on demographics, HIV, and other chronic disease risk factors and conditions. Physical activity and diet were assessed using questions from the World Health Organization (WHO) STEPwise approach to surveillance (STEPS) Instrument. Information on tests from the day of study enrollment were also abstracted from medical records. Analyses were performed to obtain both descriptive statistics and cross-tabulations. Shapiro-Wilk tests were performed to check for normality. Median values are presented for non-normally distributed data.

Results: Of the 50 participants, 26 (52%) were female, and the median age was 60 years (range=50-75). Most participants had only a primary school education (54%), were married (59%), and were employed (60%). Approximately one-third (32%) received monthly nutritional support and 30% received financial support. A little more than one-third (38%) had electricity in the home and almost all (98%) did not have a flushing toilet. The mean age at HIV diagnosis was 53 years (range=41-70 years). Participants had been diagnosed with HIV for a median of 7 years (range=1-20) and on ART for a median of 6 years (range=1-16 years). The median CD4+ count was 621 (range=201-1319) and all participants were virally suppressed (<1000 copies/mL). Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were above the upper limit of normal (ULN) among 28% (14/45 with a result) and 17% (7/41), respectively, and creatinine was above ULN for 5% (2/42), with a mean clearance of 37 mL/minute. Among the 50 participants, 6% (n=3) were current smokers, 34% (n=17) former smokers, and 60% (n=30) had never smoked. Almost all participants [88% (n=44)] reported sufficient physical activity (median=960 minutes of moderate activity/week) per WHO guidelines (≥150 minutes per week). Most activity was in the work domain, which includes household chores and other unpaid work (900 vs. 60 minutes in travel and 0 minutes in recreation). None met the WHO recommendation of ≥5 servings of fruits and vegetables per day (average serving=1.3/day). Almost half (46%) of participants reported always or often eating processed food high in salt. Among the participants, 57% (28/49) self-reported hypertension, 33% (15/45) a history of TB, 11% (5/46) diabetes, and 5% (2/39) elevated cholesterol.

Conclusions: While all OPLHIV in this pilot study showed evidence of HIV control, other chronic disease risk factors and markers were common. This indicates the need to ensure OPLHIV are screened for non-HIV risk factors and conditions and are provided with appropriate health services for HIV and other conditions.
Magnetic resonance spectroscopy evidence of accelerated aging in virally-suppressed HIV

Tran T1, Chu K1, Wei K1, Shriner K2, King K1
1Huntington Medical Research Institutes, Pasadena, United States, 2Phil Simon Clinic, Huntington Memorial Hospital, Pasadena, USA

HIV-associated neurocognitive disorder (HAND) (1,2) and accelerated neurocognitive aging (3) are a persistent problem despite effective viral suppression. MRI studies reveal increased brain white matter hyperintensity (WMH) volume (4) and atrophy (5), but these studies have primarily been performed on heterogenous groups including those without effective treatment. MR spectroscopy (MRS) studies have reported elevations in choline and myo-inositol (6) and reduction in neuronal marker N-acetyl aspartate in AIDS dementia complex (7), but no study has utilized MRS to assess aging in healthy HIV-positive patients. Our study aims to measure N-acetyl aspartate, a marker of neuronal integrity and metabolism (8) by MRS (9) to determine whether there is HIV-related brain insult resembling accelerated aging in healthy individuals with effective treatment.

Material & methods: Thirty-six patients with HIV (age 50±13) and 41 non-demented HIV-negative individuals (age 80±10) consented to participate in this IRB-approved study. MR exams were completed on a 3T GE scanner and imaging included 3D T1 FSGPR and 3D FLAIR. MR spectroscopy was obtained using short echo time (TE = 35ms) point-resolved spectroscopy (PRESS) in posterior and frontal grey matter (PGM and FGM, respectively) and analyzed using LC Model (LCM http://s-provencher.com/lcmodel.shtml) to quantify NAA and creatine (Cr); NAA/Cr was averaged for both regions. Cortical thickness was evaluated with Freesurfer (https://surfer.nmr.mgh.harvard.edu/). WMH was quantified using Lesion Segmentation Toolbox 2.0.15 (http://www.statistical-modelling.de/lst.html) with threshold at 0.3. Multilinear regression with age and sex was done using JMP Pro (SAS, V 13.0.0, Cary, NC) using a best fit model minimizing Bayesian Information Criterion for predictor variables age and HIV status with an interaction term for Age*HIV status. WMH volumes were log transformed to obtain a more normal distribution.

RESULTS
Age and HIV status were both significantly associated with NAA/Cr. Age alone showed significant correlations with log WMH and cortical thickness.

Discussion: History of HIV and older age were both associated with decreased NAA/Cr. Based on parameter estimates, NAA/Cr values for HIV+ are similar to HIV- individuals who are approximately 30 years older. HIV status was not associated with significant differences in mean cortical thickness and WMH volume. Mean cortical thickness and log WMH showed significant linear slopes with age (p<0.0001) while HIV stage did not contribute to model fit. HIV did cause a reduction in NAA/Cr but the interaction term for age and HIV status was insignificant indicating the rate of age-related decline did not significantly differ from those without HIV. This seems to suggest that there is an additional burden of insult related to HIV but which does not cause a synergistic subsequent acceleration of brain insult with aging. With aging, a decline in NAA/Cr indicates significantly increased risk for dementia. It remains uncertain whether low NAA/Cr we observe in healthy individuals living with HIV carries the same risk. A concern is that HIV may damage the brain, diminishing cognitive or metabolic reserves that will ultimately hasten the onset of clinically apparent deficits related to other accumulated insults and brain changes leading to dementia. Our study indicates that NAA/Cr provides a useful measure to track this accumulated brain insult in HIV which is not apparent on structural MRI.

Conclusion: N-acetyl aspartate reveals brain insult in chronic HIV equivalent to approximately 30 years of aging. Our results indicate that age related differences in brain cortical thickness and WMH volume are not affected by HIV infection.
Frailty phenotype is associated with antiretroviral exposure among older persons living with HIV.

Felker G1, Enel P1,2, Petit N1, Tolinchi F3, Cohen-Valensi R4, de Jaureguiberry F5, Chadapaud S5, Philibert P6, Allegret T7, Breggeon S7, Granet-Brunello P8, Pelissier L9, Pichancourt G11, Ravaux I1,12, Retornaz F2,11, Darque A1

1Assistance Publique, Hôpitaux De Marseille, Public University Hospital, Marseille, France, Marseille, France, 2Department of Public Health, Self-Perceived Health Assessment Research Unit EA3279, Aix-Marseille University, Marseille, France, 3Department of Dermatology, Saint-Joseph foundation hospital, Marseille, France, 4Department of Internal Medicine, hospital center, Martigues, France, 5Department of Internal Medicine and Oncology, Sainte-Anne Military hospital, Toulon, France, 6Department of Internal Medicine, hospital center, Hyères-les-Palmiers, France, 7Department of Internal Medicine and Infectious Diseases, European hospital, Marseille, France, 8Department of Internal Medicine and Hemato-Oncology, hospital center, Aix-en-Provence, France, 9Department of Cardiology and Pneumology, hospital center, Digne-les-Bains, France, 10Department of Internal Medicine, hospital center, Gap, France, 11Department of Clinical Hematology and Medical Oncology, hospital center, France, 12Institut Hospitalo-Universitaire Méditerranée Infection, Marseille, France

Introduction: Aging persons living with HIV may develop multiple health problems, including comorbidities, and altered physical and mental health, and frailty phenotype earlier than non-infected people. Determinants of the high prevalence of frailty are not completely understood.

Objective: We assessed the prevalence of frailty phenotype and its relationship with antiretroviral treatment (ART) in older persons living with HIV.

Methods: An 18-month, multicenter, cross-sectional study was carried out between 2013-2014 focusing on patients > 50-years of age followed-up in 12 dedicated HIV medical hospital units located in the South of France and involved the VISAGE study group. The following data were recorded: health indicators (gender, age, body mass index), comorbidities, HIV data, five frailty markers (nutrition, energy, mobility, physical activity, strength), socioeconomic, behavioral and age-related variables. Patients were defined as frail if they had 3 or more frailty markers and pre-frail if they had 1 or 2. The history of ART was documented in medical records: all cumulative exposure to any pharmacological classes of ART and all different regimens.

Results: A total of 484 patients completed the frailty evaluation and history on ART. Mean age was 58.5 ± 7.0 years and 72.9% were male. These patients received 6.01 ART regimens on average. Univariate analysis found that duration on all ART regimens, number of different ART regimens, duration on protease inhibitors (PI) and reverse transcriptase inhibitors (NRTI), number of comorbidities, presence of dyslipidemia, cancer, lipodystrophy, risk of depression, falls last past 6 months, ADL disability, and chronic pain were independent predictors for presence of at least one frailty markers. On logistic regression multivariable analysis, with factors selected at a threshold of $p \leq 0.10$ by univariate analysis and with sex, we found that the independent predictors for frailty and pre-frailty phenotype were a higher number of different ART regimens (OR=1.09 [95%CI: 1.01-1.17]), presence of cancer (OR=2.00 [95%CI: 1.02-3.92]), and chronic pain (OR=1.11 [95%CI: 1.01-1.21]) (respectively $p=0.043$, $p=0.039$ and $p=0.032$).

Conclusion: Our study confirms a significant association between presence of frailty markers and a high number of different ART regimens among older PLWHIV. As frailty phenotype could be potentially reversible, a better understanding of the underlying determinant is warranted. The burden of cancer and pain shows the importance of comprehensive care. Further studies are needed to confirm these findings.
Effect of computerized cognitive rehabilitation therapy on neurocognitive function, quality of life and frailty among older Ugandans with and without HIV infection.

Ezeamama A1, Sikorskii A1, Sankar P1, Nakasujja N2, Ssonko M3, Kaminski N4, Guwatudde D2, Boivin M1, Giordani B4

1Michigan State University, East Lansing, United States, 2Makerere University, Kampala, Uganda, 3Mildmay Hospital, Kampala, Uganda, 4University of Michigan, Ann Arbor, USA

Background: Premature neurocognitive decline is a public health challenge without known effective treatment. Computerized cognitive rehabilitation therapy (CCRT) is a promising strategy for mitigating/slowing neurocognitive decline. However, the feasibility of CCRT intervention in older Ugandan adults is unknown.

Methodology: Adults ≥50 years old (n=80) at risk of aging-(n=40) and HIV-(n=40) associated neurocognitive decline were enrolled from Wakiso District of Uganda. Participants were non-randomly allocated CCRT – i.e., 20 forty-five minute sessions of computerized cognitive training over five weeks with culturally adapted video games through Captain’s Log Software at frequency of two training days/week and four sessions/training day or standard of care (SOC, i.e. no CCRT). All subjects were tested pre and post CCRT or at beginning and study end (if SOC) using a suite of eight performance based neurocognitive tests. Quality of life (QOL) and frailty related phenotype (FRP) were measured on same schedule via the Medical Outcomes Study questionnaire and Edmonton frail scale respectively. Multivariable linear regression models estimated CCRT vs. SOC related differences (β) in neurocognitive batteries, QOL and FRP with corresponding 95% confidence intervals (CI). Effect Size were calculated to quantify clinical relevance of estimated βs. All analyses were implemented in SAS v.9.4.

Results: Target sample was enrolled within specified time frame with universal positive dispensation towards engaging with the computerized games. There was limited evidence of post-intervention increase in QOL (β=-2.64, 95%CI:-6.7, 1.4; ES=-0.28). However, adults that received CCRT vs. SOC had modestly higher performance in learning tests – specifically, interference list (β=1.00, 95% CI: 0.02-1.98; ES=0.43) and delayed recall (β=1.04, 95%CI: 0.06-2.02; ES=0.47) and in verbal fluency (β=1.25, 95%CI: -0.09-2.58, ES = 0.38). Among HIV+ older adults, CCRT was associated with: 1) clinically large improvement in three post-intervention test: immediate recall (β=0.91, 95%CI: 0.08-1.73; ES=0.69), working memory (β=0.79, 95%CI: -0.18-1.77; ES=0.51) and verbal fluency (β=1.68, 95%CI: -0.32-3.67; ES=0.51); and 2) moderately faster time to completion of color trails(ES=-0.32, p = 0.306) and timed gait (ES=-0.44, p = 0.167) tasks. Among HIV-negative controls, CCRT vs. SOC predicted modest improvement in learning tests, and a decline in FRP (β=-0.54, 95%CI: -1.00 to -0.08; ES = -0.71); however, older HIV+ adults on CCRT vs. SOC scored lower on test of simple attention (ES=-0.41, p=0.147) and had longer time to completion of visuomotor coordination task (ES=0.41, p=0.172).

Conclusion: CCRT intervention is feasible in older adults in this setting with possible beneficial impact on learning and verbal fluency regardless of HIV status. A broader array of CCRT related neurocognitive benefits was realized in HIV-infected older adults. However, given feasibility nature of the present investigation, these promising data suggests need for an efficacy trial of CCRT for aversion of premature neurocognitive decline in vulnerable older adults.
The effect of gp120 on cleavage of pro-BDNF in HIV-1 clade B & C leading to HIV associated neurocognitive disorders (HAND)

Allen C1, Arjona S1, Santerre M1, Sawaya B2
1Temple University, Philadelphia, United States

Background: HIV-1 associated neurocognitive disorders (HAND) exhibit neurocognitive impairments such as memory loss and learning difficulty. HAND remains an unsolved problem in the clinical management of HIV-1 patients because existing therapies do not prevent these impairments. Interestingly, HIV-1 sub-types contribute to HAND differently, for instance clade B, which is primarily found in North America and Europe, has a higher propensity for developing HAND than clade C, which is found elsewhere. This difference was attributed to the response of cellular factors such as Brain-derived neurotrophic factor (BDNF).

BDNF is essential for neuronal plasticity and is usually found in abundance in healthy adult brains. Active BDNF protein is normally cleaved from pro-BDNF by the protease Furin. While BDNF is associated with neuronal protection and healthy neurons through the CREB signaling pathway, pro-BDNF elicits the opposite effect through the ICER signaling pathway. Previous studies have shown that HIV-1 protein gp120 can reduce the expression of BDNF and may contribute to the development of HAND. Thus, we hypothesize that there is a blockage of cleavage of pro-BDNF with gp120 exposure. This blockage of cleavage results in pro-BDNF accumulation and a subsequent increase in ICER. The leads to long-term depression (LTD) of neurons ultimately resulting in neurocognitive decline. We also hypothesize that the increase in pro-BDNF is greater with clade B gp120 when compared to clade C gp120 and is partially responsible for the increased incidence of HAND in clade B-positive patients.

Methods: Some HIV proteins, including gp120, have been proposed as contributors to HAND because they may be shed by infected cells and find their way across the blood-brain barrier. Further, the use of antibodies revealed the presence of gp120 in CSF shed by defective pro-viruses. Therefore, to study HAND in cell culture, we used gp120 protein from clade B and C. Using SH-SY5Y cells which we dosed with 100ng/ml of HIV gp120 clade B and clade C proteins, we measured mRNA and protein levels through qPCR and western blotting respectively.

Results: Here we show that there is a reduction of CREB signaling with exposure to HIV gp120. This decrease of CREB also corresponds to a decrease in BDNF mRNA. We also show an increase in ICER expression in clade B gp120 treated cells when compared to control and clade C gp120 treated cells. We also show an increase in pro-BDNF in clade B vs control and clade C treated cells.

