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Abstracts

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Mood disorders and risk of non-communicable disease multi-morbidity among aging adults living with HIV

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Background: As persons living with HIV (PLHIV) age, accumulating ≥ 2 non-communicable diseases (NCDs), or multi-morbidity, is common. Multi-morbidity is associated with poly-pharmacy, functional decline, and increased healthcare utilization. The mood disorders of major depression and bipolar affective disorder (BPAD) are prevalent among PLHIV and are associated with increased NCD risk in the general population. The relationship between mood disorders and multi-morbidity in aging PLHIV is poorly understood.

Material & Methods: PLHIV attending the Vanderbilt Comprehensive Care Clinic in Nashville, Tennessee, between 1998-2015 contributed data. As onset date for mood disorders is imprecise in medical records, we included only patients with ≥ 1 year of follow-up and used one year after clinic entry date as baseline. Exposed patients had a documented mood disorder diagnosis during the year before baseline. Outcomes were defined by NCD diagnoses: coronary artery disease, chronic kidney disease, cerebrovascular disease, diabetes, dementia, hepatic disease, hyperlipidemia, hypertension, obesity, peripheral vascular disease, and non-AIDS-defining cancers. We also examined metabolic syndrome defined as: ≥ 3 of hypertension, hyperlipidemia, diabetes, and obesity. We used multivariable competing risk (death) models to estimate the cumulative incidence functions and adjusted sub-hazard ratios (sHR) of incident NCDs and multi-morbidity. We used Cox regression to estimate adjusted hazard ratios (HR) for mortality after multi-morbidity. Multivariable models also included sex, race, prevalent NCD, hepatitis C co-infection, substance use, tobacco use, alcohol use, and time-updated CD4 cell count (CD4), CD4/CD8 ratio, and HIV RNA.

Results: Of 4,140 adults contributing 24,686 person-years, 999 (24%) had a mood disorder. Mood disorder patients were statistically older at baseline (40 vs. 39 years) and were more likely to be female (27 vs. 22%),

of white race (68 vs. 48%), to report a history of injection drug use (12 vs. 10%), and to report prior/current tobacco use during follow-up (62 vs. 47%). At baseline, CD4 and CD4/CD8 ratio were similar by exposure status, though mood disorder patients were less likely to have HIV RNA < 400 copies/mL (57 vs. 61%) and were more likely to have ≥ 1 (57 vs. 48%) and ≥ 2 NCDs (27 vs. 21%). A higher proportion of mood disorder patients died (15 vs. 13%). The most frequent NCDs were hypertension (40% of patients), obesity (35%), and hyperlipidemia (34%). Overall, 470 mood disorder patients (47%) and 1219 (39%) non-mood disorder patients had NCD multi-morbidity. Mood disorders were significantly associated with incident NCDs (sHR=1.30, 95% confidence interval [CI]: 1.07-1.58). However, multi-morbidity risk was attenuated for ≥ 2 NCDs (sHR=1.05, 95%CI: 0.87-1.26), ≥ 3 NCDs (sHR=1.13, 95%CI: 0.92-1.38), and ≥ 4 NCDs (sHR=1.21, 95%CI: 0.94-1.55). Mood disorders were significantly associated with metabolic syndrome risk (sHR=1.28, 95%CI: 1.01-1.63), which persisted when adjusted for psychiatric medication exposure. Increased mortality risk following ≥ 2 NCDs by mood disorder status was not significant (HR=1.11, 95%CI: 0.78-1.59).

Conclusions: PLHIV with mood disorders are at increased risk of incident NCDs and may be at increased risk of NCD multi-morbidity, particularly metabolic syndrome. Focused prevention and treatment of NCDs in PLHIV with mood disorders may reduce the burden of multi-morbidity in this high-risk group.

2

Aging with HIV: I'm fine, thanks for asking

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Background: Much attention is being paid to frailty in people aging with HIV. Less attention is paid to those doing “well – thank you” yet much could potentially be learned from those doing well.

Objective: The purpose of this study is to describe the profile of people who are aging well with HIV to identify factors that place people at promise for aging well.

Methods: Data from the inaugural visit for people enrolled in the Brain Health Now cohort were analyzed cross-sectionally. Aging well was measured using the 8 subscales of the SF-36, a well-known and widely used measure of the health aspects of quality of life: Physical Function (PF), Pain, Vitality (VIT), Social Function (SF), Role Physical (RP), Role Emotional (RE), Mental Health (MH) and one question from General Health Perception (GHP) for self-rated health. Normative data from the Canadian population was used to classify people at or above norms for age and sex on each sub-scale. People with data on all these measures so classified on 7 or 8 of the 8 subscales were defined as aging well. Promise factors covered domains of socio-demographic, HIV, co-morbidity, life-style, social support, loneliness, stigma, and cognition.

Results: A total of 806 people, out of the original cohort of 856 persons (mean age 53; range 35 to 81 years), had all the data necessary to be classified as aging well (685 men and 121 women). The most common health profile (n=154; 19%) is none of the SF-36 subscales at norm. The second most common profile is all at norm (n=59; 7%). The third most common profile is only PF at norm (n=43; 5%). A total of 113 people met our aging well criteria (14%), 97 men and 16 women. Variables

unrelated to aging-well status were age, sex, Nadir CD4, BMI, current smoking, cardiovascular risk, and hours of engagement in meaningful activities. Variables showing promise for aging well were university education, having friends or family, social drinking, not being lonely, low stigma, better cognitive performance, fewer self-reported cognitive concerns, being vigorously active, and lower levels of inflammation (CRP).

Discussion: While it is not possible with this cross-sectional view to sort out the “chicken or the egg”, many of the promise factors are early life-course variables (education, friends, physical activity and inflammation), while others are more likely to contribute to aging well (stigma, loneliness, cognition) rather than being a consequence. Maintaining physical activity, cognition, and social network are three variables showing promise for aging well with HIV.

This study showed that 14% met our criteria for “superstar” status, this is in contrast to only 8% meeting criteria for frailty. Focusing on people aging well with HIV could be a fruitful avenue to explore to not only promote successful aging with HIV but also to identify ways of preventing or arresting frailty.

3

Exercise-Induced Inflammatory Changes among Older Adults with and without HIV

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Background: Regular physical activity has numerous health-related benefits, including lower levels of inflammation. Although we have previously shown greater physical function benefits with higher intensity exercise, some studies suggest that higher intensity exercise may exacerbate inflammation among people with chronic inflammation, while lower intensity exercise may lower inflammation. The effects of exercise intensity on inflammatory markers among older adults with HIV (PLWH) is unknown.

Materials and Methods: PLWH and uninfected controls, aged 50-75 were enrolled in a 3 times/week supervised cardiovascular and resistance exercise program. After 12 weeks of moderate intensity exercise, participants were randomized to continue moderate or advance to high-intensity exercise for an additional 12 weeks. Serum and plasma levels of IL-6, TNF-alpha, soluble TNF receptor (sTNFR) 1/2, CRP, sCD14, intestinal fatty-acid binding protein (iFABP), and IL-10 were analyzed pre-intervention, and at 24 weeks of exercise. Additional samples were analyzed at week 12 for IL-6, TNF-alpha and sTNFR1. Mixed and multiple regression models were adjusted for baseline level of the inflammatory marker, age and BMI. Inflammatory data were log transformed and results are reported as percent differences from baseline (mean [95% CI]). Outcomes were considered complimentary, with no adjustment for multiple comparisons.