Conclusions: In conclusion clade B gp120 causes an increase in pro-BDNF through blockage of cleavage and this increase in pro-BDNF results in an increase in ICER. This increase of ICER contributes to the development and progression of HAND in clade B patients. In the future we will explore what is responsible for the blockage in cleavage of pro-BDNF as well as transcriptional targets of ICER and CREB after exposure to gp120 clade B and C.
CMV and aging revisited: relationship of CMV IgG titers with age, HIV infection, inflammation, immune activation and influenza vaccine antibody responses.

Pallikkuth S1, de Armas L1, Rinaldi S1, Nagalla K1, Roach M1, Pan L, Pahwa R1, Pahwa S1

1University of Miami, Miami, United States

Background: Coinfection with CMV has been implicated in immunosenescence with aging, and all-cause mortality in the general population and with immune activation, non-AIDS comorbidities and accelerated disease progression in virally suppressed HIV infected (HIV+) individuals. However, the role of CMV in immune dysfunction in HIV and aging is controversial and poorly studied.

Methods: In this study, 172 virologically controlled HIV+ and 173 age-matched HIV uninfected (HIV−) volunteers were grouped by age as young (<40 yrs), middle aged (40-59 yrs) and old (≥60 yrs). Participants were administered seasonal trivalent influenza vaccine (TIV). CMV IgG titers, inflammation/immune activation, immune cell phenotypes, and vaccine responses were investigated. Data were analyzed by Mann-Whitney test or by one way ANOVA and correlation analysis by Spearman correlation.

Results: Mean CMV IgG titers determined in plasma by ELISA at baseline (pre-vaccination), were significantly higher (P <0.0001) in the HIV+ (28,067 ±41,831 IU/ml) compared to HIV- (10,434 ±13,859 IU/ml) participants and correlated with age only in HIV+ (r=0.32; p<0.0001). HIV- did not show any differences in the CMV IgG titers between young, middle aged and old groups. In HIV+, significantly higher titers were noted in middle aged (37,801 ±59,441 IU/ml) and old (27,402 ±23,790 IU/ml) compared to young (15518 ± 20,815 IU/ml) and were also higher compared to respective HIV- age groups except in the young. No relationship was evident between CMV IgG titers and antibody response to influenza H1N1, H3N2 and B antigens at 28 days post-vaccination in either HIV+ or HIV-. As expected, CMV titers did however correlate with pre-vaccination frequencies of CD4 T cell effector memory and effector subsets in both HIV+ and HIV- while an inverse correlation only in HIV+ was noted with naïve CD4, central memory CD4 and peripheral T follicular helper cells identified by Flow cytometry. In the CD8 compartment, naïve CD8 showed an inverse correlation while effector CD8 T cells showed a direct correlation with CMV titers in both groups. Analysis of CD8 immunosenescence phenotype based on the expression of CD28 and CD57 showed that in HIV-CD28+CD57- phenotype inversely correlated while in HIV+, CD28-CD57+ phenotype directly correlated with CMV titers. Plasma levels of monocyte activation marker sCD163, soluble activation marker TNFRI and intestinal fatty acid binding protein (IFABP) measured by ELISA directly correlated with CMV IgG titers in HIV+. Expression of immune activation markers HLA-DR and HLA-DR+CD38 on CD4 and CD8 T cells at pre-vaccination directly correlated with titers only in HIV+ group. Frequencies of CD56hiCD16neg NK cells inversely correlated while inflammatory monocytes directly correlated with titers in HIV+.

Conclusion: Our data support an association between CMV IgG responses with age, immune activation in HIV+ group but not in HIV- group, the common features in the two groups being altered T cell subsets distribution. A key finding was the lack of association between CMV titers and HAI response to flu vaccination in both HIV+ and HIV-. Further investigations are ongoing to understand the impact of CMV on immune responses in aging.
Flow cytometric analysis of lysosomal cathepsin B and cystatins in PBMCs from people living with HIV

Moylan D1, Sabbaj S1, Robertson K2, Taiwo B3, Overton E1, Cutter G4, Heath S1, Shacka J5

1Division of Infectious Diseases, Department of Medicine, UAB, Birmingham, AL, United States, 2Department of Neurology, University of North Carolina, Chapel Hill, Chapel Hill, NC, United States, 3Feinberg School of Medicine, Northwestern Univ., Chicago, IL, United States, 4Department of Biostatistics, UAB, Birmingham, AL, United States, 5Department of Pharmacology & Toxicology, UAB, , United States

Background: The average age of chronically infected people living with HIV (PLWH) continues to increase with successful antiretroviral (ART) therapy. Related to this increase is a higher prevalence in aging-related co-morbidities, including a large (>50) percentage of PLWH with HIV-associated neurocognitive disorder (HAND). Our lab is interested in identifying and validating biomarkers that predict disease and disease progression in the setting of HIV infection and their potential targeting to prevent progression. Recent evidence suggests the autophagy-lysosome pathway (ALP) is altered in HIV. In particular, significant changes in lysosomal cathepsin B, a cysteine protease, and cystatin B and C, endogenous inhibitors of cathepsin B, were observed previously in blood of PLWH with HIV-associated dementia (HAD) compared to cognitively normal PLWH (Cantres-Rosario et al., 2013). However, these markers have not yet been evaluated in peripheral blood mononuclear cells (PBMCs) of PLWH with mild neurocognitive disorder (MND), a more prevalent classification of HAND. Thus, we set out to determine if levels of cathepsin B, cystatin B and cystatin C were altered in T cells of PLWH compared to healthy controls; if they were further altered with MND; and if these levels were also influenced by a subsequent 48 week course of ART.

Materials & Methods: Archived PBMCs from the ACTG 5303 study (Robertson et al. 2016) were obtained from the following HIV-positive groups: cognitively normal participants before 1) and 2) 48 weeks after ART; participants with MND, 3) before and 4) 48 weeks after ART. PBMCs from healthy controls (HC) were obtained from a separate study. Levels of intracellular cathepsin B, cystatin B and C were determined for CD4+ T cells and CD8+ T cells using polychromatic flow cytometry (18-24 participants/group). Comparisons between groups were assessed using non-parametric statistics. Significant differences between groups were determined a priori as p <0.05.

Results: Cystatin B levels were significantly higher in CD4+ and CD8+ T cells of cognitively normal PLWH compared to HCs. These differences remained significant in PLWH with MND compared to HCs. However, this effect was not observed after ART in PLWH with MND. In addition, levels of cathepsin B levels were found to be significantly lower in CD8+ T cells of PLWH exhibiting MND compared to HC. Furthermore, no changes in cystatin C levels were observed.

Conclusions: These findings suggest T cell levels of cystatin B may be useful for predicting HIV and its progression, potentially in the setting of HAND. This study also highlights the therapeutic potential to target the ALP for treating age-related comorbidities such as cognitive decline, in the setting of controlled HIV infection.
TGF-β is lower in HIV infected immune non-responders and is negatively associated with T cell markers of exhaustion and senescence independent of age

Shive C1,2, Kowal C1, Rodriguez B1,3, Lederman M1,3, Anthony D1,2
1Cleveland VA Medical Center, Cleveland, United States, 2Case Western Reserve University, Cleveland, United States, 3University Hospitals, Cleveland, United States

Background: Antiretroviral therapy (ART)-treated, HIV-infected immune non-responders have undetectable levels of virus on ART, yet fail to adequately reconstitute their CD4 T cell numbers. This condition is associated with being male, white and older. Many comorbidities and elevated soluble inflammatory markers are similar among HIV-infected immune non-responders and the elderly. Because immune non-response in controlled HIV infection is associated with age, it is important to understand which immune parameters are age driven and which are attributable to HIV infection and non-responder status.

Material & Methods: We compared immune parameters of young (<50 years old) HIV-infected immune non-responders (<350 CD4 T cells/μL) and immune responders (>500 CD4 T cells/μL) who had been on ART for at least 2 years, and uninfected elderly (>65 years old) and young (<50 years old) participants. Plasma levels of cytokines and soluble receptors (IL-6, IP10, sCD14, sCD163, TGF-β) were measured by ELISA and T cell subset expression of exhaustion and senescence markers (PD-1, CD57, KLRG-1, TIGIT) were examined by flow cytometry. Differences across groups were compared by Kruskal Wallis tests, differences between individual groups were examined via Mann-Whitney U-tests, and associations between plasma markers and T cell exhaustion/senescence markers were examined using Spearman’s rank order method.

Results: Plasma levels of IL-6, IP10, sCD14, and TGF-β were elevated in treated HIV-infected patients compared to plasma levels in uninfected young participants. IP10 and sCD14 were elevated in plasma of young HIV-infected immune non-responders compared to immune responders (p = 0.028, p = 0.043 respectively) but IL-6 was not. TGF-β levels were elevated in treated HIV infection compared to uninfected groups; however, they were significantly lower in young immune non-responders compared to immune responders (p = 0.0004). Plasma levels of TGF-β were negatively associated with CD4 expression of CD57, PD-1, and TIGIT and with CD8 expression of TIGIT in the ART-treated HIV-infected groups.

Conclusions: Lower plasma levels of the immune regulatory cytokine TGF-β were observed in HIV-infected immune non-responders at an early age and may be an indication of deficiencies in immune regulation associated with the non-responder phenotype. Although plasma levels of IL-6 are strongly associated with morbidity and mortality in HIV disease, plasma levels were not significantly elevated in young HIV-infected immune non-responders compared to responders and IL-6 levels were significantly higher in uninfected elderly patients compared with HIV-infected young patients, consistent with a primarily age driven phenotype. Our results indicate that further attention on the role of immune regulation in HIV-infected immune non-responders is warranted.
Senescence-associated beta-galactosidase activity and other markers of senescence in human peripheral blood immune cells during healthy aging and HIV-Infection

Dewald H1, Martinez-Zamudio R2, Vasilopoulos T1, Swaminathan S1, Herbig U2, Fitzgerald-Bocarsly P1

1Rutgers New Jersey Medical School Department of Pathology, Immunology, and Laboratory Medicine, Newark, United States, 2Rutgers New Jersey Medical School Department of Microbiology, Biochemistry And Molecular Genetics, Newark, United States, 3Rutgers New Jersey Medical School Department of Medicine, Newark, United States

Aging is associated with a decline in immune system performance termed “immunosenescence” which leads to less robust immune responses including decreased cytokine production and simulation of the adaptive immune response. Cellular senescence is characterized by a persistent cellular growth arrest, a failure to respond to stimuli, and an overall loss of cellular function. However, whether immune cells undergo cellular senescence in vivo and whether cellular senescence plays a role in immunosenescence remains controversial due to the lack of specific markers that can reliably identify these cells in peripheral blood. Freshly isolated human peripheral blood mononuclear cells from healthy younger (22-26 y.o.) and older (56-65 y.o.) donors were fluorescently labeled for senescence-associated β-Galactosidase (SA-βGal) activity, anti-CD3, and anti-CD8 and sorted using fluorescence-activated cell sorting. Blood was collected from HIV-infected donors following IRB approved protocol and labeled for SA-βGal activity. Flow cytometric analysis was utilized to identify CD14+ monocytes, CD3+ CD4+ T cells, and CD123+ BDCA2+ plasmacytoid dendritic cells (pDC). qRT-PCR was used to quantify p16INK4a and cytokine production and immunofluorescence microscopy was used to measure DNA damage response foci. We detected a significantly higher percentage of CD8+ T cells with high SA-βGal activity in the older vs. younger cohort. CD8+ T cells that were sorted for high SA-βGal activity displayed characteristics of senescent cells, including increased levels of transcripts for GLB1, p21, p16INK4a, and inflammatory cytokines. Additionally, analysis of sorted SA-βGal positive and negative CD8+ T cells by immunofluorescence microscopy revealed that SA-βGal positive cells displayed significantly greater numbers of DNA damage response foci and p16INK4a protein levels. SA-βGal activity was also increased in CD8+ T cells, CD4+ T cells, monocytes, and pDC from an older, HIV-infected donor. Older individuals display increased in SA-βGal activity in several blood immune cell populations, most consistently in CD8+ T cells. Additionally, we observed increase SA-βGal activity in CD8+ T cells, CD4+ T cells, monocytes, and pDC from an HIV-infected donor. This indicates that HIV infection can induce cellular senescence in several immune populations. Sorting cells based on high SA-βGal activity allowed us to further characterize these cells for other senescence markers. The presence of p16INK4a and nuclear DNA damage response foci, which indicate double stranded DNA breaks or telomere dysfunction, along with the production of inflammatory cytokines clearly demonstrate that SA-βGal activity is a strong indication of cellular senescence in blood immune cells. SA-βGal activity can be leveraged to further identify senescent immune cells and elucidate cellular senescence’s role in immunosenescence. Understanding this connection and how it contributes to the decline in immune response seen in healthy aging will further our understanding of premature aging and early onset aging-associated comorbidities seen in HIV infection.
Soluble inflammatory markers correlate with VACS risk index scores among HIV infected older adults on suppressive antiretroviral therapy

Premeaux T1, Hosaka K1, Therrien N1, Greene M2, Javandel S2, Allen I2, Corley M3, Valcour V4, Ndhlovu L1

1University Of Hawaii, Honolulu, United States, 2University of California San Francisco, San Francisco, United States

Background: The prevalence of age-related comorbidities is increased in people living with HIV even despite being well controlled on antiretroviral therapy (ART). Persistent immune activation and inflammation may play pivotal roles, however, the burden of morbidities and the extent of this link among an older HIV infected population may be exacerbated.

Material & Methods: In a cross sectional study comprised of 45 participants from the San Francisco HIV Elders Study, we examined for associations between 14 inflammatory mediators, measured by Luminex or ELISA, and the Veterans Aging Cohort Study (VACS) Index, a predictor of multimorbidity and mortality, and the individual VACS components (age, CD4 count, hemoglobin, Fibrosis-4 [FIB-4] score, estimated glomerular filtration rate [eGFR], and hepatitis C virus infection) by linear regression analysis and unpaired t-tests for continuous and categorical variables, respectively.

Results: All HIV-infected participants were virally suppressed (<50 HIV copies/mL), on ART, 60 years or older, and primarily white (86.7%) males (91.1%). Plasma levels of monocyte and macrophage activation markers (neopterin, sCD163, sCD14, and MCP-1) and glycan binding immunomodulatory proteins (galectin (Gal)-1, Gal-3, and Gal-9) were assessed, including inflammatory biomarkers previously linked to the VACS Index (CRP, Cystatin C, TNF-α, TNFRI, IL-6, and D-Dimer) for comparison. In regression analysis, neopterin correlated with the VACS index in models unadjusted (β = 0.41; p = 0.006) and adjusted for estimated duration of infection (EDI; β = 0.45; p = 0.003). Upon analysis of individual VACS components, we observed neopterin associations with age (β = 0.49; p = 0.001), CD4 count (β = -0.40; p = 0.008), and eGFR (β = -0.49; p = 0.001). Gal-9 also correlated with VACS index scores in models unadjusted (β = 0.37; p = 0.014) and adjusted for EDI (β = 0.41; p = 0.008), and this correlation was primarily driven by associations with FIB-4 (β = 0.34; p = 0.024) and eGFR (β = -0.47; p = 0.001). As expected, Cystatin C, TNF-α, and TNFRI were associated with VACS index scores, as well as a trend with D-Dimer. A direct interaction between neopterin and Gal-9 was noted (p < 0.001) and multiple associations among several plasma markers were observed, including neopterin levels positively associating with IP-10, Cystatin C, TNF-α, and TNFRI (p < 0.05), as well as Gal-9 levels positively associating with IP-10, Gal-1, CRP, Cystatin C, IL-6, TNF-α and TNFRI (p < 0.05).