Results: Of 69 participants (32 PLWH, 37 Controls), the mean age was 57.8 (SD 6.4) years, BMI 28.7 (SD 4.8)kg/m², and the majority were male (91%). At

baseline, PLWH had higher levels of inflammation than Controls: IL-6 (34 [3,74]%, p=0.033), CRP (103 [28,223]%, p=0.004), sCD14 (17 [2,33]%, p=0.026), sTNFR2 (29 [4,60]%, p=0.022), and iFABP (113 [19,281]%, p=0.014). Between 0 and 12 weeks, decreases from baseline levels were observed in IL-6 (controls: -14 [-25,0.5]%, p=0.058) and in sTNFR1 (PLWH: -5 [-9,-0.9]%, p=0.02). Between 0 and 24 weeks, significant increases were observed for a subset of markers by HIV serostatus: sCD14 (PLWH: 8 [2,14]%, p=0.014, controls: 11 [5,17]%, p<0.001), IL-10 (controls: 66 [18, 134]%, p=0.005). Between 0-24 weeks, decreases in iFABP (-51 [-75,-2]%, p=0.045) were seen in PLWH. Changes in inflammatory markers did not differ between PLWH and controls (p>0.11). By exercise intensity (between 0-24 weeks), significant differences were observed among those randomized to high-intensity exercise : CRP (-24 [-41,-2]%, p=0.033) and sCD14 (14 [8,19]%, p<0.001); compared to those randomized to moderate intensity, the CRP was 30% lower ([2,-51]%, p=0.062) and sCD14 8% higher ([0,16]%, p=0.043) among those randomized to high-intensity exercise. Finally, a 10% increase in adherence to exercise was associated with a 5% ([1,9]%, p=0.018) lower IL-6 level and 42% ([21,63]%, p=0.002) lower CRP at 24 weeks.

Conclusions: Overall, despite higher baseline inflammation among PLWH, an exercise intervention did not significantly decrease inflammatory markers. Similar responses were seen in both PLWH and uninfected controls. Increases in sCD14 across both arms raise questions regarding the role of monocyte activation and changes in gut permeability with exercise. Lastly, significant increases in IL-10 (an anti-inflammatory cytokine associated with exercise) among uninfected controls but not PLWH suggests a need for additional investigation into anti-inflammatory cytokine responses in older PLWH.

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The Impact of Number of Medications on Falls in Aging Persons Living with HIV

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Background: Despite heightened awareness of aging complications in persons living with HIV (PLWH), the risk factors for falls among HIV-infected adults remain incompletely described. This study describes the impact of number of medications on falls in aging PLWH.

Methods: PLWH at least 50 years of age who were seen at our institution from September 2012 to August 2017 were included in a retrospective analysis. Unique participants meeting inclusion and exclusion criteria were selected for either a case or control cohort depending on presence of a documented fall. Characteristics of the two cohorts were compared using chi-square for categorical variables and student's t-test for continuous variables. Logistic regression was performed using variables that were significant in the univariate analysis.

Results: Fall was documented for 643 patients compared to 1,565 without a fall during the same time period. There was no difference between the two cohorts based on race, ethnicity, CD4 count, or viral load at the time of fall. In the univariate analysis, being older (mean 59.0 vs. 57.5, $p < 0.0001$), female gender (17.1% vs. 10.3%, $p < 0.001$), taking a higher total number of medications (mean 11.2 vs. 7.5, $p < 0.001$), and taking a higher number of antiretrovirals (ARVs) (mean 3.8 vs. 3.3, $p < 0.0001$) were associated with falls. All variables remained significant in the multivariate analyses with female gender resulting in the highest odds of a fall (OR 1.56, 95% CI 1.18-2.05). Each additional medication taken increased the odds of a fall by nearly 10% (OR 1.09, 95% CI 1.07-1.11).

Conclusions: In this cohort, older age, female gender, total number of non-ARV medications, and total number of ARVs, was associated with having a fall. These results demonstrate the clinical impact of polypharmacy on aging PLWH. Future studies evaluating the impact of de-prescription should be considered in aging PLWH with a greater number of

ARVs or overall greater number of medications in order to prevent harmful outcomes.

Key Words: Polypharmacy, Falls, Aging, HIV

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Muscle mitochondrial function and contemporary anti-retroviral therapy

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Background: Despite ART, some people living with HIV (PLWH) exhibit reduced physical function or frailty. The underlying pathological mechanisms remain poorly understood. Maintenance of normal mitochondrial function in skeletal muscle is important in healthy ageing. We therefore investigated whether PLWH on contemporary ART have evidence of mitochondrial dysfunction.

Methods: Tibialis anterior biopsies were obtained from 37 PLWH: 13 ART naïve, and 24 ART treated. All treated subjects were currently exposed to contemporary NRTIs (TDF, ABC, 3TC, FTC), but 14 also had past exposure to older NRTIs known to be associated with mitochondrial DNA (mtDNA) damage (AZT, d4T, ddI, ddC).

Multiplex immunofluorescence was performed on 10µm cryo-sections with automated quantification of the abundance of mitochondrial respiratory chain complexes I and IV (CI, CIV) and mitochondrial mass within individual myofibres. Quantitative PCR using the MT-ND1/MT-ND4 multiplex assay was then performed on individual myofibres severely deficient (z score <-6), deficient (z<-3) and positive for mitochondrial complexes I (CI) and IV (CIV).

Results: Mean age was 48 years. A mean of 1229 myofibres were analysed per subject.

Compared with ART naïve (group 1), subjects with past exposure to older NRTIs (group 3) showed a significantly higher proportion of myofibres deficient in CI (p=0.01) and CIV (p=0.004). Subjects with exposure to only contemporary ART (group 2) also showed a deficiency of CI (p=0.05) but not CIV. This pattern was also true of severely deficient fibres. Subjects in group 3 had a significantly higher proportion of myofibres severely deficient in CI (p<0.0001) and CIV (p=0.04) compared to group 1, while group 2 had a trend towards higher proportion of myofibres severely deficient in CI (p=0.08) but not CIV. Preliminary molecular analysis of individual myofibres suggests that this deficiency in mitochondrial

electron transport chain complexes is caused by deletions in mtDNA.

There were no associations between mitochondrial defects and age, current or nadir CD4 count, or duration of diagnosed HIV infection or ART (after controlling for type of NRTI exposure).

Conclusions: Automated multiplex immunofluorescence is a reliable tool for the objective quantification of mitochondrial defects in skeletal muscle of PLWH.

As expected, mitochondrially deficient myofibres were most abundant in subjects with exposure to historical NRTIs. Surprisingly however, PLWH who only had exposure to contemporary ART showed intermediate levels of mitochondrial defects.

Future studies should confirm these observations in larger numbers of subjects and explore their relevance for physical function. Furthermore, we show for the first time that affected myofibres are predominantly deficient in CI, which is of relevance for potential therapeutic interventions.

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Metabolic Syndrome is Associated with Neurocognitive Deficits in Persons Living with HIV

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Background: Metabolic syndrome (MetS) is a cluster of metabolic abnormalities associated with an increased risk of developing cardiovascular or cerebrovascular disease. Among HIV-uninfected (HIV-) persons, the presence of MetS has been associated with worse neurocognitive functioning. Regardless of HIV serostatus, components of MetS have been linked to neurocognitive impairment; however, the impact of MetS, as a whole, on neurocognitive impairment in persons living with HIV (PLHIV) has not been sufficiently explored.

Our aims were to examine the association between MetS and neurocognitive deficits among persons with and without HIV, and to assess the potential modifying role of HIV serostatus on this association. We hypothesized the association between MetS and neurocognitive deficits would be stronger among PLHIV than HIV- persons. A secondary aim was to further examine the association between MetS and neurocognitive deficits among PLHIV, after considering the impact of other HIV disease factors. We hypothesized that, even after accounting for these covariates, the association between MetS and neurocognitive deficits would remain significant.

Materials & Methods: Participants included 109 PLHIV and 92 HIV- persons participating in the Multi-Dimensional Successful Aging cohort study at the University of California, San Diego. Participants completed comprehensive neuromedical, psychiatric, and neurocognitive assessments. Our main outcome was the global deficit score (GDS), which captures the severity of neurocognitive deficits across 15 neurocognitive tests assessing seven domains. MetS was assessed via standard criteria and determined by the presence of three or more of the following:

abdominal obesity, elevated serum triglycerides, low high-density lipoprotein cholesterol, elevated blood pressure, and elevated glucose. Examined covariates included demographics, psychiatric comorbidities, and HIV disease characteristics in models within PLHIV.

To examine if HIV status modified the association between MetS and neurocognitive deficits, we modeled GDS in a multivariable linear regression analysis using as predictors: HIV, MetS, HIV x MetS interaction, and significant covariates (determined via univariable analyses for their association with GDS). To further investigate the association between MetS and GDS among PLHIV, a multivariable linear regression analysis was used with MetS and significant covariates as predictors.