Conclusions: Both galectin-9 and neopterin independently emerged as additional plasma markers that can potentially assist in differentiating multimorbidity and mortality risk in older HIV-infected individuals on suppressive ART, but more importantly, also serve as novel mediators in understanding the pathogenic mechanisms of these age-related disorders.
The effects of aging and HIV infection on the function of dectin-1, an innate immune receptor for the recognition of fungal organisms

Zapata H1, Vander Wyk B2, Allore H2, Bakarat L3, Shaw A1
1Yale School of Medicine, Section of Infectious Diseases, Department of Internal Medicine, New Haven, United States, 2Yale University Program on Aging, United States, 3Yale University, Yale AIDS Care Program, United States

Dectin-1 is a pattern recognition receptor that recognizes and binds \(-\text{1,3/1,6-}\) glucans, a component of the fungal cell wall, and is primarily expressed on myeloid cells, including: dendritic cells, and monocytes. Through the recognition of \(-\text{glucans, Dectin-1 can recognize several human pathogens, including; Aspergillus, Candida, Coccidioides, and Pneumocystis. Invasive fungal infections in humans carry unacceptably high rates of mortality that can exceed 50% despite our current anti-fungal drugs. Older adults are at increased risk for invasive fungal infections due to increased risk of developing malignancies, increased need of organ/bone marrow transplantation, and increased underlying co-morbidities. HIV infected individuals are at the highest risk of invasive fungal infections when CD4 counts are below 200, with decreasing rates at higher CD4 counts, although still a concern for people living with HIV/AIDS. With the advent of effective antiretroviral regimens, HIV-infected adults are living longer, reaching normal life expectancies and consequently facing the maladies of advancing age. Therefore, we examined Dectin-1 function in a cohort of HIV-infected and uninfected young (21-35 yrs) and older adults (>60 yrs). Most of the HIV-infected cohort were on antiretroviral therapy (ART), and had CD4 counts >200/mm3. Peripheral blood mononuclear cells (PBMCs) were isolated from blood, and stimulated with whole glucan particles (1,3/1,6-\(-\text{-glucan). Cells were then surface stained for monocyte and dendritic cell markers, and intracellular cytokines and then analyzed using multi-color flow cytometry. We determined intracellular IL-10, IL-12, IL-6 and TNF-\(\alpha\) production in classical (CD14+CD16lo), inflammatory (CD14+CD16+), activated (CD11b+CD14+) and non-classical monocytes (CD14+CD16hi) monocytes. We also determined IFN-\(\alpha\), TNF-\(\alpha\), IL-12, and IL-6 production in both myeloid and plasmacytoid dendritic cells (mDC and pDC). Overall, we found both age and HIV-associated differences in the inflammatory response in both monocytes and dendritic cells. However, the HIV-associated differences were more consistent and prominent in all monocyte and dendritic cell subsets. Specifically, HIV-infected individuals consistently produced more IL-12 and TNF-\(\alpha\) in all monocyte subsets with Dectin-1 stimulation than HIV-negative age matched counterparts. Differences in IL-10 and IL-6 production were also noted that were individual to monocyte subset. When we looked at the single cell level (assessed by Boolean gating) we also noted that monocytes from HIV-infected individuals we more inclined to produce multiple cytokines than monocytes from HIV-negative individuals. When myeloid dendritic cells were examined, both older adults and HIV-infected individuals produced more IFN-\(\alpha\), TNF-\(\alpha\), and IL-12 in response to Dectin-1 stimulation. Plasmacytoid dendritic cells were notable for only showing increased production of IFN-\(\alpha\), TNF-\(\alpha\), IL-12 in the setting of HIV-infection. Dectin-1 surface expression (via Mean Fluorescence Intensity) was significantly higher in both older adults and HIV-infected individuals in inflammatory, classical and activated monocytes. Dectin-1 surface expression in both mDCs and pDCs was only significantly elevated in HIV-infected individuals. Clinical variables of gender, race, smoking, drug use, and co-morbidities such as diabetes were also collected for each subject and included in the analysis. Overall, these findings provide insight into the host response to fungal organisms in the setting of aging and HIV-infected population.

Presented at the International Workshop on HIV & Aging 2019

Material is strictly view only
Role of autophagy in premature immune aging during HIV infection

Mu W1, Hamid P1, Rezek V1, Martin H1, Zhen A1
1University of California, Los Angeles, Los Angeles, United States

Cellular immune responses play a crucial role in controlling viral replication in HIV-infected individuals. However, chronic immune activation drives the pathogenesis of HIV-1 infection, leading to loss of CD4+ T cells and exhaustion and senescence of antiviral cellular immunity, which is characterized by poor anti-viral responses against HIV. Using the humanized bone-marrow-liver-thymus (BLT) mouse model of HIV infection, a small animal model that recapitulates HIV immunopathogenesis, we previously demonstrated that blocking persistent type I interferon (type I IFN) receptor signal during chronic HIV infection can significantly reduce chronic inflammation and improve anti-viral T cell responses, resulting in lower viral loads in vivo. When combined with combination anti-retroviral therapy (cART), type I IFN receptor blockade therapy also accelerates viral decline and reduces latent HIV reservoirs. These findings illustrate the connection between chronic inflammation and T cell immune dysfunction during HIV infection. However, as type I IFNs are key regulators for antiviral immune responses, blocking interferon receptor to all type I IFNs may have unwanted consequences. Therefore, additional study for safer and more specific drugs to curb chronic inflammation is necessary.

Autophagy is a homeostatic mechanism that is involved in the disposal of damaged cellular organelles and the elimination of intracellular pathogens. It is a key quality control mechanism for cellular homeostasis and it is coupled to cellular senescence. Interestingly, it is also intricately involved in T cell function and it is impaired during HIV infection. Here we report that autophagy inducers rapamycin and spermidine can curb inflammation by down-regulating STING-activated type I interferon signaling in macrophages. In addition, treatment with rapamycin and spermidine improved proinflammatory cytokine production and killing activity of in vitro cultured anti-HIV T cells. More importantly, we found that in vivo treatment of spermidine in HIV infected humanized BLT can significantly reduce persistent immune activation, lower expression of exhaustion markers on T cells, improve T cell responses, and lower viral load during chronic HIV infection. Our data suggests that therapeutically targeting autophagy may be used to treat persistent immune activation and improve immune control of HIV replication.
Poorer muscle quality and quantity with ART initiation is associated with greater inflammation and immune activation

ERLANDSON K1, Moser C2, Olefsky M2, Brown T3, Currier J4, McComsey G5, Scherzinger A1, Stein J6, Lake J7

1University of Colorado Denver, Aurora, United States, 2Harvard T.H. Chan School of Public Health, Boston, United States, 3Johns Hopkins University, Baltimore, United States, 4University of California Los Angeles, Los Angeles, United States, 5Case Western Reserve University, Cleveland, United States, 6University of Wisconsin, Madison, United States, 7University of Texas Health Sciences Center at Houston, Houston, United States

Background: People with HIV (PWH) tend to experience a greater burden of physical function impairment, suggesting impairment in muscle quality. Fat accumulation within skeletal muscle, as determined by the density on computed tomography (CT) scan, is strongly linked to physical function impairments in populations both with and without HIV. We have previously shown that initiation of antiretroviral therapy is also associated with both a decrease in skeletal muscle density (greater fat accumulation) and an increase in total fat (includes fat surrounding the muscle) but not the lean component of skeletal muscle area. These findings suggest that gains in lean body mass seen in many ART studies may reflect gains in low quality, fatty muscle. Here we focus on the psoas muscle and explore the link between fat accumulation and markers of inflammation and immune activation.

Methods: AIDS Clinical Trials Group A5260s, a cardiometabolic sub-study of A5257, randomized ART-naïve PWH to raltegravir or ritonavir-boosted atazanavir or darunavir, each with tenofovir disoproxil fumarate/emtricitabine. Single-slice abdominal CT scans from baseline and week 96 were re-analyzed for total psoas density and lean psoas area. We compared baseline and week 96 muscle density and area and % change to levels of circulating markers of inflammation (IL-6, hs-CRP) and immune activation (sCD14, sCD163, %CD38+HLADR+ on CD4+ or CD8+ T-cells) using Spearman’s correlations. Analyses were limited to participants with virologic suppression who remained on their randomized ART at 24 weeks and beyond.

Results: Of 328 participants, 222 had available inflammation/ immune activation markers and paired CT scans and that could be re-read for muscle endpoints. The majority of participants were male (90%) with a median age 36 (IQR 28-45) years and BMI 24.5 kg/m2 (22.3-27.8); 44% were white; 30% black and 21% Hispanic. At baseline, lower total psoas density (greater fat) correlated with higher IL-6 (r -0.26, p<0.001) and sCD163 (r -0.15, p=0.03) concentrations. Lower baseline lean psoas area correlated with higher IL-6 (r -0.30), hs-CRP (-0.13), sCD14 (r -0.26), sCD163 (r -0.18), and %CD38+HLADR+ on CD4+ T-cells (r -0.18; all p<0.05). Between baseline and week 96, small decreases in total psoas density (media -1.34 [-6.15, 3.04]) and increases in lean psoas area (0.18 [-6.04, 6.84]) were seen. At week 96, lower total psoas density correlated with higher IL-6 (r -0.24), hs-CRP (r -0.28; both p<0.001), and weakly with sCD163 (r -0.12; p=0.07); lean psoas area correlated with hs-CRP (r-0.15; p=0.03). Greater % decrease in total psoas density (more fat) correlated with greater increase in IL-6 (r -0.14; p=0.04); greater % decrease in lean psoas area correlated greater increase in IL-6, sCD14, sCD163, and %CD38+HLADR+ on CD8+ T-cells (r -0.15 to -0.18; all p<0.04).

Discussion: Greater fat infiltration within the psoas muscle (lower density) and greater loss in lean psoas muscle was associated with higher inflammation and immune activation, which may portend important effects on muscle function and cardiometabolic risk.
The behavioral and biological effects of electronic cigarette provision in HIV-positive smokers who are not motivated to quit

Cioe P1, Lechner W2, Tidey J1, Kahler C1
1Brown University School Of Public Health, Providence, United States, 2Kent State University, Kent, United States

Introduction: People living with HIV (PLWH) smoke at higher rates and suffer significantly more smoking-related morbidity and mortality compared with the general population of smokers. Past studies have shown that smoking cessation rates are substantially lower among PLWH and some HIV-positive smokers report ambivalence about quitting. Switching to electronic cigarettes (ECs) may be a viable option for smokers who are unable or unwilling to quit smoking combustible cigarettes (CCs). The purpose of this open pilot study was to examine the acceptability and health-related effects of ECs in HIV-positive smokers who were not seeking smoking cessation treatment.

Methods: Twenty HIV-positive adult smokers were recruited from two HIV clinics in the Northeastern U.S. Following a baseline (BL) visit in which assessments were obtained and ECs were provided, each participant was seen for 8 weekly visits in which self-report and biological assessments were obtained. E-liquid was provided weekly and participants were encouraged to use the EC whenever they would normally smoke a cigarette. Blood specimens were obtained at baseline and week 8; sCD14, hs-CRP, IL-6, D-dimer, and sCD163 levels were measured. Follow-up assessments were obtained at week 12.

Results: At BL, all participants were stable on antiretroviral therapy, 17 (85%) had an undetectable HIV viral load), 6 (30%) were female, mean age 52.7 (SD 9.3), mean duration of years living with HIV 21.1 (SD 10.2), mean FTCD = 5.7 (SD 2.2). At week 8, cigarettes per day (CPD) was reduced by more than 80% from 15.1 (SD 9.6) at BL to 1.79 (SD 2.2) at week 8, and remained significantly lower at week 12 (M=6.74, SD=3.89), p<.001). Cigarette dependence scores and respiratory symptoms (such as coughing and wheezing) reduced significantly, while intention to quit increased significantly over time. At week 8, perceived benefits related to EC use remained high and harms remained low, showing stability over time. The means of two biomarkers of inflammation (hs-CRP, sCD163) were lower at week 8 than at baseline; however, these changes were not statistically significant. The linear effect of time was not a significant predictor of cigarettes smoked per day or biologically verified abstinence from smoking.

Conclusions: These results suggest that switching from combustible cigarettes to ECs in daily HIV-positive smokers is feasible and acceptable. Beneficial effects were seen such as reduced toxicant exposure (CO), reduced CC use and dependence, and increased motivation to quit. The linear effect of time was not a significant predictor of reduced smoking or abstinence; it appears that smoking reductions occurred soon after e-cigarette provision and remained stable over time. ECs may be promising as a harm reduction approach, reducing exposure to carbon monoxide among smokers who are unable to quit, and increasing motivation to quit among non-treatment-seeking smokers with HIV.
Characteristics associated with exercise adherence in the setting of a supervised intervention

Abdo M1, MaWhinney S1, Wilson M1, Jankowski C1, Erlandson K1
1University of Colorado Denver, Aurora, United States

Background: We have previously shown that exercise is an effective intervention to reverse impairments in physical function among older people with HIV (PWH). Despite the known benefits of exercise, however, long-term adherence remains low. Here we explored factors associated with adherence to exercise within the setting of a 24-week exercise intervention.

Methods: Sedentary adults (50-75 years) with or without HIV enrolled in a 24-week supervised endurance/resistance exercise intervention. PWH had suppressed HIV-1 RNA for ≥ 2 years. After 12 weeks of moderate-intensity exercise, participants were randomized to continue moderate- or advance to high-intensity exercise for an additional 12 weeks. Adherence to the intervention was calculated as the number of attended exercise sessions divided by the number of expected exercise sessions. Linear regression models were used to determine the effect of baseline covariates (demographics, HIV characteristics among those with HIV, physical function/frailty, and comorbidity count, quality of life [SF-36], or depressive symptoms [CES-D]) on adherence; bivariate models were adjusted singly for age, BMI, and HIV status, as relevant.

Results: Among 32 PLWH and 37 controls, 27 PWH and 29 controls completed the intervention. The overall median adherence was 88% (IQR=74, 91) among PWH and 85% (67, 89) among controls. The mean age was 57.8 (SD 6.4) and BMI 28.7 (4.8), the majority of participants were male (91%), white (74%) and non-Hispanic (83%). Neither sex (females vs males) (β=-17.2%; 95% confidence interval -36.8, 2.5; p=0.09), HIV serostatus (3.4%; -8.0, 14.7; p=0.55), nor exercise intensity (moderate vs high) was significantly associated with adherence (3.1%; -3.1, 9.3; p=0.32). Each 5-year increase in age was associated with 6.0% (1.8, 10.3; p=0.006) greater adherence, which remained significant after adjusting for HIV serostatus (6.4%; 2.1, 10.6; p=0.004) or BMI (5.4%; 1.5, 9.3; p=0.008). Each 1 unit greater BMI was associated with 1.9% lower adherence (-3.0, -0.8; p<0.001), and remained significant after adjusting for age and HIV serostatus (-1.7%; -2.8, -0.6; p=0.003). Similarly, for every 10 pound increase in body weight since high school, adherence decreased by 2.7% (-4.5, -0.9; p=0.004). Race/ethnicity, baseline physical function, quality of life by SF-36, depressive symptoms, HIV characteristics, comorbidity burden, or use of antidepressants or antihypertensives were not significantly associated with adherence. In contrast, participants on antipsychotic medications had 20% lower adherence compared to nonusers (-38.6, -2.3; p=0.028), with a greater difference after adjusting for HIV serostatus (-25.8%; -45.1, -6.6; p=0.009) but attenuated and no longer significant after adjusting for age (-15.6%, -33.5, 2.3; p=0.09).

Conclusions: PWH of older age and lower BMI are more likely to adhere to an exercise intervention. Additional strategies are needed to better engage and promote adherence in other PWH that are at high risk of nonadherence but likely to benefit from regular exercise.
Chronic pain management and opioid reduction among adults living with HIV: an innovative physical therapy intervention

Pullen S1, del Rio C1,2, Marconi V1,2
1Emory University School of Medicine, Atlanta, United States, 2Emory University Rollins School of Public Health, Atlanta, United States

Background: People living with HIV (PLWH) may be at increased risk of experiencing both chronic pain and opioid dependence. Physical therapy (PT) has been shown to be effective as a non-pharmacological strategy for mitigating chronic pain in the general population, however, there is gap in research investigating PT to reduce both chronic pain and opioid use among PLWH. This pilot study examined the feasibility of an innovative PT intervention to decrease chronic pain and opioid use at a multidisciplinary HIV clinic.

Methods: Participants (n=4) were evaluated and given an individualized PT “package” comprised of manual therapy, exercise prescription, Transcutaneous Electrical Nerve Stimulation (TENS) and pain coping strategies. Pre- and post-intervention outcomes were measured using an original questionnaire created by the investigator as well as the Short-Form 36 (SF-36), the Brief Pain Inventory (BPI), the numerical (0-10) rating scale for pain, and morphine milliequivalents (MME), which calculates a standard value for different opioids.

Results: After the PT intervention, all participants reported pain improvement over five times the minimal clinically important difference for pain and a decrease in opioid use ranging from 60% to 100% reduction in MME. SF-36/quality of life scores showed a trend of improved health concepts in all eight health domains. A paired t-test showed a significant difference (<.05) in the pre-intervention and post-intervention pain scores and MME values.

Conclusion/implications: Results of this pilot study suggest that PT is a feasible approach to mitigating chronic pain and reducing opioid use among PLWH.

Larger intervention studies to power for effectiveness should be conducted.
The relationship between high risk behavior and HIV testing among older adults

Alsen M1, Kelvin E1,2

1Department of Epidemiology and Biostatistics, CUNY Graduate School of Public Health and Health Policy, City University of New York, New York, United States, 2CUNY Institute for Implementation Science in Population Health, City University of New York, New York, United States

Background: Studies suggest that older adults are less likely to test for HIV compared to younger adults. This lower HIV testing rate could be related to less risk in this age group, but there is limited research on whether low risk behavior explains the lower testing rates among older adults, and in New York City (NYC), the proportion of people diagnosed with HIV concurrent with an AIDS diagnosis is highest among people age 50 and older, suggesting a need for some older adults to test more frequently.

Materials and Methods: Using data from the 2017 NYC Community Health Survey (CHS), we conducted logistic regression to examine the association between HIV testing and age, controlling for HIV risk behavior. We further assessed whether the association between HIV risk behavior and HIV testing differed by age by adding an interaction term for age*condomless sex at last sex and, if we found significant interaction, we stratified on age group to describe the direction of the effect modification.

Results: Adults over 50 years of age had 0.41 times lower odds of HIV testing in the past year compared to younger adults (p<0.001). There was significant interaction between age and condom use at last sex (p=0.026). When stratifying on age group, not using a condom at last sex was associated with a higher odds of HIV testing among those <50 (OR=1.2, p=0.09) that was of borderline significance, while there was no association between unprotected sex and HIV testing among those age 50+ (OR=1.0, p=0.957).

Conclusion: Adults age 50+ were less likely to test for HIV than their younger counterparts, and while condomless sex was associated with higher odds of HIV testing among younger adults, as would be expected, it was not associated with HIV testing among older adults. This suggests that risk behavior is not being appropriately assessed for making HIV testing decisions among older adults, which may explain the higher rates of late HIV diagnosis among older adults. Sexual health interventions targeting older adults to help them evaluate risk behavior that may warrant regular HIV testing are needed.
Evaluating the impact and feasibility of a yoga intervention on cognition and balance in people living with HIV: a randomized pilot trial

Quigley A1, O'Brien K1,4, Brouillette M5, MacKay-Lyons M5,7,8
1Department of Health, Dalhousie University, Halifax, Canada, 2Department of Physical Therapy, University of Toronto, Toronto, Canada, 3Rehabilitation Sciences Institute, University of Toronto, Toronto, Canada, 4Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto, Canada, 5Department of Psychiatry, McGill University, Montreal, Canada, 6Department of Physiotherapy, Dalhousie University, Halifax, Canada, 7Department of Medicine, Dalhousie University, Halifax, Canada, 8Nova Scotia Health Authority, Halifax, Canada

Background: People living with HIV (PLWH) are experiencing high rates of cognitive and balance impairments. This is the first randomized controlled trial (RCT) to evaluate the feasibility and impact of a yoga intervention on cognitive and physical function among PLWH.

Objectives: The main purpose of this pilot RCT was to assess the feasibility of participant recruitment and assessments, as well as satisfaction with a 12-week yoga intervention in order to inform future RCTs. Secondary objectives were to evaluate change among PLWH in cognition, balance, walking speed, mood, medication adherence, physical activity, and quality of life in the yoga group compared to controls.

Methods: We recruited 22 PLWH aged ≥35 years from community and health organizations in Halifax, Canada. Assessments were conducted at baseline and 12 weeks by blinded assessors and included demographics, a computerized cognition measure [the Brief Cognitive Ability Measure (B-CAM)], an HIV-specific self-reported cognitive questionnaire [(the Communicating Cognitive Concerns Questionnaire (C3Q)], the Community Balance and Mobility Scale (CB&M), the 10-metre walk test, the Rapid Assessment of Physical Activity, Accelerometer data (Fitbit™), the Simplified Medication Adherence Questionnaire, the Medical Outcomes Survey-HIV (MOS-HIV), and the Hospital Anxiety and Depression Scale. Following baseline assessment, participants were randomly assigned to the yoga (n=11) or control group (n=11) using a random computer generator. Yoga group participants engaged in supervised group-based Hatha classes for 60 minutes, 3 times weekly for 12 weeks at a yoga studio. Control group participants were instructed to maintain their physical activity levels. Feasibility outcomes [participant recruitment, attrition, attendance (a priori criterion was attendance at 70% of classes)] were recorded, and a post-participation questionnaire with Likert scale and open-ended questions measured participant satisfaction. Secondary outcomes were analyzed with intention-to-treat methods using univariate and repeated-measures ANOVA with bootstrapped confidence intervals, Mann-Whitney, and Wilcoxon Signed Rank tests and an alpha of .05.

Results: The recruitment rate was .96 (22 participants recruited/23 months) and 22 of 29 (76%) participants approached by the study coordinator were successfully recruited. Two participants withdrew from the yoga group. Mean attendance to total yoga classes was 81.8% and 88.9% of participants in the yoga group were adherent to the intervention. All (100%) yoga participants enjoyed the sessions, 100% felt there was some benefit, 100% felt safe during the sessions, and 100% agreed or strongly agreed that they felt comfortable during the sessions. The two groups differed at baseline in age and B-CAM scores. The yoga intervention did not induce any significant within or between group differences in B-CAM (yoga group mean at post-test=22.27±4.38, mean change=.36±3.55; control post-test mean=18.22±5.69, mean change=1.97±4.29), C3Q (yoga post-test group mean=28.11±5.49, mean change=1.78±5.14; control post-test mean=25.45±7.24, mean change=2.27±11.19), or CB&M performance (yoga group post-test mean=73.67±27.05, mean change=1.2±7.46; control group mean= 64.64±18.26, mean change=5.18±9.91). There was a trend (p = .058) toward between-group differences in MOS-HIV social domain scores (yoga group mean at post-test=95.56±8.82, mean change=4.44±19.44; post-test control mean=78.18±24.42, mean change=1.82±27.5).

Conclusion: This 12-week yoga intervention was feasible as determined by participant recruitment, attendance, attrition, and satisfaction. The excellent adherence and low attrition rates observed in this study indicate that future large-scale RCTs evaluating cognitive and physical outcomes among PLWH could make power calculations with anticipated low attrition rates. We did not observe significant changes in cognitive or physical performance among 22 PLWH but the study was underpowered to detect change in these outcomes.
Development of an HIV-specific cardio-vascular health status measure

Mayo N, Scott S, Brouillette M, Fellows L, Durand M, Daskalopoulou S

1Research Institute of McGill University Health Centre, Montreal, Canada, 2 Montreal Neurological Institute, McGill University, Montreal, Canada, 3 Centre de recherche du Centre Hospitalier de l’Université de Montréal, Montreal, Canada

Background: Cardio-vascular (CV) “health” is typically measured using indicators of CV disease through imaging of the vascular bed or by estimating risk of CV events. Imaging is expensive and is usually only justified for people with clinical indications. The risk method is population-based using weights for each CV risk factor based on the estimated probability of a CV event and, thankfully, most people will not have an event. What is lacking in the field is a true measure of CV health yet many of the factors that indicate CV health are routinely available from tests made during the course of care.

Objective: The purpose of this study is to develop a method of measuring CV health by combining the results of biological and clinical measures routinely collected during clinical care of people with HIV.

Methods: Data were available from two Canadian cohorts: the Positive Brain Health Now (BHN) cohort (n=817; mean age 53 years; range: 35 to 81) and the Canadian HIV and Aging (CHIVA) cohort (n= 800 HIV+). The results from 13 tests and measures were available for up to 6 time points yielding 2544 observations for the BHN cohort and 2085 for the CHIVA cohort. The value for each test item was converted into 6-10 ordinal categories and Rasch analysis was used to test the extent to which each item fit a linear hierarchy that underlies the requirement for a true measure. Optimal measurement properties on the logit scale is mean 0 and standard deviation (SD) 1 with an optimal span from -4 to +4 logits. Here higher values indicate less optimal CV health status. The BHN cohort served as a test cohort and the CHIVA cohort served as a validation cohort.

Results: For the BHN cohort, 9 of the 13 items (BMI, waist-to-hip ratio, systolic BP, lipid total cholesterol, lipid triglycerides, total cholesterol to HDL ratio, blood fasting glucose, HbA1C, and CRP) fit the Rasch model with 3 to 5 response categories, yielding 26 thresholds for measurement. For the CHIVA cohort data on waist-to-hip ratio was not available so there were only 24 thresholds.

The hierarchy of the 8 matching items was similar for the two cohorts and the item locations ranged essentially from -3 to +3 logits. For both cohorts, people who were under or normal weight had the best CV health status, and people with body mass index ≥35 had poorest or close to poorest CV health status. Internal validation on the BHN cohort yielded the expected gradations for poorer CVD health for men compared to women, with increasing age, and with increasing risk of CVD events and metabolic syndrome.

Discussion: The method used here, Rasch Analysis, converted multiple (n=13) commonly used clinical measures of CV health into one value on a continuum. The results can be displayed as a ladder providing a useful clinical tool. The HIV-CV Health Status Measure could be used to evaluate the outcome of trials to reduce CV disease eliminating the need multiple correlated tests of CV disease.
A collaborative approach to develop a community based model of care to identify people living with HIV who may be at risk of developing HIV associated neurocognitive disorder.

Cummins D1, Crawford D

1Community Health, Sydney Local Health District, camperdown, Australia

Background: People living with HIV (PLHIV) may be at risk of developing HIV associated neurocognitive disorder, or HAND. The diagnosis of HAND is multifactorial and is often achieved by the exclusion of other medical conditions. PLHIV may experience signs and symptoms that can be mild, which they may attribute to other causes such as morbidity associated with ageing. Community based nursing and allied health professionals are well placed to observe changes in cognition and a person’s environment whilst providing care in the home; especially to those PLHIV who live alone or do not have the support of an informal caregiver.

Material & Methods: A mixed method study using semi structured interviews and a modified Delphi Method with four HIV specialist services to develop an initial and annual monitoring risk assessment tool. Additionally following an online quantitative survey two resources were developed in collaboration with a peer support HIV NGO.

Results: Several themes were identified following seven semi structured interviews with allied health professionals: how to identify signs and symptoms of HAND, the importance of communication and counselling regarding cognitive changes, changes in memory affecting adherence and medical monitoring, promoting new skills in PLHIV and the need for more education.

Over 80% consensus was reached with four community based HIV services following three rounds of the Delphi method. All panel experts had completed higher education and cared for PLHIV who had a diagnosis of HAND for up to 16 years. Key areas were identified to incorporate into both risk assessment tools to be developed. A flow chart was designed as a guide for community based staff: firstly initial screening by multidisciplinary staff with the outcome of screening being annual monitoring if no signs and symptoms of cognitive changes were identified or further assessment by the clinical nurse consultant and/or occupational therapist which would be provided to medical doctor for review with the PLHIV. The initial assessment tool was pilot tested to PLHIV by allied health members and completion of the tool took 20 minutes. Additionally during the assessment PLHIV would be provided with resources that were developed following an online survey with peer HIV NGO regarding HAND. Of the 126 eligible survey responses from across Australia, 94 (75%) had heard of HAND and 74 (59%) had noticed symptoms of HAND in themselves and in others. Forty-nine (39%) of respondents indicated that they would like further guidance to initiate discussion about HAND with their doctor, caregiver or other PLHIV. Collaboration of nursing and allied health professionals with peer HIV NGO has led to this model of care for community based professionals to identify those PLHIV at risk of developing HAND. A longitudinal study has been commenced using this model of care and assessment tools.

Conclusion: As PLHIV age they are at risk of developing HAND. Development of a model of care was an important strategy to be able to monitor and assess those at risk of developing HAND and arrange referral for formal assessment by their medical professional.

Presented at the International Workshop on HIV & Aging 2019

Material is strictly view only
The SAGE Clinic: The introduction of a new HIV frailty service at our London centre

Stafford A1, McClintock-Tiongco A1, Burns F1, Cope N1, Katiyar A1, Procter A1, Swaden L1, Williams J1, Barber T1
1Royal Free London NHS Trust, London, United Kingdom

Background: Recent work has identified 101 HIV positive patients over 70 years old who are known to our service. Of these, 50% were classified as “frail” on the Electronic Frailty Index, with 4% of patients having a “severe” frailty status.

In response to this ageing HIV population, our centre has introduced a dedicated HIV frailty service: The SAGE Clinic. This clinic provides joint clinical reviews with an HIV specialist and Elderly Care physician as well as input from occupational therapy, physiotherapy and HIV specialist pharmacists. With this multi-disciplinary team approach, we aim to provide a service which effectively tackles the biggest challenges seen amongst our ageing HIV population, namely multi-morbidity, polypharmacy and functional decline.

Patients can gain access to the clinic through onward referral from other clinicians based upon individual assessment of need. Our referral guidelines are: HIV positive, >50 years old and >1 co-morbidity or polypharmacy.