Results: Rates of MetS were nearly two-times higher among PLHIV than HIV- participants. In the overall sample, a multivariable linear regression analysis on GDS with HIV status, MetS, their interaction, and significant covariates (i.e., estimated premorbid functioning/quality of education) as predictors showed a marginally significant HIV by MetS interaction ($p=.07$). Follow-up analyses stratified by HIV status showed that MetS was significantly associated with GDS among PLHIV (Estimate=0.22, SE=0.10, $p=.03$), but not HIV- persons (Estimate=-0.01, SE=0.09 $p=.93$). Among PLHIV, a multivariable model of GDS showed that MetS continued to be significantly associated with GDS ($p<.05$) even after accounting for significant covariates (i.e., estimated premorbid functioning/quality of education and nadir CD4).

Conclusions: MetS, a cluster of metabolic abnormalities, is significantly associated with global neurocognitive deficits among PLHIV. These findings underscore the need for early identification of PLHIV at risk for MetS, and the implementation of preventive and treatment approaches to lessen the development of MetS and its potential impact on neurocognitive impairment among PLHIV.

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Hepatic Steatosis Is Common in Both Younger and Older Adults Living with HIV and Associated with Divergent Immuno-Metabolic Profiles

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Background: Fatty liver disease is believed to be common in people living with HIV (PLWH), but the prevalence, risk factors and biomarkers of disease are not well defined, including differences by age.

Methods: PLWH (n=160) were enrolled in a cross-sectional study of FibroScan[®] with controlled attenuation parameter (CAP) and liver stiffness measurement (LSM), medical record review and circulating immuno-metabolic biomarker measurement (ELISA or Luminex platform). Quantile regression determined factors associated with CAP and LSM values. Subset analyses compared differences in older (age ≥50 years) vs younger participants.

Results: Participants were 58% male, 31% female and 11% transgender women; mean age 51 years, BMI 29 kg/m², CD4 T cell count 640 cells/mm³, time with HIV 14 years, and time on HIV treatment 9 years. Mean (standard deviation, SD) CAP and LSM were 260 (49) dB/m and 5.8 (4.3) kPa. In multivariate analyses, higher CAP values were significantly (p<0.05) associated with Hispanic ethnicity and higher BMI (trend for higher triglycerides, p=0.09), but not age. Higher LSM values were associated with higher BMI and AST levels, and active hepatitis B virus (but not current/past hepatitis C virus) co-infection (trend for lower CD4 T cell count, p=0.07), but not age.

39% of older patients met criteria for significant hepatic steatosis (CAP >260 dB/m) vs 49% of younger patients. Compared to younger patients with hepatic steatosis (n=38, mean age=42), older participants (n=35, mean age=59) with hepatic steatosis were more likely to be female, Black and have a diagnosis of hypertension or cirrhosis (all p<0.05), and had longer time with HIV infection (16 vs 12 years) and on ART (12 vs 7 years).

CAP and LSM scores were similar for older (CAP 256 [51] dB/m, LSM 6.1 [5.5] kPa) vs younger (CAP 266 [51] dB/m, 5.4 [2.4] kPa LSM) participants with NAFLD, as were mean BMI and circulating biomarker levels. Older participants with hepatic steatosis were more likely to be obese (BMI 33 vs 27 kg/m², p<0.0001) and have higher Fetuin A levels (906 vs 677 ng/mL, p<0.0001) than older participants without hepatic steatosis (n=55), with trends towards increased frequency of Hispanic ethnicity, cirrhosis diagnosis and triglyceride levels, but less prevalent cardiovascular disease, observed among older participants with hepatic steatosis compared to older PLWH without steatosis (p≤0.10).

Conclusions: In this convenience sample of PLWH, hepatic steatosis by CAP was very common among both older (≥50 years old) and younger adults. Among older PLWH, obesity was the major clinical factor associated with a diagnosis of hepatic steatosis. Obesity prevention and treatment among both younger and older adults is imperative in preventing the development of hepatic steatosis with advancing age.

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Memory loss: T cell subsets associated with mortality in HIV+ and HIV- veterans

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Introduction: Chronic cellular immune activation is a hallmark of HIV infection. The relative depletion of naïve CD4+ and CD8+ T cells and the expansion of memory cell subsets, including pro-inflammatory effector memory (TEM) and effector memory RA+ (TEMRA), are associated with increased risk of cardiometabolic diseases in the general population, but there are fewer data on health outcomes among HIV-infected (HIV+) individuals.

Purpose of the Study: We assessed whether the proportional size of the naïve, activated, memory, TEM and TEMRA compartments was associated with subsequent mortality in HIV+ versus uninfected (HIV-) persons.

Methods: We analyzed data on 1089 subjects (684 HIV+ and 405 HIV-) from the Veterans Aging Cohort Study – Biomarker Cohort, a prospective, longitudinal study of HIV+ veterans and age-, sex-, race/ethnicity- and clinical site-matched HIV- veterans. VACS BC archived peripheral blood mononuclear cells from study subjects in 2005-2007 (defined as baseline). We performed flow cytometry to measure the proportion of 10 classes of CD4+ and CD8+ T cells: naïve, activated CD38+, memory CD45RO+; TEM cells CD45RO+CD28-, and TEMRA cells CD45RA+CD28-CD57+. Deaths occurring through September 30, 2015 were ascertained from the medical record and death certificates. We compared the median baseline proportions of T cell subsets among subjects who subsequently died versus those who remained alive, stratified by HIV status, using Mann-Whitney U tests.

Results: Subjects were predominantly male (95%) and African-American (68%). Among the measured subsets, naïve CD4+ and memory CD8+ T cells were lower in both the HIV+ and HIV- persons who died during follow-up ($p \leq 0.04$ for all). However, HIV+ persons who died also had lower CD4+CD45RO+ memory T cells (40.0% in

deceased vs. 47.7% in alive, $p < 0.001$) and higher CD4+ TEMRA cells (5.5% vs. 4.4%, $p = 0.02$) at baseline, but these associations were not observed in the HIV-. Furthermore, if CD4+ TEMRA cells were alternately defined as CD4+45RA+CD27-, the mortality difference among the HIV+ persons was consistent (4.0% in deceased vs. 2.8% in alive; $p = 0.007$). Of note, the median percentage of CD4+ TEMRA cells at baseline was approximately 2-fold higher in the HIV+ group compared to the HIV- group among persons aged <45 (5.5% vs. 2.0%), 45-55 (4.2% vs. 2.2%), and >55 (4.8% vs. 2.7%, $p < 0.0001$ for all).

Conclusions: In both HIV+ and HIV- veterans, the depletion of naïve CD4+ cells, possibly reflecting accelerated immunosenescence, was associated with higher risk of death as previously reported. CD4+ TEMRA cells, defined according to two common surface marker phenotypes, were 2-fold higher in HIV+ compared to HIV- persons, and in the HIV+ group CD4+ TEMRA cells were high

Effects of Comorbidity Burden and Age on Brain Integrity in HIV

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Aim: Persons living with HIV (PLWH) represent a clinically heterogeneous population vulnerable to central nervous system injury due to HIV as well as to comorbid conditions, including those that occur with aging. HIV-associated neurocognitive disorders (HAND) criteria require that neurocognitive impairment be attributable, at least in part, to HIV disease but not primarily to comorbid conditions. Although greater comorbidity burden increases risk for neurocognitive impairment, the relationship between comorbidity severity, aging, and brain integrity remains unclear. We hypothesized that among PLWH, a) greater comorbidity burden and older age would independently be associated with greater abnormalities on magnetic resonance spectroscopy (MRS) and structural brain imaging, and b) older age would exacerbate the deleterious influence of comorbidity burden.