Methods: We are measuring baseline and 6-monthly outcomes in four main areas:

1. Improvement in the disability status and quality of life patients - this will be assessed using World Health Organization Quality of Life in HIV-infected Persons instrument (WHOQOL-HIV-BREF) and WHO Disability Assessment Schedule (WHODAS).
2. Improvement in patients’ mood (depression and/or anxiety) – this will be assessed using Patient Health Questionnaire-9 (PHQ-9) and Generalized Anxiety Disorder 7 (GAD-7).
3. Patient and staff satisfaction - this will be assessed using patient and staff retention, as well as satisfaction/acceptability questionnaires.

Results: Since the establishment of the SAGE Clinic in March 2019, we have seen a total of 15 patients – 12 male and 3 female, with a mean age 65 years (range 55-81). The mean number of co-morbidities per patient was 4 (range 1-8) and the mean number of medications the patient was receiving was 10 (range 3-19).

Baseline results:

WHODAS: No disability n=1, mild n=0, moderate n=2, severe n=3, extreme n=6. Mean 33.9 (n=12, range 0.375-87.5)

WHOQOL: Domain I “Physical” mean 11.6 (range 6-20); Domain II “Psychological” mean 11.8 (range 6.4-17.6); Domain III “Level of Independence” mean 10.9 (range 5-20); Domain IV “Social Relationships” 13.4 (range 6-17), Domain V “Environment” mean 13.4 (range 7.5-17.5); Domain VI “Spirituality/Religion/Personal Beliefs” mean 14.6 (range 9-19).

PHQ-9: Minimal symptoms n=4, mild depression n=0, moderate n=4, moderately severe n=3, severe n=2. Mean 11.5 (n=13, range 3-23).

GAD-7: No anxiety n=5, mild anxiety n=5, moderate n=1, severe n=2. Mean 6.4 (n=13, range 0-16)

Conclusion: The vast majority (92%) of patients had at least moderate disability at presentation to the clinic, with 50% scoring as “severe”. In addition, the majority of the patients have a baseline mood disorder, with 15% of patients exhibiting severe depression and 15% severe anxiety. Preliminary results have shown that therapies have had the biggest impact on patients. Data collection is still ongoing, but we hope this clinic will help improve the care of ageing HIV patients within our centre, and may provide data that helps support introduction of similar services at other centres.
Frailty index (FI) and age predict neurocognitive functioning in a real life large prospective HIV+ cohort

Mille J1, Corni M1, Bardi E1, Venuta M1, Malagoli A1, Carli F1, Franconi T1, Mussini C1, Bloch M1, Cysique L4,5, Guaraldi G1

1Modena HIV Metabolic Clinic, University of Modena and Reggio Emilia, Modena, Italy, 2Clinical and Experimental Medicine PhD Program, University of Modena and Reggio Emilia, Modena, Italy, Modena, Italia, 3Holdsworth House Medical Practice, Sydney, NSW, Australia, Sydney, Australia, 4Neuroscience Research Australia, Randwick, Sydney, Australia, 5School of Medical Sciences, UNSW Medicine, UNSW Sydney, Sydney, Australia

Background: Frailty has been associated with neurocognitive impairment (NCI) in cross-sectional studies. It is unclear whether frailty is predictive of neurocognitive function (NF) in aging HIV+ patients who are otherwise clinically stable. We aimed to evaluate in a large prospective HIV+ cohort the association between baseline frailty and NF at 12 months.

Methods: Consecutive people living with HIV (PLWH) ≥50yrs attending Modena HIV Metabolic Clinic were assessed for NF at baseline and follow-up using the computerized CogState battery comprising 6 domains: simple speed processing, complex speed processing, attention/working memory, visual learning/memory, verbal learning, verbal memory. Each individual CogState raw score was transformed into z-score correcting for age and gender. A global NF performance score was defined as the mean of z-score by averaging individual task z-scores. Normal, mild and moderate/severe impairment was defined according to the global deficit score (GDS) method. Frailty was assessed by 67-item frailty index (FI) generated by a standardized comprehensive geriatric assessment. Multivariable logistic regression model was used to assess the relationship between baseline frailty and NF at follow-up.

Results: Total 761 PLWH were included, median age 57 years, 74% males. All tasks except verbal memory and simple speed processing showed improvement at follow-up (p<0.05). Baseline NF was described as normal in 631 (82.9%) patients, mildly impaired in 52 (6.8%) and moderate-severely impaired in 78 (10.3%). Follow up NF was normal in 646 (84.8%) patients, mildly impaired in 50 (6.6%) and moderate-severely impaired in 66 (8.7%). GDS improvement was observed in 75 (9.9%), GDS worsening 34 (5.6%), while 635 (83.5%) remained normal out of 761 patients. CDC HIV classification, nadir CD4 count and current CD4/CD8 ratio were not associated with NF. FI and GDS score were linearly associated both at baseline and at follow up (p<0.01). In the multivariate logistic regression, independent predictors of NCI at follow-up were NCI and age. PLWH with moderate/severe NCI at baseline had the 2.85-fold (CI=1.95-4.32) probability of GDS increase at follow-up of per any 0.1 increment of FI at baseline. PLWH with mild NCI at baseline had the 1.68-fold (CI=1.18-2.39) probability of GDS increase at follow-up of per any 0.1 increment of FI at baseline. In PLWH without NCI impairment at baseline, low FI at baseline protected against GDS increase at follow up (OR=0.66, CI=0.44-0.96). Model was corrected for baseline GDS.

Conclusions: Frailty was associated with NCI at both baseline and follow up. Age and baseline frailty predicted neurocognitive impairment at follow up in this clinically stable and virally suppressed HIV+ cohort. Frailty screening may be used as a prognostic tool for neurocognitive impairment.
Older age exacerbates negative effects of HIV and binge drinking on neurocognitive functioning

Paolillo E1, Saloner R1, Kohli M1, Watson C1, Heaton R2, Moore D2

1San Diego State University/UC San Diego Joint Doctoral Program in Clinical Psychology, San Diego, United States, 2UC San Diego, Department of Psychiatry, San Diego, United States

Background: The population of older persons living with HIV (PLWH) is rapidly growing. Binge drinking is also common among PLWH; however, its effects on neurocognition among this population are understudied, especially in the context of aging. The current study examined independent and interactive effects of HIV status (+/-), binge drinking status (+/-), and age on neurocognition. We hypothesized that: 1) HIV disease and binge drinking would have detrimental synergistic effects on neurocognition, and 2) the deleterious effect of age on neurocognition would be largest among HIV+/binge+ participants as compared to other HIV/binge drinking groups (i.e., HIV+/binge-, HIV-/binge+, and HIV-/binge-).

Material & Methods: Participants were 85 PLWH and 61 HIV- adults (mean[age] = 42.3; SD[age] = 12.3). All participants were current alcohol drinkers. A semi-structured interview was used to identify engagement in at least one episode of binge drinking (i.e., ≥4 drinks for women and ≥5 drinks for men in two hours) in the last 30 days. Neurocognition was examined using demographically-corrected T scores measuring global and domain-specific (verbal fluency, executive functioning, processing speed, learning, delayed recall, working memory, and motor skills) neurocognitive performance. Covarying for history of dependence on non-alcohol substances, multiple linear regressions examined: 1) independent and interactive effects of HIV and binge drinking statuses on neurocognition, and 2) independent and interactive effects of age and HIV/binge drinking group on neurocognition.

Results: Thirty PLWH and 23 HIV- participants met criteria for at least one binge drinking episode in the last 30 days. HIV status and binge drinking status did not interact to predict global or domain-specific neurocognition; however, additive independent effects were detected for global neurocognition (HIV: b = -2.57, p = 0.027; binge drinking: b = -3.80, p = 0.004) and processing speed (HIV: b = -3.17, p = 0.029; binge drinking: b = -3.74, p = 0.022). Next, a significant interaction between age and HIV/binge drinking group was detected for neurocognitive domains of learning (b = -0.38, p = 0.036), delayed recall (b = -0.42, p = 0.018), and motor skills (b = -0.61, p = 0.005), such that the negative effect of age was significantly stronger in the HIV+/binge+ group compared to the HIV-/binge- group.

Conclusions: Older age increases vulnerability to physiological insult from heavy alcohol use, including multi-organ damage with downstream effects on the brain. Given that HIV disease similarly reduces physiological reserve, older PLWH may be particularly vulnerable to the adverse effects of alcohol. The current findings suggest a tripartite model by which HIV disease, binge drinking, and older age synergistically increase risk for poor neurocognition. Given the recent rise in heavy alcohol use among older adults and the rapidly aging population of PLWH, close clinical screening for alcohol misuse among older PLWH is warranted to help preserve cognitive health.
The burden of neuropsychiatric conditions in patients living with HIV-1 treated with antiretroviral therapies – a perspective from US Medicaid

Song J¹, Hardy H¹, Chow W¹, Connolly N¹, Wu B¹
¹Janssen Scientific Affairs, LLC, Titusville, United States

Background: Mental health disorders, such as depression, anxiety, and substance use disorder occur more frequently in people living with HIV-1 compared with the general population. Also, neuropsychiatric conditions (NPCs), such as headache, fatigue and insomnia, have been reported with antiretroviral therapies (ART). The occurrence of NPCs potentially lead to discontinuation of ART, resulting in poorer clinical outcome and increased risk of transmission; yet, little is known about their prevalence and associated economic impact. This study describes the demographics and pre-treatment comorbidities of patients living with HIV-1 who begin therapy with ART, and estimates the all-cause and NPC-related healthcare costs during the 6 months after ART initiation.

Material & Methods: A retrospective cohort study using administrative claims data from the IBM MarketScan® Multi-State Medicaid Database (MDCD) during the study period between 1/1/2014 and 12/31/2017 was conducted. The database includes hospital and outpatient diagnoses, procedures and pharmacy claims for geographically diverse Medicaid enrollees. Patients with a HIV-1 diagnosis, aged ≥18 years, who were newly initiated on an ART regimen and had continuous health plan enrollment [12 months prior to (baseline period) and 6 months following the start of ART (post-period)] were included. We estimated the post-period prevalence of NPCs and, among the entire study population, assessed total all-cause healthcare costs (medical + pharmacy costs) and total NPC-related costs (NPC-related medical + NPC-related pharmacy costs). The NPCs examined were anxiety, major depressive disorder, other depression, bipolar disorder, dizziness, fatigue, headache, insomnia/sleep disorder, trauma and stressor related disorders, cognitive impairment/poor concentration [combined diagnosis codes for specific memory loss, mild cognitive impairment, and other specified cognitive deficit], suicidal ideation and suicide attempt.

Results: Among 1,971 patients included in the study, the mean (SD) Quan-Charlson Comorbidity Index, a measure of comorbidity burden to which HIV/AIDS contributes 4 points, was 4.2 (2.2). The most common comorbidities observed during the baseline period were hypertension (32.1%), hyperlipidemia (13.4%) and obesity (10.9%). Mean age (SD) was 38.5 (12.7) years (14% ≥55 years) and 41.4% were female. During the post-period, 51.4% of patients had a claim for at least 1 NPC, 25.1% had at least 2 distinct NPC claims and 11.7% had at least 3 distinct NPC claims. The most common NPC claims were for depression (26.1%), anxiety (15.8%), headache (11.9%), bipolar disorder or mania (10.1%) and fatigue (9.7%). The mean (SD) total all-cause healthcare costs during the post-period were $16,632 ($33,928), of which $2,914 ($18,233) were NPC-related.

Conclusions: In this Medicaid study of HIV-1 patients newly initiated on ARTs, approximately half experienced a NPC over a 6-month follow up period. Over the same time period, the incremental NPC-associated costs were considerable at 17.5% of the total all-cause healthcare costs.
Integrated HIV persists in brain nuclei of an elderly woman with 20 years of therapy-induced viral suppression

Plaza-Jennings A1, Morgello S1, Smith M1, Murray J1, Akbarian S1
1Icahn School Of Medicine At Mount Sinai, New York, United States

Background: HIV can persist despite long-standing treatment with combination antiretroviral therapy (cART); while the major reservoir is the resting CD4+ T cell, other cellular compartments have not been ruled out.

Materials & Methods: Herein, we report the presence of integrated HIV DNA in brain nuclei isolated from a patient with a 20 year history of viral suppression on cART.

Results: The patient was an 81 year old woman diagnosed at the age of 61, when she presented with a CD4 T cell count of 208 cells/mm3 and a peak plasma HIV RNA load of 54,700 copies/ml. She was placed on an initial regimen of Indinavir, Lamivudine, and Zidovudine, and her plasma viral load decreased to undetectable (limits of detection for early assays were 400 copies/ml). Her cART regimens were continuous, with evolution to Indinavir and Combivir, Combivir and Efavirenz, and then Atripla, with which she was treated for the last 10 years of her life. Her viral loads remained undetectable (with decreased limits of detection to 50 and then 20 copies/ml) for the duration of her therapy, with the exception of one blip to 109 copies/ml 3 years after diagnosis, and another blip to 98 copies/ml 9 years prior to demise. A total of 56 plasma HIV RNA determinations were conducted during this 20 year period. At autopsy, nested PCRs for gag and pol sequences were positive in frontal lobe brain tissue. Using a ligation mediated PCR-based approach, a total of 58 viral integration sites were identified in nuclei sorted from the frontal cortex of this patient. No integration sites were found in nuclei from the brain of an HIV-negative control, and 11,635 integration sites were identified in the nuclei from the brain from a patient with HIV encephalitis (HIVE). Sequencing of viral integration sites from the spleens of the patient with HIVE and the patient with long-term viral suppression produced 1,094 and 208 integration sites respectively.

Conclusions: This shows that integrated HIV can persist in the brains of patients even with 20 years of viral suppression, raising the possibility that the brain, in addition to CD4 T-cells, may be a reservoir site.
Head-to-head comparison of classifications of cognitive impairment for explaining presenteism among HIV+ workers in the Positive Brain Health Now (PBHN) aging Canadian cohort

**Brouillette M**, Fellows L, Brew B, Koski L, Cysique L, Mayo N

1McGill University Health Centre, Montreal, Canada, 2The University of New South Wales, St. Vincent’s Hospital, Sydney, Australia, 3Montreal Neurological Hospital and Institute, Montreal, Canada

**Background:** HIV-Associated Neurocognitive Disorder (HAND) requires impairment in ≥ 2 cognitive domains, each assessed with ≥ 2 measures. Controversy persists about: the best cut-off on normalized NP scores to determine domain impairment; whether functional impairment is associated with domain impairment versus global NP performance; and about the role of measured versus self-reported cognition in explaining everyday function. Here, to anchor the debate in real-life outcomes, we compare domain versus global NP impairment on the extent to which they explain function among HIV+ workers. The hypothesis was that cognitive impairment explains function both directly and indirectly through self-reported difficulties.

**Methods:** The data came from the PBHN aging Canadian cohort study that enrolled participants aged >35 years diagnosed with HIV for >1 year. At each cohort visit, cognition is measured with a brief computerized cognitive test (B-CAM, higher score is better, covers the full range of cognitive ability). Selected participants in the PBHN study underwent NP testing that covered 7 domains with 2-4 measures per domain. Domain impairment was determined by applying 5 different published methods, yielding 5 classifications, and we computed a continuous measure of cognition, the Global Deficit Score (GDS, range: 0-5, higher is worse, covers only the impaired range). Function was conceptualized as an individual’s self-report of cognitive difficulties in everyday activities measured using the 20-item Perceived Deficits Questionnaire (PDQ) with a score ≥ 40/80 considered impaired; and presenteemism, a widely used measure of a worker’s ability to concentrate and accomplish work despite health problems, calculated from the Stanford Presenteeism Scale (scored from 0-100, higher scores are better). Path analysis was used to test the hypothesized relationships along with age and education.

**Results:** Information on NP testing and presenteemism was available for 98 participants. They were on average 52.8 (SD: 7.4) years old with 14.2 (2.5) years of education. Rates of NP impairment using 5 different methods ranged from 20.4% to 73.5%. Scores on the GDS, B-CAM and presenteemism had respective means of 0.46 (SD: 0.53), 21.0 (SD: 4.7) and 73.5 (SD:15.9). PDQ was impaired in 15 (15.3%) of participants. GDS did not explain impaired PDQ (Odds Ratio per 1 unit (95% CI): 1.75 (0.70-4.37) or presenteemism (Beta (SE): -3.69 (3.09), p=0.231). B-CAM explained presenteemism directly (Beta (SE): 1.09 (0.33), p<0.001), but mostly indirectly, through impaired PDQ: B-CAM explaining PDQ: Odds Ratio per 1 unit (95% CI): 0.76 (0.64 - 0.91; and impaired PDQ explaining presenteemism (Beta (SE): -15.9 (4.1), p<0.001). None of the 5 classifications of NP impairment explained either impaired PDQ or presenteemism.

**Conclusions:** Rates of impairment when applying 5 different published classification methods varied by as much as 53%; however, none of these explained self-reported cognitive difficulties or presenteemism, reflecting that they align poorly with this aspect of function. Lesser ability to function at work was predicted by the B-CAM but not by the GDS, suggesting that a measure of global NP function that covers the entire spectrum of ability is required to explain function. The presence of self-reported cognitive difficulties plays a central role in explaining function. In order to understand the impact of cognition on function, an evidence-based evaluation needs to consider cognition in the non-impaired range, as well as self-reported difficulties.
Feedback-related negativity shows promise as an electrophysiological marker of apathy in older men living with HIV.

Castaneda G1, Fernandez Cruz A1, Hum S1, Brouillette M3, Mayo N4, Fellows L1

1Department of Neurology and Neurosurgery, Montreal Neurological Institute, McGill University, Montreal, Canada; 2School of Physical and Occupational Therapy, Faculty of Medicine, McGill University, Canada; 3Department of Psychiatry, Faculty of Medicine, McGill University, Montreal, Canada; 4Division of Clinical Epidemiology, Department of Medicine, McGill University, Montreal, Canada

Apathy, a highly prevalent condition in people living with HIV, affects mental and physical health-related quality-of-life, medication adherence, and is associated with more cognitive decline. The causes of apathy in HIV, and the underlying brain mechanisms, are unknown. Recent work in Parkinson’s Disease found a relationship between apathy and the brain response to incentives measured with EEG (i.e. the amplitude of the feedback-related negativity (FRN)). Here, in a large sample (N=70) of older men with well-controlled HIV, we asked if apathy measured with a modified version of the Starkstein Apathy Scale was related to FRN amplitude. Participants were drawn from the Positive Brain Health Now cohort, a longitudinal Canadian study of mental health and cognition in HIV+ people over age 35, taking antiretroviral therapy. High-density EEG was recorded while participants completed a gambling task in which they received either positive or negative feedback after each trial. The FRN was measured at frontocentral electrodes (Fz, Fcz, Cpz) between 200 to 300ms post-feedback. Participants were divided into more-aphatic (N=22) and less-aphatic (N=38) groups, based on a median split. A typical FRN response was observed in both groups, with higher frontocentral negativity after negative than positive feedback. The more-aphatic group had a significantly smaller amplitude after both types of feedback at Fcz and Cpz electrodes compared to the less-aphatic group, controlling for age. This is the first EEG study of incentive processing in HIV. We provide preliminary evidence of mesocorticolimbic dysfunction resulting in lower-amplitude brain responses to positive and negative feedback in those with more self-reported apathy. This is a step towards a clearer understanding of the pathophysiology of apathy in HIV, and identifies a possible biomarker to advance further research.
Resting state EEG is more sensitive than structural MRI to the brain changes underlying cognitive performance in people living with HIV

Fernandez Cruz A1, Chen C1, Salcin K, Sanford R1, Dadar M1, Collins D1, Brouillette M1, Mayo N1, Fellows L1

1Department of Neurology and Neurosurgery, Montreal Neurological Institute, Faculty of Medicine, McGill University, Montreal, Canada,
2Department of Psychiatry, Faculty of Medicine, McGill University, Montreal, Canada, 3Division of Clinical Epidemiology, Department of Medicine, McGill University, Montreal, Canada

Cognitive impairment is common in people living with HIV, even with effective systemic viral suppression. The causes and underlying mechanisms remain uncertain, and there is no consensus on how to treat this quality-of-life-limiting problem. Here, we tested whether EEG oscillations at different frequency bands and brain structure assessed with MRI were related to cognitive performance in older men with effectively-treated HIV infection. High-density EEG was recorded at rest in 89 men from the Positive Brain Health Now cohort, a Canadian study of brain health in older persons with well-controlled HIV. Structural MRI was also available in 58. Multiple linear regression showed that the power of occipital and parietal alpha and delta bands measured with EEG related to cognitive ability, independent of age effects. Neither variation in global volumes or regional cortical thickness, assessed with voxel-based morphometry and cortical modeling, nor subcortical brain volumes assessed with deformation-based morphometry, nor white matter hyperintensities related to cognitive ability. None of the structural or functional brain measures were predicted by nadir or current CD4 counts. These results suggest resting state EEG is a sensitive method to assess brain function related to cognitive ability in older HIV+ individuals with longstanding, well-controlled HIV infection. This is the first direct comparison of candidate EEG and structural MRI biomarkers. Resting-state EEG seems a promising potential biological marker that, with further validation, could enhance our understanding of the pathophysiology of cognitive impairment in HIV, and provide new clinically-relevant outcome measures for treatment studies.
Clinical information about immune activation does not explain depression, cognition, fatigue or motivation in older men with HIV: results from the Positive Brain Health Now Canadian cohort

Matout M1, Isnard S2, Fellows L2, Routy J1, Mayo N1, Brouillette M1
1Research Institute of the McGill University Health Center, Montreal, Canada, 2Montreal Neurological Hospital and Institute, Montreal, Canada

Introduction: Several aspects of brain health have been associated with indicators of immune activation or with the presence of infections that drive this activation. Depression, poor cognition, decreased motivation and fatigue have all been associated with laboratory markers of immunity, mostly in the research setting. It is unclear if information available clinically can identify an immune profile that is associated with poor brain health.

Objective: The purpose of this study is to estimate, among older adults living with HIV, the strength of the association between clinical information about immune activation and several indicators of poor brain health.

Methods: The data came from the inaugural visit of the Positive Brain Health Now Canadian cohort study that enrolled participants aged >35 years diagnosed with HIV for >1 year. Data was collected from chart review, direct measurements (blood samples) and self-report questionnaires. Immune profile was assessed by (i) 2 hypothesized drivers of immune activation: co-infection with CMV or HSV (ii) 2 clinical markers of inflammation: CRP and CD4:CD8 ratio. The indicators of poor brain health were: depression (Mental Health Index of the RAND-36), fatigue (vitality index of the RAND-36), motivation (3 questions from Starkstein’s apathy scale); and a computerized measure of cognition, the B-CAM, that yields a single score of cognitive ability. First, co-infection (CMV and HSV) and inflammation (CRP and CD4:CD8) were considered as latent variables. Regression models (linear if the outcome was reasonably normal, otherwise ordinal) were used to estimate the strength of the relationship between the brain health outcomes with co-infection and inflammation, adjusting for age, use of amphetamine/cannabis/alcohol/cigarettes, and the Charlson comorbidity index. Because sex and ethnicity were considered confounders, we limited the analysis to the largest group, Caucasian men.

Results: Data were available on 513 men (mean age 54.1 (SD: 8.2). Neither the co-infection variables nor the inflammation variables could be combined: they were modeled as 4 separate outcomes. The final model comprised 4 explanatory variables and 6 adjustment variables. The only variable associated with brain health outcomes was CRP. The strongest association was with the B-CAM (Beta (CI): -0.068 (-0.112, -0.025)) such that a 29-unit difference on the CRP would lead to a difference in the B-CAM of 0.5 SD. An association, even more modest, was present between CRP and fatigue (Proportional Odds Ratio (CI): 0.976 (0.951, 1.000)) and MHI (Proportional Odds Ratio (CI): 0.978 (0.954, 1.003). No association with poor motivation was found.

Conclusion: In this cross-sectional analysis of a large cohort of older men with HIV, only CRP showed a very modest association with cognition that would only be clinically meaningful at very high CRP values. The other explanatory variables tested, CMV, HSV and CD4:CD8 ratio, did not show an association with cognition, depression, fatigue or motivation. While promising results are reported between brain health outcomes and immune measures available in the research setting, we did not find any evidence that information available clinically provides useful indication of about the presence of an immune profile that would explain poor brain health.
Gait speed is associated with cognitive function among older adults with HIV

Derry H1, Johnston C1, Burchett C1, Siegler E1, Glesby M1
1Weill Cornell Medicine, New York, United States

Background: Older adults with HIV have elevated risk for cognitive impairment, and strategies to mitigate cognitive decline are needed. Cross-sectional studies suggest that self-reported physical activity may improve cognitive function among those aging with HIV, but relationships with objective markers of physical function have been less explored.

Materials and Methods: In a sample of HIV-positive adults ages 55 and older, we tested relationships between cognitive function and physical function. Participants (N=162) were patients from an HIV clinic in New York City who completed a biomedical research visit as part of a larger study. The visit included objective tests of gait speed (4-meter walk test) and cognitive function (MoCA) as well as subjective reports of their cognitive and physical function (using the MOS-HIV self-report survey).

Results: At baseline, gait speed was correlated with MoCA scores (r = 0.25, p = 0.001); those with slower gait speed had worse overall cognitive function than those with faster gait speed. This association remained in an adjusted regression model controlling for age, sex, race, and assistive device use. Using MoCA subtest data, gait speed was related to visuospatial (r = 0.17, p = 0.03) and attention domains (r = 0.22, p = 0.006) and marginally associated with delayed recall (r = 0.14, p = 0.07); links between gait speed and other domains were weaker and not statistically significant. We also examined relationships among subjective and objective variables. Self-rated physical function was moderately related to objective gait speed (r = 0.42, p < 0.001) and weakly predictive of MoCA scores (r = 0.19, p = 0.01). Although self-rated cognitive function was correlated with objective cognitive function (r = 0.30, p < 0.001), subjective cognitive function was more strongly associated with emotional well-being (r = 0.52, p < 0.001), consistent with prior work.

Conclusions: In cross-sectional analyses, HIV-positive older adults with faster gait speed performed better on the MoCA than those with slower gait speed. Subjective and objective ratings of physical function were moderately correlated with each other; subjective cognitive function shared a stronger relationship with emotional well-being than with objectively-measured cognitive function. These findings expand the literature on the relationship between cognitive and physical function among adults aging with HIV, and suggest that longitudinal studies are warranted, as improving physical function could have cognitive benefits.
HIV-1 gp120 and spatial memory impairments: role of CREB protein

Allen C1, Shrestha J1, Santerre M1, Arjona S1, Chin J1, Sawaya B1,3

1Molecular Studies of Neurodegenerative Diseases Lab, FELS Institute, United States, 2Department of Neurology; Lewis Katz School of Medicine - Temple University, Philadelphia, United States, 3Memory & Brain Research Center, Department of Neuroscience Baylor College of Medicine, Houston, United States

Background: HAND remains an unsolved problem in the clinical management of HIV-1 carriers, because existing anti-retroviral therapies, while suppressing viral replication, do not prevent neurocognitive impairment such as spatial memory loss. Some viral proteins, including gp120, have been proposed as contributors to HAND, because it is shed by infected cells and find its way across the blood-brain barrier. The use of antibodies revealed the presence of gp120 in CSF even in the cART era. Further, the cAMP response element binding (CREB) protein has long been known to be a star player in memory. CREB exerts its effect partially through turning on the gene for BDNF. CREB and BDNF levels are low in the brains of people with neurodegenerative diseases and a dearth of CREB and/or BDNF is associated with cognitive decline.

Methods and Results: We have obtained data showing that gp120 contributes to neurodegeneration via disruption of the CREB pathway, hence altering synaptic plasticity and neurite outgrowth leading to spatial and declarative memory loss. Our data was validated in vitro (primary human and mouse neurons and neuronal cell line, SH-SY5Y) and in vivo (gp120-tg animal and mice injected with gp120). Loss of CREB function was also associated with decreased of ATP levels and lower mtDNA copy number. The negative effect of gp120 was alleviated in cells and in animals in the presence of Rolipram.

Conclusion: Thus, we concluded that HIV-1 gp120 protein contributes to memory impairments via inhibition of CREB protein activity.
Assessment of the health-seeking behavior of people living with human immunodeficiency virus (PLHIV) enrolled in a treatment facility in a tertiary hospital

Quitos L1, Salamat M1, Gregorio E2
1Section of Infectious Diseases, Department of Medicine, University of the Philippines - Philippine General Hospital, Manila, Philippines, 2Department of Health Promotion and Education, College of Public Health, University of the Philippines, Manila, Philippines

Background: The health-seeking behavior of key populations at risk for human immunodeficiency virus (HIV) infection has been evaluated, and knowledge regarding the disease, cost, and trust on health care providers were among the significant factors in seeking treatment. This study aimed to determine the health-seeking behavior of people living with HIV enrolled in STD/AIDS Guidance, Intervention, and Prevention (SAGIP) clinic in Philippine General Hospital, a tertiary university hospital.

Material and methods: This was a questionnaire-guided, analytic cross-sectional study. A revised version of the questionnaire by Bhutto and Nisar was used in assessing the health-seeking behavior of the participants and their satisfaction with the treatment facility. The sociodemographic and clinical profile of the participants and their satisfaction with the services provided by the facility were correlated with their health-seeking behavior. Descriptive statistics were used to determine and describe the characteristics of the participants. Student T-test was used to assess associations of outcomes.

Results: A total of 348 participants were included in the study analysis. Majority of the participants (266, 76.4%) had positive health-seeking behavior and 293 (84.2%) were satisfied with SAGIP. The factors significantly associated with negative health-seeking behavior were being young (19-24 years old) (17.1% vs. 9.0%; p=0.041), high school level (22.0% vs. 11.3%; p=0.014), being a student (11.0% vs. 4.5%; p=0.032), living with HIV for ≤2 years (39.0% vs. 26.7%; p=0.032), those who lack disease awareness (53.7% vs. 26.7%; p=<0.050), those who felt stigma (50.0% vs. 19.2%; p=<0.050), cost of >Php 200 per visit (64.6% vs. 51.9%; p=0.042), and dissatisfaction with the treatment facility (28.0% vs. 13.5%; p=<0.050). In contrary, the factors associated with positive health-seeking behavior were living with HIV for >2 years (73.3% vs. 61.0%; p=0.032), lesser cost per visit (≤ Php 200) (47.7% vs. 35.4%; p=0.049), and satisfaction with the services provided by the treatment facility (86.5% vs. 72.0%; p=0.002). There was no significant difference in the number of participants with undetectable viral load among both groups. Interestingly, there were significantly more patients with <200 baseline CD4 cell count in participants with positive health-seeking behavior (62.4% vs. 50.0%; p=0.045). There was also no significant difference in the presence and types of opportunistic infections except for Cytomegalovirus (CMV) retinitis, wherein more patients with negative health-seeking behavior had CMV retinitis compared to the positive group (3.7% vs. 0.4%; p=0.015).