Methods: 288 PLWH [age=44.2 (7.74)] underwent structural MRI and MRS to assess volumes of cortical and subcortical gray matter, total cerebral white matter, and abnormal white matter along with metabolite levels in the basal ganglia (BG), frontal white matter (FWM), and frontal gray matter (FGM). Participants also underwent neuromedical and neurocognitive assessments. Each case was reviewed by a senior clinician (R.K.H.) to determine whether neuromedical and neuropsychiatric comorbidity burden was incidental (normal/mild), contributing (moderate), or confounding (severe) to a diagnosis of HAND. Comorbidity group comparisons of demographic, clinical, and neurocognitive data were conducted using analysis of variance or chi-square tests. Multiple regression modeling predicted neuroimaging outcomes as a function of comorbidity group, age (continuous), and their interaction.

Results: Comorbidity classifications were 176 (61%) incidental, 77 (27%) contributing, and 35 (12%) confounding. As expected, these groups differed in multiple demographic and clinical characteristics (e.g., confounding participants displayed the lowest education and estimated premorbid verbal IQ, the highest rates of neurocognitive impairment and lifetime substance use disorders), although they did not differ in HIV disease characteristics. Relative to incidental and contributing groups, the confounding group had smaller cortical and subcortical gray matter volumes, larger abnormal white matter volume, and in FWM and BG, more neuroinflammation (choline, myo-inositol) and less neuronal integrity (N-acetylaspartate: $p < .05$). Older age increased the impact of comorbidity burden: the confounding group had larger abnormal white matter ($p = .017$), smaller total white matter ($p = .015$), and smaller subcortical gray matter ($p = .014$) volumes with increasing age. In contrast, older age was associated with less cortical gray for incidental ($\beta = -.26$; $p < .001$) and contributing ($\beta = -.19$; $p < .001$) groups, while confounding participants displayed low cortical gray matter volumes at a younger age and demonstrated no further age-related effect ($\beta = -.04$; $p = .644$).

Conclusions: Greater comorbidity burden is associated with greater brain abnormalities in PLWH, including evidence of neuroinflammation and reduced neuronal integrity in cortical, subcortical, and white matter tissues. Findings support the importance of including comorbidity classifications during HAND diagnostic decision-making. Metabolic and structural brain alterations present in PLWH with substantial comorbidity burden may reflect HIV-related neural injury coupled with distal (e.g., neurodevelopmental disabilities) and/or proximal (e.g., stroke, overdose) neural insults. Older age amplifies these subcortical and white matter effects beyond typical brain aging in PLWH with severe comorbidity burden, warranting increased clinical attention to this population as it ages.

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Persistent Pro-Inflammatory HIV-mediated Glycomic Alterations Associate with Neurological Impairment During Suppressive Therapy.

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Background: A comprehensive understanding of the pathophysiological mechanisms driving HIV-associated chronic inflammation can lead to the development of strategies to delay or prevent age-associated comorbidities that are increasingly prevalent despite suppressive antiretroviral therapy (ART). Glycans on circulating glycoproteins and antibodies are known to modulate systemic inflammatory responses and are closely linked to both chronological and biological age in the general population. However, whether HIV-associated chronic inflammation, at least in part, is promoted by alterations in the host glycome remains unknown.

Methods: Using capillary electrophoresis and a lectin array, we profiled the glycomes of plasma and immunoglobulin G (IgG) from n=40 chronic HIV+ individuals (ART-suppressed and viremic) and n=10 age/gender-matched HIV- controls, including a subset of ART-suppressed individuals with variation in levels of HIV associated cognitive impairment as measured by clinical global deficit scores (GDS). We also measured levels of 16 pro- and anti-inflammatory cytokines, and markers of T-cell activation, using luminex and flow cytometry, respectively. Non-parametric Mann-Whitney U and Spearman's r tests were used for statistical analyses. False discovery rates (FDR) were computed to adjust for multiple comparisons.

Results: HIV infection was associated with persistent alterations in plasma and IgG glycomes, including

decreased levels of the anti-inflammatory sialylated glycans when compared to HIV- controls (FDR < 0.05). Levels of the highly-sialylated glycans in IgGs were reduced with age in HIV+ ART-suppressed individuals ($\rho = -0.72$, $p = 0.005$). When we investigated links between sialylated glycans and immune markers, we found that levels of specific plasma highly-sialylated glycans (A4G4S3) correlate with higher levels of CD4 T cell count ($\rho = 0.57$, $p = 0.03$), higher levels of CD4 T cell percentage ($\rho = 0.67$, $p = 0.01$), and lower levels of CD4+ T cell activation ($\rho = -0.66$, $p = 0.004$). We also found that levels of di-sialylated glycans on IgGs negatively correlate with levels of the pro-inflammatory cytokine TNF α ($\rho = -0.8$, $p = 0.0009$), and positively correlate with levels of the anti-inflammatory cytokine IL-10 ($\rho = 0.77$, $p = 0.019$). Finally, when we compared levels of glycan structures between HIV+ ART-suppressed individuals with and without cognitive impairment (with comparable CD4 count and nadir CD4, and viral load <50 copies/ml), we found that levels of seven glycan structures were statistically different between the two groups (FDR<0.05; tested using multiple linear regression with age added as an independent variable). When the levels of these seven glycan structures were correlated with GDS, we found that levels of hypo-sialylated oligosaccharides positively correlate with the degree of neurological impairment ($\rho = 0.84$, $p = 0.0001$).

Conclusions: Our data show that altered glycosylation patterns persist even after long-term suppressive ART, and suggest that lower levels of sialylated glycans, with documented anti-inflammatory roles, may contribute to immune activation, chronic inflammation, and the pathogenesis of combinatorial HIV- and age-associated co-morbidities affecting the central nervous system.

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The relationship between synaptodendritic neuropathology and HIV-associated neurocognitive disorders is moderated by age

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Background: Approximately 45% of people living with HIV (PLWH) develop HIV-associated neurocognitive disorders (HAND) in the era of effective antiretroviral therapy. Given the rising rates of older PLWH, it is important to determine whether older PLWH are more vulnerable to the effects of HIV disease processes on HAND. In this study, we examined whether age moderates the relationship between synaptodendritic neuropathology and cognitive performance and rates of HAND. We hypothesized that minimal to moderate levels of neuropathology would be more strongly associated with cognitive function in older versus younger PLWH, whereas severe neuropathology would be strongly associated with cognitive function regardless of age.

Methods: Analysis included 100 HIV-seropositive post-mortem cases (mean age=46.7, [SD=9.5], mean education=12.9 yrs [SD=2.8], 83% male, 66% White) who were enrolled in the National NeuroAIDS Tissue Consortium and were diagnosed as HAND or no HAND within one year of death. Synaptodendritic neuropathology was determined based on the density of (1) synaptophysin (SYP, a marker of presynaptic terminals) and (2) microtubule-associated protein-2 (MAP2, a marker of neuronal cell bodies and dendrites) immunoreactivity in sections of the frontal cortex. A composite score of SYP and MAP2 was divided into tertiles representing minimal, moderate and severe neuropathology. HAND was diagnosed according to Frascati criteria. We used Fisher's exact test to examine differences in HAND rates among neuropathology groups within older (≥ 50 years old; n=39) and younger (<50 years old; n=61) cases. In a subset of cases with demographically-corrected, standardized T-scores from 15 neuropsychological tests (N=77), T-scores were averaged to create a global T-score, and linear regressions were used to examine the interactive effect

of age and neuropathology group on global T-scores. Analyses were adjusted for relevant demographic and clinical factors (e.g., education, sex, estimated duration of HIV infection, CD4+ T-cell count).

Results: Among those with moderate and severe neuropathology, rates of HAND diagnoses were similar between younger (moderate: 87%, severe: 100%) and older cases (moderate: 87%, severe: 91%); however, among those with minimal neuropathology, older cases had rates of HAND that were higher than younger cases (61.5% vs. 28.5%, $p=.08$), although not significant, and similar to older cases with moderate neuropathology (61.5% vs. 86.7%, $p=.20$). Conversely, among younger cases, rates of HAND were lower in those with minimal versus moderate neuropathology (28.5% vs. 86.7%, $p=.001$). There was a significant age by neuropathology group interaction on global T-scores ($p=.04$), whereby the relationship between severe (versus minimal) neuropathology and poorer global T-scores was stronger among older ($B=-14.67$, $p=.001$) versus younger ($B=-5.59$, $p=.03$) cases. The comparisons of moderate versus minimal and moderate versus severe neuropathology with global T-scores did not differ by age group ($p's>.05$).