Conclusions: This study described the factors and overall health-seeking behaviors of this population and correlated the sociodemographic and clinical profiles of the patients with their health-seeking behavior. Majority of the PLHIV enrolled in SAGIP clinic had a positive health-seeking behavior and their satisfaction with the services provided may have been a factor in their continuing engagement to HIV care. A lower cost of treatment also significantly contributed to this favorable behavior. All efforts should be driven to the care of younger patients, who lack disease awareness, felt stigma and discrimination, had a higher cost of treatment, and those who are not satisfied with the services provided by the treatment facility, for they are prone to exhibit negative health-seeking behavior.
Disruption of MAM in premature brain aging and HIV-associated neurocognitive disorders (HAND)

Arjona S1, Allen C1, Santerre M1, Sawaya B1
1Temple University, Philadelphia, United States

Patients infected with HIV-1, including those using combinatorial Anti-Retroviral Therapy (cART), suffer from impairment of vital organs such as brain, heart, etc. Studies involving HIV-infected patients using cART showed signs of HIV-1 associated neurocognitive disorders (HAND). In other neurodegenerative conditions such as aging, AD, PD, and ALS/FTD there is a dysregulation of neuronal functions including calcium exchange, lipid exchange, intracellular trafficking, and mitochondrial biogenesis which contribute to pathogenesis. Interestingly, the Mitochondrial-Associated ER Membrane (MAM) regulates many of these cellular functions. The MAM is the contact between the membrane of the endoplasmic reticulum (ER) and the outer membrane of the mitochondria and is vital for mitochondria health and function. It has only recently been implicated in neurodegenerative conditions. The MAM plays a major role in mitochondrial fission and fusion as well as calcium homeostasis especially in neurons which are extremely sensitive to changes in mitochondrial health and calcium signaling.

In order to demonstrate the role the MAM plays in the progression of HAND, we used SH-SY5Y cells which we exposed to the HIV-1 protein TAT. The cells were treated with 100ng/mL of TAT protein. Some cells were fixed and imaged using electron microscopy (EM); others were used in fractionation of the MAM to quantify expression of key proteins involved in the communication between the ER and the mitochondria using western blotting. To assess the effect TAT had on the functional aspect of the MAM, some cells were stained with a calcium sensitive dye to measure calcium influx.

Here we show that the mitochondria in Tat treated cells are significantly damaged physically based on our EM image analysis. We also show that calcium signaling is dysregulated in our TAT treated cells suggesting mitochondria are not healthy further implicating MAM dysfunction in HAND.

Future studies of the MAM will involve exploring changes in mitochondrial fission/fusion and movement all using HIV-1 TAT treated cells. By targeting the MAM dysfunction, we hope to develop new approaches for the treatment of HAND.
Tenoforv-diphosphate in dried blood spots is associated with HIV-related aging factors

Coyle R1, Seifert S1, Abdo M1, MaWhinney S1, Anderson P1, Erlandson K1

1University of Colorado-AMC, Aurora, United States

Background: Improved efficacy and tolerability of modern antiretroviral therapy (ART) has led to greater life expectancy but increasing comorbid burden for persons living with HIV (PLWH). Decreased kidney function and frailty may accentuate the impact of ART toxicity, in part through increased drug exposure. This study compared associations between intracellular tenofovir-diphosphate (TFV-DP) arising from tenofovir disoproxil fumarate (TDF) with bone mineral density (BMD), falls, and physical function among older and younger PLWH.

Methods: Intracellular TFV-DP concentrations were analyzed in dried blood spots (DBS) using previously validated methods. BMD, lean body mass (LBM), and total fat mass was assessed using dual-energy x-ray absorptiometry (DXA), physical function with a short physical performance battery (SPPB) and 400-m walk, and falls by self-report in the prior 6 months. Linear and logistic regression methods were used to evaluate the association between TFV-DP with falls, BMD, and physical function. Bivariate models adjusted for sex, age, LBM, and total fat mass.

Results: A total of 45 participants were enrolled. There were 23 younger participants (ages 18 - 36) and 22 older (age >60). The majority of participants were white (64%), male (87%), overweight/obese (56%), and had no falls in the preceding six months (91% younger, 59% older). Every 500 fmol/punch increase in TFV-DP was associated with decreased hip BMD (-0.021 g/cm² [95% CI: -0.040, -0.002], P=0.03), but not spine BMD (-0.018 g/cm² [95% CI: -0.039, 0.003], P=0.09). After adjusting for either LBM or total fat mass, the association between hip BMD with TFV-DP was attenuated and no longer statistically significant (P=0.06 and P=0.10, respectively). Every 500 fmol/punch increase in TFV-DP was associated with higher odds of reporting a fall in the prior 6 months (odds ratio [OR]: 1.7 [95% CI: 1.1, 2.8]), P=0.02; this effect remained significant after controlling for either sex, age, LBM, or total fat mass (all P=0.02). Every 500 fmol/punch increase in TFV-DP was strongly associated with longer time to complete a 400-m walk (14.78 sec [95% CI: 3.81, 25.76], P=0.01), which remained significant after controlling for either sex (P=0.003), age (P=0.01), LBM (P=0.01), or total fat mass (P=0.0001). Although TFV-DP was not associated with SPPB in unadjusted analyses (P=0.12), after controlling for sex or total fat mass, every 500 fmol/punch increase in TFV-DP was associated with higher odds of SPPB impairment (score <10; adjusted OR [aOR]: 1.6 [95% CI: 1.0, 2.4], P=0.04; aOR: 1.6 [95% CI: 1.0, 2.5], P=0.04, respectively). Every 500 fmol/punch increase in TFV-DP was also associated with significantly longer time to complete 10 chair rises after adjusting for total fat mass (1.47 sec [95% CI: 0.31, 2.64]), P=0.01.

Conclusions: Higher TFV-DP levels were associated with lower hip BMD, greater risk for falls, and poorer physical function, a combination highly concerning for increased fracture risk. Whether higher TFV-DP is associated with additional confounders that increase risk of poor outcomes or is playing a direct role cannot be determined from this study. Further research is needed to determine if TFV-DP might help identify individuals at high risk for fractures.
Food insecurity and neurocognitive function among women living with HIV in the US

Tan J, Weiser S

1University of California San Francisco, Center for AIDS Prevention Studies, San Francisco, United States; 2Division of HIV, ID and Global Medicine, University of California, San Francisco (UCSF), San Francisco, United States

Background: Food insecurity (FI) is highly prevalent among women living with or at risk for HIV. FI contributes to HIV-related inflammation and has negative impacts on HIV disease outcomes. The effects of FI and HIV on neurocognitive function are not well understood among women, who may be particularly vulnerable to its deleterious effects.

Methods: From 2013 to 2015, 1324 (900 HIV-seropositive) participants from the Women’s Interagency HIV Study (WIHS) completed a comprehensive neuropsychological test battery (e.g., learning, memory, attention/working memory) and a measure of food insecurity (U.S. Household Food Security Survey Module). Multivariable linear regression models were conducted to examine associations between FI and neurocognitive performance (T-scores; M=50; SD=10) after adjusting for socio-demographic, behavioral, and clinical characteristics.

Results: Over one-third (36%) of women were food-insecure, of whom 68% were women living with HIV. In the adjusted analysis in the overall sample (Table 1), having any FI (vs. high food security) was associated with lower scores on executive function (β=-1.7, SE=0.59, p<0.01), processing speed (β=-1.4, SE=0.59, p<0.05), and motor function (β=-1.7, SE=0.62, p=0.01). FI was not associated with attention/working memory, learning, memory, or verbal fluency (ps>0.10). Being HIV-positive was associated with lower scores on attention/working memory (β=-1.5, SE=0.62, p=0.01), but was not associated with executive function, processing speed, motor function, learning, memory, or verbal fluency (ps>0.10).

Conclusions: FI was associated with lower executive function, processing speed, and motor function, and impairments in attention/working memory was observed among women living with HIV. Longitudinal research is needed to investigate directionality and potential mediators, such as stress.
Statin use is a major risk factor for Type 2 Diabetes Mellitus in PLWH

1University Of Alabama At Birmingham, Birmingham, United States

Introduction: For persons living with HIV-1 infection (PLWH), combination antiretroviral therapy (cART) effectively suppresses viral load and partially restores immunologic health, yet various comorbidities continue to rise in the aging PLWH population. Our study aimed to assess the risks of incident type 2 diabetes (T2D) in a clinical setting.

Methods: We analyzed retrospective data from PLWH who had multiple clinical visits between 1999 and 2018 as part of routine care at a southeastern US clinic. Patient characteristics, including demographics, body mass index (BMI), HIV-1-related outcomes, protease inhibitor use, hepatitis C virus (HCV) co-infection, statin use and various co-morbidities were screened in univariable regression models as potential correlates for T2D occurrence. Multivariable logistic regression models were used to identify factors that are independently associated with incident T2D.

Results: Among a total of 3,975 PLWH with 26,256 person-years (PY) of active follow-up during the study period, 354 newly diagnosed T2D cases were included for analysis. Incidence rates of T2D were 125 (95% confidence interval, CI: 102-148), 143 (CI: 133-161), and 115 (CI: 64-165) per 10,000 PY for ages 18-44, 45-64, and >65 years, respectively. In univariable models, age, sex, BMI, HIV-1 viremia, use of statin and enrollment period were associated with incident T2D (p <0.05 for all). Based on adjusted effect size (odds ratio, OR), the top 3 risk factors identified by a reduced multivariable model were (i) statin use regardless of specific types (<0.5 years: OR=8.9; ≥ 0.5 year: OR= 10.0; p<0.0001 for both), (ii) HIV-1 viremia >200 copies/mL (OR=2.2, p<0.0001), and BMI ≥30 kg/m2 (OR=3.4, p<0.0001).

Conclusion: In addition to confirming previously known factors for T2D, statin was a major factor in our study and warrants further investigation.
Low social support prevalent in midlife and older Human Immunodeficiency Virus-positive men who have sex with men attending an urban clinic.

Wasserman P1, Aratoon K1, Yoon J1, Turett G1,2
1New York Presbyterian/Queens, New York, United States, 2Weill Cornell Medical College, New York, United States

Background: Social support is the individual’s perception of the availability of supportive communications, affectionate and instrumental care, and positive interactions with close others, if needed. The adverse impacts of meager social networks on health outcomes and mortality rates, are thought to be mediated by low levels of social support. Our aim was to determine if low social support was prevalent in midlife and older men who have sex with men (MSM), in care for Human Immunodeficiency Virus (HIV) infection, and if it was associated with poor physical function, self-rated health, and/or poor skeletal muscle mass.

Methods: MSM aged ≥ 45 years, presenting for routine care, were invited to participate in this cross-sectional period-prevalence study. Overall, and by domain, perceived social support was assessed using the 19-item Medical Outcomes Study Social Support Survey instrument (scored 0-100). Low social support was defined as overall score < 50. Self-rated health was evaluated by a 5 point scale (poor to excellent). Transfer/sensorimotor function was assessed by 5 times sit-to-stand, physical function by hand-grip strength and timed walk. Skeletal muscle mass was assayed by mid-upper arm muscle circumference (MUAMC). Sarcopenia was defined as low MUAMC and low hand-grip strength or low gait speed; pre-sarcopenia low MUAMC only. Multivariate logistic regression models were used to determine associations with low social support. Variables that were associated with low social support at P ≤ .10 in the univariate analyses were retained as co-variates in regression analyses.

Results: Between 6/25/2018 and 2/11/2019, 88 community-dwelling HIV+ MSM participated in this study. Hispanic ethnicity (67.1%) was predominant. The mean age 55.3 years, mean time of known HIV infection 16.5 years, and mean CD4+ T cell count 764. The prevalence of low social support was 23.9%, sarcopenia 11.4 %, pre-sarcopenia 35.2 %, low hand-grip strength 28.4%, low gait speed 6.8%, slow 5 times sit-to-stand 45.5%, poor/fair self-rated health 5.7%. Multivariate regression analyses were modeled for age, ethnicity, marriage/partnership, height, hand-grip strength, gait speed, sarcopenia, and receipt of a lipid-modifying or antithrombotic agent. Older age (odds ratio, OR, 0.59, 95% confidence interval, CI, 0.41 – 0.85; P = .004) and higher hand-grip strength (OR 0.77, 95% CI 0.63 – 0.94; P = .009) were negatively associated with low social support. Clinically low hand-grip strength remained associated with low social support in analysis with the same covariates (OR 373, 95% CI 7-1000; P = .004).

Conclusions: Low Social support was prevalent (essentially 1-in-4) in this population. Our observation that participants experiencing low social support were younger suggests onset in or entry into midlife with it. This association may be subsequent to carriage of a potentially stigmatizing diagnosis, in addition to sexual minority status. The associations of low social support with hand-grip strength but not more global measures of function may reflect less engagement with testing instrumentation, due to mood/psychological functioning.
Depression is associated with low CD4:CD8 T-cell ratio among PLWH over 55 with mild cognitive impairment

Dobbins S1, Merrilees J1-2, Moskowitz J1, Javendal S2, Brijesh B3, Valcour V2

1UCSF School of Nursing, Oakland, United States, 2UCSF Memory and Aging Center, San Francisco, United States, 3Northwestern University Medical Social Sciences, Chicago, United States

HIV affects the immune system, the nervous system, and causes chronic inflammation in the body. Low CD4:CD8 ratio is a marker of T-cell balance and indicates chronic immune activation despite effective antiretroviral treatment and viral suppression. Even when HIV is well-managed, inflammation may increase risk of age-associated conditions. Although evidence suggests loneliness and depression may contribute to dysregulated inflammatory processes, there is little research about psychosocial variables and immune function among older people living with HIV (PLWH). We examined the association of CD4:CD8 ratio with loneliness, social isolation, and depression in a sample of PLWH over 55 who have a confirmed neurocognitive disorder (N=171).

Methods: This study is a secondary analysis of a cohort recruited for a mindfulness based stress reduction intervention study. We described the sample social network and examined the association of low CD4:CD8 ratio with social isolation, loneliness, and depression. These variables were measured with the Norbeck Social Support scale, UCLA-20 item loneliness scale, the Geriatric Depression Scale (GDS), and self-reported history of depressive episode in the past 2 years. The Norbeck and UCLA scales do not have validated cutoff scores, and a score 10 on the GDS indicates above-normal symptoms. CD4:CD8 is an absolute serum cell count ratio. Other variables: Age, perceived stress, self-reported history of substance dependence/abuse, years living with HIV, past hepatitis C (treated), current medication treatment for depression, and nadir CD4 cell count. All skewed variables were transformed.

We estimated the association of CD4:CD8 cell ratio with loneliness, social support, and depression while adjusting for hypothesized confounders using maximum likelihood with full information and bootstrap standard errors. Alpha was set to 0.05.

Results: Our sample was 92% male, 73% White, mean 64 years of age (SD 5.3), and had a mean 26 years living with HIV (SD 6.8). All had Mild Neurocognitive Disorder. 49% had past substance use, 52% has a past depressive episode, and 32.9% had current depressive symptoms on the GDS.

Mean CD4 and CD8 cell counts were 613.9 (SD 279.8) and 798.9 (SD 346.1). The CD4:CD8 cell ratio had a median of 0.77 (IQR 0.24-2.15) and low ratio was defined as less than 1.0 (71%).