Conclusions: Findings indicate that age moderates the relationship between synaptodendritic neuropathology and neurocognitive performance. In the presence of minimal neuropathology, older PLWH are more likely to have HAND than younger PLWH. When severe neuropathology is present, almost all PLWH have HAND regardless of age; however, HAND may be more severe in older PLWH compared to younger PLWH.

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Associations of loneliness with cognitive function and quality of life (QoL) among older adults living with HIV

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Background: Loneliness, a perceived state of undesirable social isolation, is associated with adverse emotional and physical health outcomes. People living with HIV often face unique challenges that heighten their risk for loneliness and its consequences, including stigma, depression, substance use, lack of social connections, and physical symptoms related to HIV or comorbid conditions. Using a theoretical model supported from the literature, the purpose of this study is to estimate, among older adults living with HIV, the strength of the associations between loneliness and (i) factors hypothesized to contribute to loneliness and (ii) factors hypothesized to be consequences of loneliness.

Materials & Methods: Positive Brain Health Now is a prospective longitudinal cohort study conducted at five HIV outpatient clinics in Canada, enrolling participants aged ≥ 35 years diagnosed with HIV for ≥ 1 year. For this analysis, data collected from personal interviews, direct measurements, and self-report questionnaires at the first study visit were analyzed cross-sectionally. Loneliness was assessed by one item from the OARS Social Resource Scale: "Do you find yourself feeling lonely: quite often, sometimes or almost never?" Cognitive function was assessed using a computerized battery of cognitive tests (B-CAM) and the perceived deficit questionnaire (PDQ). Proportional odds regression and multiple linear regression were used to estimate the strength of the association between loneliness and brain and other health outcomes, adjusting for age, sex and education.

Results: Of 856 participants enrolled between 9/10/2013 and 8/6/2016, 836 responded to the loneliness question and were included in this analysis (85% men; mean age 52.0 years, SD 8.3). Almost 18% (n=148) said they "quite often" felt lonely and 46% (n=383) said they were "sometimes" lonely; these proportions did not differ between men and women. Factors associated with increased likelihood of loneliness ($p < 0.001$) were lower economic status, more HIV-specific symptoms, experiencing HIV-related stigma, restricted social network, lack of motivation (no plans or goals), pain, fatigue, poorer physical function, and less physical activity. Participants 35-45 years of age, those not working or volunteering, and those who watched more hours of television per week were more likely to report feeling lonely ($p < 0.05$). There was no association with smoking, alcohol consumption, marijuana use or use of most other drugs, except opioids which were associated with loneliness independently of pain ($p < 0.05$). In comparison to "never" feeling lonely, feeling lonely "sometimes" or "quite often" was consistently associated ($p < 0.001$) with poorer emotional and physical health outcomes including those reflecting cognitive ability, stress, depression, and anxiety, and those reflecting self-rated health, health-related QoL, and overall QoL.

Conclusions: In this cohort of HIV+ adults aged ≥ 35 years, 64% experienced loneliness "sometimes" or "quite often". The results support that physical symptoms (e.g. pain, fatigue), apathy, stigma, and restricted social network contribute to loneliness; and that loneliness has consequences for reduced activity, poor lifestyle choices, impaired cognition, stress, and depression, all of which contribute to poor quality of life. Interventions to engage people in socially in meaningful activities, shown to be effective for loneliness in other conditions, should be developed for older adults living with HIV.

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The relationship between amnestic mild cognitive impairment and biomarkers of inflammation among adults living with HIV

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Background: As people living with HIV (PLHIV) age, it becomes increasingly important to differentiate HIV-Associated Neurocognitive Disorders (HAND) from other common causes of neurocognitive impairment, such as Alzheimer's disease (AD) and amnestic mild cognitive impairment (aMCI). While aging is the greatest risk factor for AD, little is known about how aging in the context of HIV affects risk for AD/aMCI. HIV may influence AD/aMCI risk via inflammation, as both HIV infection and aMCI/AD are associated with higher levels of chronic, low-grade inflammation. Therefore, we classified PLHIV into HAND or aMCI groups and hypothesized that plasma biomarkers of inflammation would be highest in older PLHIV with aMCI.

Material & Methods: Analysis included 244 PLHIV (age range: 24-68, 86% male, 59% non-Hispanic white) on antiretroviral therapy with undetectable viral load (i.e., <50 copies/ml plasma). Participants completed comprehensive neurobehavioral and neuromedical evaluations. Three plasma biomarkers of inflammation (i.e., TNF- α , MCP-1, and IL-6) were measured by immunoassay, and all biomarkers were log-transformed. HAND was classified using Frascati criteria. We used an empirically-based neuropsychological diagnostic approach for aMCI (Jak/Bondi criteria) that was adapted to distinguish HAND from aMCI by focusing on recognition memory impairment which is characteristic of aMCI but not HAND. Participants that met criteria for aMCI, regardless of HAND classification, were classified into one aMCI+ group. Participants who were not classified as aMCI+ were separated into HAND (HAND+/aMCI-) and no HAND (HAND-/aMCI-) groups. Multinomial logistic regression modeling analyzed the relationship

between classification group and age. Multivariable linear regressions predicting inflammatory markers were used to examine the relationship among classification group, age, and inflammation. Comorbidities and demographic variables related to the outcome at $p < 0.10$ were included as covariates; age and sex were also included in models predicting inflammatory biomarkers.

Results: Using the articulated classification approach, 85 PLHIV were classified as aMCI+ (78% HAND), 66 HAND+/aMCI-, and 93 HAND-/aMCI-. Increase in age significantly increased the odds of being in the aMCI+ (odds ratio=1.05, $p=0.01$), but not in the HAND+/aMCI- group ($p=0.33$). There were no significant differences in inflammatory biomarkers (i.e., TNF- α , MCP-1, and IL-6) between the three classification groups (all p 's > 0.05). Separate multivariable models examined the associations between inflammatory biomarkers and classification group \times age (i.e., <50 vs. ≥ 50 years) interactions. The interaction term when comparing the aMCI+ group to the HAND+/aMCI- group in the model predicting TNF- α was significant, such that older aMCI+ PLHIV demonstrated higher TNF- α levels (suggesting more inflammation) than younger aMCI+ PLHIV ($\beta=0.05$, $p < 0.01$). When comparing the aMCI+ group to the HAND-/aMCI- group, however, the interaction was not significant ($p=0.16$). A similar trend was seen with the classification group \times age interaction in the aMCI+ group with MCP-1 ($p=0.08$), but not for IL-6.

Conclusions: These findings suggest that some inflammatory biomarkers are more strongly associated with older age in aMCI and may be a mechanism of aMCI particularly in the context of HIV. Longitudinal studies that include adults without HIV infection are needed to further examine biomarkers of inflammation and cognitive trajectories, such as conversion to aMCI or AD.

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Frailty Phenotype: A Clinical Marker of Age Acceleration in the older HIV-Infected Population

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Introduction: The HIV-infected population is aging nonhomogeneously. The identification of patients who are at risk of unhealthy aging has become relevant for the care of older HIV patients. Frailty is a geriatric syndrome that results from an age-associated decline. It has been proven to be related to worse clinical prognosis but with a chance of successful outcome if detected early. DNA methylation at specific genomic sites is a known epigenetic hallmark of accelerated aging. Age acceleration is a predictor of mortality, independently of health status, lifestyle, and genetic factors. An association between DNA methylation and frailty has already been assessed in the general population, but there are no data about this for the HIV-infected.

Aim: To evaluate the usefulness of frailty status as a simple clinical marker to identify age acceleration.

Methods: Frailty was assessed according to Fried's frailty phenotype. DNA methylation was analyzed on PBMCs at three previously described CpG sites from 10 frail patients and compared with 10 robust control patients, all with HIV. Predicted age was inferred using the formula implemented by Weidner: Predicted age (years) = 38.0 - 26.4 α - 23.7 β + 164.7 γ . Age acceleration was assessed using the difference between predicted and chronological age.

Results: We observed that HIV-infected frail patients had significantly higher biological predicted age than chronological age (mean age acceleration: 10.3 years; p = 0.012), whereas HIV-infected robust patients did not show acceleration (mean age acceleration: -0.67 years; p = 0.63).

Conclusions: Here, we link age acceleration and frailty in an older HIV population. This finding is important for

clinical practice because frailty can now be used as a clinical marker of accelerated aging and, consequently, for implementing specific approaches for older HIV frail patients.

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Correlation between HIV-Index (HIVI), Protective Index (PI) and frailty in an HIV ageing population.

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Background: Currently, the impact of HIV and protective social-environmental conditions on frailty in HIV ageing population is not known. Frailty can be operationalized as a deficit accumulation, building a scale which can be used to standardise accumulated deficits in order to estimate survival probability without reference to chronological age.

Aim of this study was to evaluate the relationship between frailty and HIV and social vulnerability using two health indexes previously developed by our group, HIV and Protective Indexes, (HIVI, PI).

Material and methods: This study was performed within the Modena HIV Metabolic Clinic (MHMC) prospective cohort. Frailty was evaluated with a 72-items frailty index (FI). All patients with a FI score ≥ 0.25 were considered frail. HIVI and PI were built using commonly recollected HIV and social vulnerability data. Multivariate linear and logistic models were used to evaluate predictors of frailty among all variables and Indexes.

Results: 1565 subjects were included. Mean age 53.15 \pm 8.03, 73.9% males. Mean FI was 0.19 \pm 0.08. Mean HIVI and PI were 0.48 \pm 0.17 and 0.63 \pm 0.14 respectively. Independent predictors of frailty were: CDC class (OR=2.20, $p < 0.001$), duration of HIV (OR=3.86, $p < 0.001$), time from diagnosis to initiation of ART (OR=1.65, $p = 0.002$), lipodystrophy (OR=1.86, $p = 0.001$), current CD4+ (OR=1.66, $p < 0.001$) and a higher HIVI score (OR=1.025, $p < 0.001$). Social protective factors were: higher years of education (OR=0.24, $p < 0.001$), white collar profession (OR=0.41, $p < 0.001$), higher income (OR=0.26, $p < 0.05$), no history of injective drug use (OR=0.49, $p < 0.001$), no smoking habit (OR=0.44, $p < 0.001$), physical activity (OR=2.94, $p < 0.001$) and a higher PI score (OR=0.972, $p < 0.001$).

Conclusion: Our work suggests that HIV and social vulnerability factors contribute to frailty in an HIV

ageing cohort. Interestingly, higher HIVI and lower PI scores correlate with frailty. Taking into consideration the medical and socioeconomic burdens affecting older people living with HIV, a more holistic approach to the assessment of global health and care must be favored, resorting to geriatric assessment tools even for patients who would not normally be classified as geriatric on the basis of their chronological age.

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How Different Are Invisible and Visible Disabilities in HIV?

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Background: HIV infection has evolved from an infectious disease to a chronic disease in the post-cART era. As people with HIV live into their senior years, they accumulate health challenges both from aging and from HIV. The typical manifestations of chronic diseases in older persons are under-studied in HIV. Disability is one of the results of aging and of living with a chronic disease, but these disabilities are not always visible.

Objective: The specific objective is to estimate the prevalence of impairments, activity limitations, and participation restrictions in people living with HIV and the effect of age and sex on these disabilities.

Methods: The data came from the Positive Brain Health Now study, a Canadian cohort of older people living with HIV. The BHN cohort was fully characterized on measures under the framework of the International Classification of Functioning, Disability, and Health model (ICF). Specific ICF model variables included physical, emotional, and cognitive impairments, capacity and performance in everyday activities, participation in usual activities and expected life roles, as well as personal and environmental factors. Binary indicators of these disabilities were generated based on self-reported problems and logistic regression was used to assess the contribution of age and sex to the frequency of disability.

Results: A total of 858 men and women (723 men, 135 women) were enrolled in the Brain Health Now study. The mean age of the men was 53.3 (SD:8.3) and the women was 50.5 (SD:7.5) years.

The prevalence of invisible disabilities (pain, fatigue, low mood, negative body image, low self-esteem, low sleep quality, and cognitive problems) ranged from 15% (negative body image) to 95% (any memory concerns). Other prevalent invisible disabilities were planning and organization challenges (55%), symptoms of depression and anxiety (38%), fatigue (32%), and pain (32%).

The prevalence of more visible disabilities (related to physical capacity, engagement in physical activities and usual roles) ranged from 4% (limitations in self-care activities) to over 42% for restrictions in social activities and over 66% for performing physically demanding activities. Of moderate level activities, the highest prevalence of disability was seen for climbing several flights of stairs (47%), bending, kneeling, or stooping (38%), lifting and carrying (30%).

The only significant differences in prevalence across age groups was for the oldest group, 60+, who had the lowest rates of invisible disabilities (other than pain) and the highest rates of visible disabilities. Women reported higher rates of disabilities, invisible or visible, than men.

Discussion: Although HIV is now a health condition that can be managed, disabilities remain prevalent and invisible disabilities are common. Regular screening for these invisible disabilities is warranted as they may not come to attention without direct query. The most prevalent visible disabilities are those related to more strenuous activities and indicate that the HIV population may be at risk for future disability arising from inactivity. As most of the disabilities are actionable, behavioural and rehabilitative interventions should be considered as part of front-line therapy to change this disability profile.

Abstracts

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Frailty Predicts Fractures Among HIV-infected and Uninfected Women: Results from the Women's Interagency HIV Study

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Background: Frailty is associated with numerous adverse outcomes among elderly HIV-uninfected persons, including falls, fractures, disability, and death. However the relationship between frailty and fracture risk in middle-aged HIV-infected women is unknown.

Material & Methods: Prospective longitudinal cohort study of 1332 HIV-infected and 532 uninfected women. We evaluated associations between baseline frailty status (defined as ≥ 3 of 5 Fried Frailty Index components: slow gait, reduced grip strength, exhaustion, unintentional weight loss, and low physical activity) and frailty components, with first and second incident fractures. Cox proportional hazards models determined predictors of time to first and second fracture; similar models evaluated frailty components.

Results: HIV-infected women were older (42 vs. 39 yr, $p < 0.0001$) and more often frail (14% vs. 8%, $p = 0.04$) than uninfected women; median follow-up was 10.6 years. Frailty was independently associated with time to first fracture in all women [adjusted hazard ratio, (aHR) 1.71, 95%CI: 1.30-2.26; $p = 0.0001$], and among HIV-infected women only (aHR 1.91, 95%CI: 1.41-2.58; $p < 0.0001$), as well as with time from first to second fracture among HIV-infected women only (aHR 1.92, 95% CI: 1.18 - 3.12; $p = 0.0091$). HIV infection was independently associated with time to first fracture (aHR 1.32, 95% CI: 1.02 - 1.70, $p = 0.035$), but not with time to second fracture.

In analyses of frailty components, exhaustion (aHR 1.60, 95%CI: 1.26-2.04, $p = 0.0001$), unintentional weight loss (aHR 1.44, 95%CI: 1.06-1.94, $p = 0.019$), and reduced grip

strength (aHR 1.35, 95%CI: 1.06-1.72, $p = 0.017$), were independently associated with time to first fracture in all women, as well as among HIV-infected women only [exhaustion (aHR 1.57, 95%CI: 1.20-2.07, $p = 0.0012$), unintentional weight loss (aHR 1.44, 95%CI: 1.03-2.01, $p = 0.032$), and reduced grip strength (aHR 1.36, 95%CI: 1.03 - 1.79, $p = 0.028$)]. Only exhaustion was associated with time from first to second fracture in all women (aHR 1.98, 95% CI: 1.34-2.93, $p = 0.0007$), and among HIV-infected women only (aHR 2.19, 95%CI = 1.35 - 3.46, $p = 0.0013$). HIV status was not significantly associated with time to fracture in models containing frailty components.

Conclusions: Frailty is a strong independent predictor of fracture risk among middle-aged women with or at-risk for HIV. As HIV-infected women continue to age, early frailty screening may be a useful clinical tool to identify those at greatest risk of fracture.