Loneliness scale had a mean score of 44.4 (SD 11.7). A median of 7 people were listed in social networks (IQR 4 – 24) on the Norbeck scale. 3% of participants listed nobody in their network, 33% listed a partner/spouse, 78% listed friends (mean 4.8), 72% listed family (mean 2.9), 47% listed healthcare providers (mean 1.2), and 22.5% listed counselors/therapists (mean 1.4). 32% reported losing an important relationship in the past year.

In adjusted analyses, we found that a depressive episode in the past 2 years increased the odds of having a low CD4:CD8 cell ratio (OR 2.61, 95% CI:1.06, 6.48). This data suggests that depression may have a unique contribution to immune function in aging PLWH who have mild neurocognitive disorder. Loneliness, isolation, and GDS score were not associated with low ratio.

PLWH have a higher prevalence of depression and nearly half of PLWH in the US are 50 and over. Given the putative link between loneliness, depression, and cognitive trajectories, further research on social connections and mental health in aging with HIV may reveal modifiable risk factors for HIV-associated cognitive impairment and other health outcomes in aging.
<table>
<thead>
<tr>
<th>Name</th>
<th>Abstract title</th>
<th>Abstract #</th>
<th>Page #</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jankowski, Catherine</td>
<td>Blunted Increase in Muscle Mass After Exercise Training in People Aging with HIV</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Tan, Judy</td>
<td>FOOD INSECURITY AND FRAILTY AMONG WOMEN IN THE U.S.</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Masters, Mary Clare</td>
<td>Impact of testosterone use on grip strength in men aging with HIV</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Achenbach, Chad</td>
<td>Epigenetic Age Acceleration and Non-AIDS Defining Cancers Among HIV Infected Adults</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Bowman, Emily</td>
<td>Lipidome abnormalities and altered macrophage phenotype may contribute to cardiovascular disease risk in the aging HIV population</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>Johnston, Carrie</td>
<td>Elevated Cardiac Risk Score by ASCVD Calculation is Associated with Albuminuria in Older People Living with HIV</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>Sun, Jing</td>
<td>The Association between Mitochondrial DNA Copy Number and Longitudinal Lung Function Decline among People with or at Risk of HIV</td>
<td>7</td>
<td>9</td>
</tr>
<tr>
<td>Rozanova, Julia</td>
<td>The Aging of HIV Epidemic in Ukraine: new HIV diagnoses from 2015-2018 and related mortality among adults ≥50 years</td>
<td>8</td>
<td>10</td>
</tr>
<tr>
<td>Psomas, Christina K.</td>
<td>FRAILTY PHENOTYPE IN OLDER VIROLOGICALLY SUPPRESSED PLWHIV IS STRONGLY CORRELATED WITH SPECIFIC COMORBIDITIES AND TOBACCO USE</td>
<td>9</td>
<td>11</td>
</tr>
<tr>
<td>Hunt, Matthew</td>
<td>Cellular and molecular assessment of muscle function as a predictor of ageing phenotype in older PLWH</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td>Morgello, Susan</td>
<td>HIV infection does not increase the frequency of phosphorylated tau and beta amyloid in brain in late middle age</td>
<td>11</td>
<td>13</td>
</tr>
<tr>
<td>Diaz, Monica</td>
<td>Predictors of longitudinal neuropathic pain in older patients with HIV-associated distal sensory polyneuropathy</td>
<td>12</td>
<td>14</td>
</tr>
<tr>
<td>Sundermann, Erin</td>
<td>The Utility of Olfactory Function in Distinguishing Early Stage Alzheimer’s Disease from HIV-associated Neurocognitive Disorder: A Pilot Study</td>
<td>13</td>
<td>15</td>
</tr>
<tr>
<td>Dobbins, Sarah</td>
<td>The structure and correlates of loneliness and social isolation among PLWH over 55 with mild neurocognitive disorder</td>
<td>14</td>
<td>16</td>
</tr>
<tr>
<td>Austin-Keiller, Amanda</td>
<td>What is the lived experience of loneliness in older men living with HIV? A qualitative analysis to guide service development</td>
<td>15</td>
<td>17</td>
</tr>
<tr>
<td>Guaraldi, Giovanni</td>
<td>Intrinsic capacity but not frailty predicts functional status in PLWH: a multi-centre prospective study</td>
<td>16</td>
<td>18</td>
</tr>
<tr>
<td>Lake, Jordan</td>
<td>Traditional Risk Factors and Darunavir Use Associated with Muscle and Fat Quality and Quantity in Adults With HIV on Antiretroviral Therapy</td>
<td>17</td>
<td>19</td>
</tr>
<tr>
<td>Olson, Alex</td>
<td>Persistent low-level HIV-1 transcription associated with systemic inflammation and age related comorbidities</td>
<td>18</td>
<td>20</td>
</tr>
<tr>
<td>Name</td>
<td>Abstract title</td>
<td>Abstract #</td>
<td>Page #</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>---------------------------------------------------------------------------------</td>
<td>------------</td>
<td>--------</td>
</tr>
<tr>
<td>Erlandson, Kristine</td>
<td>Frailty, Physical Function Impairment, Comorbidity Burden, and Falls are Predictive of Mortality Among Middle-Aged Adults with HIV</td>
<td>19</td>
<td>21</td>
</tr>
<tr>
<td>Balon, Emily</td>
<td>Increased frailty symptoms relate to poorer self-reported sleep quality among older people living with HIV</td>
<td>20</td>
<td>22</td>
</tr>
<tr>
<td>Bhondoekhan, Fiona Sharma, Anjali</td>
<td>Frailty Predicts Recurrent Falls among Older Women With and Without HIV</td>
<td>22</td>
<td>24</td>
</tr>
<tr>
<td>Psomas, Christina K. Inceer, Mehmet</td>
<td>Comparison of 2 frailty scores in HIV infected people aged 50 and over: SOF index and FRIED phenotype</td>
<td>23</td>
<td>25</td>
</tr>
<tr>
<td>Montano, Monty</td>
<td>Physical Activity in Asymptomatic Middle-Aged Men With and Without HIV infection is Associated with Routine Blood-Based Biomarkers</td>
<td>25</td>
<td>27</td>
</tr>
<tr>
<td>Brañas, Fatima</td>
<td>LONG-TERM PRE-HAART SURVIVORS OF HIV: A SPECIFIC GROUP WITH SPECIFIC NEEDS</td>
<td>26</td>
<td>28</td>
</tr>
<tr>
<td>Kim, Connie</td>
<td>Characterizing Gender Differences in Canadians Living with HIV to Improve Management of Comorbidities</td>
<td>27</td>
<td>29</td>
</tr>
<tr>
<td>Harris, Tiffany G. Tran, Thao</td>
<td>Physical Health of Older People Living with HIV in Eswatini</td>
<td>28</td>
<td>30</td>
</tr>
<tr>
<td>Felker, Gwendoline Ezeamama, Amara</td>
<td>Magnetic resonance spectroscopy evidence of accelerated aging in virally-suppressed HIV</td>
<td>29</td>
<td>31</td>
</tr>
<tr>
<td>Allen, Charles</td>
<td>The Effect of gp120 on Cleavage of pro-BDNF in HIV-1 Clade B &amp; C Leading to HIV Associated Neurocognitive Disorders (HAND)</td>
<td>32</td>
<td>34</td>
</tr>
<tr>
<td>Pallikkuth, Suresh Shacka, John</td>
<td>CMV and Aging Revisited: Relationship of CMV IgG titers with Age, HIV infection, inflammation, immune activation and influenza vaccine antibody responses.</td>
<td>33</td>
<td>35</td>
</tr>
<tr>
<td>Shive, Carey</td>
<td>TGF-b is lower in HIV infected immune non-responders and is negatively associated with T cell markers of exhaustion and senescence independent of age</td>
<td>35</td>
<td>37</td>
</tr>
<tr>
<td>Dewald, Hannah</td>
<td>Senescence-Associated Beta-Galactosidase Activity and Other Markers of Senescence in Human Peripheral Blood Immune Cells During Healthy Aging and HIV-Infection</td>
<td>36</td>
<td>38</td>
</tr>
<tr>
<td>Premeaux, Thomas</td>
<td>Soluble Inflammatory Markers Correlate with VACS Risk Index Scores Among HIV infected Older Adults on Suppressive Antiretroviral Therapy</td>
<td>37</td>
<td>39</td>
</tr>
<tr>
<td>Name</td>
<td>Abstract title</td>
<td>Abstract #</td>
<td>Page #</td>
</tr>
<tr>
<td>------------------------</td>
<td>---------------------------------------------------------------------------------</td>
<td>------------</td>
<td>--------</td>
</tr>
<tr>
<td>Zapata, Heidi</td>
<td>The Effects of Aging and HIV Infection on the Function of Dectin-1, an Innate Immune Receptor for the Recognition of Fungal Organisms</td>
<td>38</td>
<td>40</td>
</tr>
<tr>
<td>Zhen, Anjie</td>
<td>Role of Autophagy in premature immune aging during HIV infection</td>
<td>39</td>
<td>41</td>
</tr>
<tr>
<td>Erlandson, Kristine</td>
<td>Poorer Muscle Quality and Quantity with ART Initiation is Associated with Greater Inflammation and Immune Activation</td>
<td>40</td>
<td>42</td>
</tr>
<tr>
<td>Cioe, Patricia</td>
<td>The behavioral and biological effects of electronic cigarette provision in HIV-positive smokers who are not motivated to quit</td>
<td>41</td>
<td>43</td>
</tr>
<tr>
<td>Erlandson, Kristine</td>
<td>Characteristics Associated with Exercise Adherence in the Setting of a Supervised Intervention</td>
<td>42</td>
<td>44</td>
</tr>
<tr>
<td>Pullen, Sara</td>
<td>Chronic Pain Management and Opioid Reduction Among Adults Living With HIV: An Innovative Physical Therapy Intervention</td>
<td>43</td>
<td>45</td>
</tr>
<tr>
<td>Alsen, Mathilda</td>
<td>The relationship between high risk behavior and HIV testing among older adults</td>
<td>44</td>
<td>46</td>
</tr>
<tr>
<td>Quigley, Adria</td>
<td>Evaluating the Impact and Feasibility of a Yoga Intervention on Cognition and Balance in People Living with HIV: A Randomized Pilot Trial</td>
<td>45</td>
<td>47</td>
</tr>
<tr>
<td>Mayo, Nancy</td>
<td>Development of an HIV-Specific Cardio-Vascular Health Status Measure</td>
<td>46</td>
<td>48</td>
</tr>
<tr>
<td>Cummins, Denise</td>
<td>A collaborative approach to develop a community based model of care to identify people living with HIV who may be at risk of developing HIV associated neurocognitive disorder.</td>
<td>47</td>
<td>49</td>
</tr>
<tr>
<td>Stafford, Adam</td>
<td>The SAGE Clinic: The introduction of a new HIV frailty service at our London centre</td>
<td>48</td>
<td>50</td>
</tr>
<tr>
<td>Milić, Jovana</td>
<td>FRAILTY INDEX (FI) AND AGE PREDICT NEUROCOGNITIVE FUNCTIONING IN A REAL LIFE LARGE PROSPECTIVE HIV+ COHORT</td>
<td>49</td>
<td>51</td>
</tr>
<tr>
<td>Paolillo, Emily</td>
<td>Older age exacerbates negative effects of HIV and binge drinking on neurocognitive functioning</td>
<td>50</td>
<td>52</td>
</tr>
<tr>
<td>Chow, Wing</td>
<td>The Burden of Neuropsychiatric Conditions in Patients Living with HIV-1 Treated with Antiretroviral Therapies – A Perspective from US Medicaid</td>
<td>51</td>
<td>53</td>
</tr>
<tr>
<td>Plaza-jennings, Amara</td>
<td>Integrated HIV Persists in Brain Nuclei of an Elderly Woman with 20 Years of Therapy-Induced Viral Suppression</td>
<td>52</td>
<td>54</td>
</tr>
<tr>
<td>Brouillette, Marie-Josée</td>
<td>Head-to-head comparison of classifications of cognitive impairment for explaining presentism among HIV+ workers in the Positive Brain Health Now (PBHN) aging Canadian cohort</td>
<td>53</td>
<td>55</td>
</tr>
<tr>
<td>Castaneda, Gloria</td>
<td>Feedback-related negativity shows promise as an electrophysiological marker of apathy in older men living with HIV.</td>
<td>54</td>
<td>56</td>
</tr>
</tbody>
</table>
Resting state EEG is more sensitive than structural MRI to the brain changes underlying cognitive performance in people living with HIV

Clinical information about immune activation does not explain depression, cognition, fatigue or motivation in older men with HIV: results from the Positive Brain Health Now Canadian cohort

<table>
<thead>
<tr>
<th>Name</th>
<th>Abstract title</th>
<th>Abstract #</th>
<th>Page #</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fernandez Cruz, Ana Lucia</td>
<td>Resting state EEG is more sensitive than structural MRI to the brain changes underlying cognitive performance in people living with HIV</td>
<td>55</td>
<td>57</td>
</tr>
<tr>
<td>Matout, Mohamad</td>
<td>Clinical information about immune activation does not explain depression, cognition, fatigue or motivation in older men with HIV: results from the Positive Brain Health Now Canadian cohort</td>
<td>56</td>
<td>58</td>
</tr>
<tr>
<td>Derry, Heather</td>
<td>Gait speed is associated with cognitive function among older adults with HIV</td>
<td>57</td>
<td>59</td>
</tr>
<tr>
<td>Sawaya, Bassel E</td>
<td>HIV-1 gp120 and Spatial Memory Impairments: Role of CREB protein</td>
<td>58</td>
<td>60</td>
</tr>
<tr>
<td>Quitos, Leonell Albert</td>
<td>Assessment of the Health-Seeking Behavior of People Living with Human Immunodeficiency Virus (PLHIV) Enrolled in a Treatment Facility in a Tertiary Hospital</td>
<td>59</td>
<td>61</td>
</tr>
<tr>
<td>Arjona, Sterling</td>
<td>Disruption of MAM in premature brain aging and HIV-associated neurocognitive disorders (HAND)</td>
<td>60</td>
<td>62</td>
</tr>
<tr>
<td>Coyle, Ryan</td>
<td>Tenofovir-diphosphate in dried blood spots is associated with HIV-related aging factors</td>
<td>61</td>
<td>63</td>
</tr>
<tr>
<td>Tan, Judy</td>
<td>FOOD INSECURITY AND NEUROCOGNITIVE FUNCTION AMONG WOMEN LIVING WITH HIV IN THE U.S.</td>
<td>62</td>
<td>64</td>
</tr>
<tr>
<td>Ye, Yuanfan</td>
<td>Statin Use Is a Major Risk Factor for Type 2 Diabetes Mellitus in PLWH</td>
<td>63</td>
<td>65</td>
</tr>
<tr>
<td>Wasserman, Peter</td>
<td>Low social support prevalent in midlife and older Human Immunodeficiency Virus-positive men who have sex with men attending an urban clinic.</td>
<td>64</td>
<td>66</td>
</tr>
<tr>
<td>Dobbins, Sarah</td>
<td>Depression is associated with low CD4:CD8 T-cell ratio among PLWH over 55 with mild cognitive impairment</td>
<td>65</td>
<td>67</td>
</tr>
</tbody>
</table>