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Differences between older HIV-infected women and men regarding immunological recovery, comorbidity, physical function and quality of life

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Background: Despite a 20% of the persons living with HIV in developed countries are women few studies are focus on this specific group. HIV population is aging and the interest of the way it happens is growing up quickly but nothing is known about the specific characteristics of the older HIV-infected women neither if they have special needs.

Objectives: to evaluate differences between women and men within older HIV-infected population regarding HIV variables, comorbidity, physical function and quality of life.

Methods: Retrospective cohort study. Between June 15 2016 and May 15 2018, patients >50 years seen at the Modena HIV clinic were included in the study. They were stratified by gender. We recorded sociodemographic data, comorbidities, and variables related to HIV infection. We also recorded data on body composition (muscles mass) and on physical function using Short Physical Performance Battery (SPPB) and walking speed. Quality of life was measured by EQ5D5L.

Results: We evaluated 1126 older HIV-infected adults. 284 (25.2%) were women. Median age was 55 (IQR 53-59) years. Median Nadir CD4+ T-cell was 195 (IQR 88-296), , 76.6% were undetectable HIV RNA without significant differences between women and men. Median current CD4+ T-cell count was 758 (IQR 367) in women and 699 (IQR 356) in men (p 0.03). Mean CD4/CD8 ratio was [1.1 women vs 0.93 men (p 0.0001)]. The percentage of patients in B or C stage according to CDC classification was [57.8% women vs 52.4% men p 0.001]. History of AIDS wasting was [21.1% of the women vs 8.9% of the men (p0.0001)].

There were differences between women and men regarding: alcohol consumption [none 229(80.6%) vs

560(66.5%), mild or intense 55(19.4%) vs 282 (33.5%) p 0.0001], CVD [8(2.8%) vs 93(11%) p 0.0001], hypertension [110(38.7%) vs 508 (60.3%) p 0.0001], DM [33(11.6) vs 193(22.9%) p 0.0001], renal failure [94(33.1%) vs 151(17.9%) p 0.0001]. No differences between women and men were found regarding: physical activity, be smoker, dyslipemia, COPD, lipodistrophy, cirrhosis, vitamin D insufficiency, osteoporosis by DEXA, AIDS malignancy and no-AIDS malignancy. Women mean BMI was 23.4, men mean BMI was 24. 9. Sarcopenia was found in [117 41.2%] women vs 396 (47.1%) men (p 0.08)]. Regarding physical function there was significant differences in SPPB dichotomised as <9 or ≥ 9. SPPB <9 [31 (11.1%) in women vs 45 (5.6%) in men p 0.002] but there was not significant differences in walking speed between women and men (1.12m/s vs 1.07m/s p=0.3). EQ5D5L was 0.87 in women vs 0.89 in men [p 0.002]

Conclusions: In our cohort of older HIV-infected adults women represent one in fourth of the total patients. Despite the fact that women have better immunological recovery measured by CD4 T cell count and CD4/CD8 ratio, and less CVD and CV risk factors than men, their physical function and their quality of life are worse. So, older HIV-infected women have special characteristics and the assessment of physical function in this group seems to be crucial.

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Acute Exercise-Induced Inflammatory Response among Older Adults with and without HIV

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Background: Acutely, a single bout of exercise stimulates production and release of IL-6, independent of the TNF-alpha pathway. After repeated episodes of acute IL-6 elevation (chronic exercise training), a paradoxical reduction in the resting level of systemic inflammatory cytokines is seen. An exercise intensity that is too low may not generate great enough IL-6 stimulus acutely, and result in minimal to no decline in inflammatory cytokines over time. Alternatively, under certain conditions, (e.g., compromised immune function or heightened systemic inflammation), a high-intensity exercise may cause muscle damage, resulting in a maladaptive acute increase in TNF-alpha and an increase in chronic systemic inflammatory cytokines. Our goal was to measure inflammatory responses to a single bout of exercise early in training and following 24 weeks among older adults with and without HIV.

Materials and Methods: People with HIV (PLWH) and uninfected controls, aged 50-75 were enrolled in a 3 times/week supervised cardiovascular and resistance exercise program. After 12 weeks of moderate-intensity exercise, participants were randomized to continue moderate- or advance to high-intensity exercise for 12 additional weeks. Pre-training, and at weeks 12 and 24, blood was collected for IL-6, sTNFR-1, and TNF-alpha prior to and at 0, 60 and 90 minutes after a single, high-intensity exercise session. AUC was calculated for inflammatory levels post-exercise (relative to 0). Outcomes were log transformed and reported as % difference. Mixed models were adjusted for baseline, age and BMI. Outcomes were considered

complimentary, with no multiple comparison adjustment.

Results: Of 69 participants (32 PLWH, 37 Controls), with mean age 57.8 (SD 6.4), BMI 28.7 (4.8), the majority were male (91%). Pre-training, no statistically significant differences in maximum % change or AUC were observed in IL-6, sTNFR-1, or TNF-alpha by HIV serostatus ($p > 0.12$). Compared to pre-training, the maximum % change in IL-6 during an exercise bout was significantly lower at week 12 among all participants: -11 [-19,-2]%, $p = 0.021$, with no HIV effect (-6 [-23,14]%, $p = 0.52$). The maximum % change in TNF-alpha with after an exercise bout was significantly higher in PLWH than controls (23 [4,47]%, $p = 0.02$). Compared to controls, PLWH also tended to have greater sustained TNF-alpha levels immediately following exercise (AUC post-exercise) at week 12 (16 [-0.5,35]%, $p = 0.058$). All participants tended to have lower IL-6 AUC at week 12 compared to pre-training (-7 [-15,1]%, $p = 0.08$), with no HIV effect (1 [-15,19]%, $p = 0.92$). For participants in the high arm, change in TNF-alpha levels were 16% ([-2,31]%, $p = 0.08$) lower at 90 minutes post-exercise at week 24 than the moderate arm. Additionally, we found no significant differences in maximum % changes at week 24 by HIV serostatus for any marker ($p > 0.57$), no effect of exercise intensity on outcomes at week 24 ($p > 0.11$), no significant differences in sTNFR1 at week 12 or 24 by HIV serostatus or intensity ($p > 0.24$), and no significant difference in % change immediately post-exercise ($p > 0.10$).

Conclusion: During a single bout of exercise, PLWH had higher inflammatory response (TNF-alpha) in the initial training period, but differences were no longer seen after sustained training of 24 weeks.

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Aging Trends at a Large American Academic HIV Clinic

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Background: Overall, persons with HIV are living longer as a result of improving antiretroviral therapy. Further, people are being newly diagnosed with HIV at older ages. Together, this points to a possible increase in HIV clinics caring for greater numbers of older patients than earlier in the epidemic. Since the effect of chronological age can substantially impact HIV and non-HIV related disease processes, understanding the change in patient ages over time can help identify needs of large HIV clinics.

Objective: To determine age trends among persons with HIV in the UCSD Owen Clinic from 2000 to 2018, and evaluate illness severity among different age categories.

Methods: Using our electronic database, adult patients were categorized by age in 5 different years (2000, 2005, 2010, 2015 and 2018). To determine illness severity, the Veterans Aging Cohort Study Index (VACS Index) was calculated and number of medications prescribed per patient in 2018.

Results: From 2000 to 2018 the number of patients living with HIV in the Owen Clinic expanded from 1844 to 3251, and the mean age of patients rose by more than 8 years from 39.8 years to 48.6 years (ANOVA $p < 0.00001$) and the median age increased by 11 years from 39 to 50 years (trend $p < 0.00001$). Compared with the year 2000, the percentage of patients 50 years and older in 2018 grew from 12.5% to 52.1%. The number of patients 65 years and older has risen by more than 1000% (from 19 to 246) since 2000. Similar age trends were observed across men and women, and all races. The median VACS Index for patients under 50 years was 6, for those between 50 and 64 years was 22 and for those 65 years and older was 43. The median number of medications per patient younger than 50 years was 6 and for patients 50 years and older it was 11 medications.

Conclusions: There has been a significant shift towards patients of older ages at the UCSD Owen Clinic over the

past 18 years. These older patients have a higher burden of medications and based on their VACS Index are at greater risk for adverse outcomes including mortality. Medical providers of patients living with HIV need to be adept at caring for an aging population.

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The effect of aging on the peripheral transcriptome of HIV infected individuals following influenza vaccination

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Background: The life expectancy of people living with HIV (PLHIV) on antiretroviral therapy is now near normal. The comorbidities associated with aging, however, are greater in PLHIV and appear earlier in their lifetimes by approximately 5-10 years

Methods: We selected 24 healthy (HC) and 24 HIV infected (HIV) individuals under viral control for at least 1 year from the FLORAH influenza vaccination study. Participants were grouped by age as Young (<40 years) and Old (>60 years). RNA was extracted (QIAGEN RNeasy plus mini kit) from cryopreserved PBMC pre- and 7 days post-vaccination and sequenced (Illumina NextSeq500; 75 bp, paired-end, 40 million reads/sample). Differentially expressed genes (DEG) determined by two-group t test ($P \leq 0.05$) were organized into top pathways by P value ($P \leq 0.05$) via gene set variation analysis (GSVA) in R Bioconductor.

Results: Immune features of aging (Old Vs Young) were similar but quantitatively reduced in HIV compared to HC (139 vs 1377 DEG). HIV however interacted with aging (148 DEG) and as a consequence the effect of HIV was different between age groups. In Young HC and HIV, post-vaccination transcriptional modulation was of similar magnitude (260 vs 310 DEG) but of lower magnitude (19 DEG) in Old HC compared to Old HIV (1359 DEG). Aging interacts with the vaccination signature but this effect was limited to HC (476 vs 3 DEG). These conclusions were also confirmed by pathway analyses, which also implicated the role of immune activation and cell signaling in this interaction.

Conclusion: This study identifies a novel transcriptional perturbation induced by the simultaneous effect of

aging and HIV in resting conditions or after in vivo immune stimulation, reinforcing the concept of dysregulated immune aging in PLHIV, and introduces evidence for an HIV-induced aging mechanism for further validation.

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Efficacy and safety of darunavir/cobicistat/emtricitabine/tenofovir alafenamide (D/C/F/TAF) in treatment-experienced, virologically suppressed (EMERALD) and treatment-naïve (AMBER) patients: week 48 subgroup analysis by age

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Background: D/C/F/TAF 800/150/200/10 mg is an oral, once-daily, single-tablet regimen approved in Europe and under regulatory review in the US for the treatment of patients with HIV-1 infection. The efficacy and safety of D/C/F/TAF were demonstrated in two randomized, phase 3 studies. In this subgroup analysis, outcomes in patients >50 and ≤50 years for each study through 48 weeks were examined.

Materials & Methods: In EMERALD, treatment-experienced, virologically suppressed patients switched to D/C/F/TAF or continued their current boosted protease inhibitor+emtricitabine/tenofovir disoproxil fumarate regimen (2:1). In AMBER, treatment-naïve patients initiated D/C/F/TAF or darunavir/cobicistat+emtricitabine/tenofovir disoproxil fumarate (1:1). Efficacy was evaluated by proportion of patients with virologic rebound (EMERALD) and virologic response <50 copies/mL using FDA snapshot (both studies). Safety was assessed by adverse events (AEs), bone and renal biomarkers, and laboratory parameters.

Results: Of the 1,141 patients treated in EMERALD, 382 (33.5%) were >50 years and 759 (66.5%) were ≤50 years. Virologic rebound rates were low for D/C/F/TAF and control in patients >50 years (2.3% [6/256] vs 0.8% [1/126]; Δ1.6%; 95% CI, -2.3% to 4.4%) and ≤50 years (2.6% [13/507] vs 2.8% [7/252]; Δ-0.2%; 95% CI, -3.3% to 2.1%). Virologic response rates were high and similar with D/C/F/TAF and control in patients >50 years (93.8% [240/256] vs 93.7% [118/126]; Δ0.1%; 95% CI, -

4.9% to 6.4%) and ≤50 years (95.5% [484/507] vs 93.7% [236/252]; Δ1.8%; 95% CI, -1.5% to 5.9%). No emergent resistance to study drugs was observed. Few patients in the D/C/F/TAF and control arms, respectively, discontinued due to an AE (>50 years: 2.0% vs 3.2%; ≤50 years: 1.2% vs 0.4%) or had a serious AE (>50 years: 5.9% vs 7.1%; ≤50 years: 3.9% vs 3.6%). Among patients using D/C/F/TAF, hip and spine bone mineral density (BMD; g/cm² [substudy]) generally increased, and β-2 microglobulin:creatinine and urine albumin:creatinine ratios generally decreased, from baseline to Week 48 regardless of age, consistent with known benefits of TAF.

Similar outcomes were observed in AMBER; a total of 725 patients were treated, with 68 (9.4%) >50 years and 657 (90.6%) ≤50 years. High virologic response rates were seen for D/C/F/TAF and control in patients >50 years (88.9% [32/36] vs 87.5% [28/32]; Δ1.4%; 95% CI, -15.5% to 19.8%) and ≤50 years (91.7% [299/326] vs 88.5% [293/331]; Δ3.2%; 95% CI, -1.4% to 8.0%). No resistance to darunavir or tenofovir was observed; one patient (D/C/F/TAF) was identified with M184I/V. In the D/C/F/TAF and control arms, respectively, few patients discontinued due to an AE (>50 years: 0.0% vs 9.4%; ≤50 years: 2.1% vs 3.9%) or had a serious AE (>50 years: 11.1% vs 9.4%; ≤50 years: 4.0% vs 5.4%). Bone (hip and spine BMD [substudy]) and renal (mean estimated glomerular filtration rate by serum cystatin C) biomarkers were generally more favorable for D/C/F/TAF versus control regardless of age, but sample sizes were small.

Conclusions: In treatment-experienced, virologically suppressed and treatment-naïve patients, D/C/F/TAF was well tolerated with a high genetic barrier to resistance, and demonstrated similar efficacy and generally more favorable bone and renal safety than control, regardless of age.

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HIV-1 Viremia is an Independent Risk Factor for Falls Among Older Men with or at risk for HIV Infection

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Background: Falls and the risk factors associated with falls are common in people living with HIV. We sought to identify fall risk factors among older men with and without HIV infection.

Methods: Men aged 50-75 with (n=279) and without HIV (n=379) from the Bone Strength Substudy of the MACS were included. Falls were collected prospectively in real-time over 2 years. Multinomial logistic regression modelled faller status, adjusting for HIV serostatus, age, race, study site, enrollment period, BMI, illicit use, peripheral neuropathy, diagnosis of and medications for depression, diabetes, and hypertension.

Results: Men with HIV tended to be younger, have a lower BMI, greater prevalence of diabetes, greater use of depression medications, and differed by race and study site. Forty-one percent of men with HIV and 39% of uninfected men had at ≥ 1 fall; 20% with HIV and 17% of uninfected men experienced recurrent falls. In multivariate models, the odds of being a recurrent faller was greater among men reporting illicit drug use (OR 1.6 [1.0, 2.6], p=0.04), taking diabetes medications (2.6 [1.3, 5.1], p=0.007) or depression medications (2.0 [1.2, 3.3], p=0.008), and with peripheral neuropathy (2.4 [1.4, 4.0], p=0.001); obesity was associated with a lower fall risk (0.5 [0.3, 0.96], p=0.04). In HIV-restricted models, detectable HIV-1 RNA (3.9 [1.2, 12.0], p=0.02), use of efavirenz (3.5 [1.3, 10.0], p=0.02), diabetes medications (2.2 [1.1, 4.6], p=0.03), illicit drug use (2.2 [1.1, 4.6], p=0.03), and peripheral neuropathy (2.2 [1.0, 4.6], p=0.049) were associated with a greater odds of being a recurrent faller. The association with detectable HIV-1 RNA remained significant when detectability was limited to low-level viremia of HIV-1 RNA 50-500 copies/mL (n= 4 excluded; OR 5.5 [1.6, 18.5] p=0.007).

Conclusions: Even low-level HIV-1 viremia was associated with increased fall risk, after accounting for other fall risk factors, emphasizing the importance of ART adherence in comorbidity management. Several additional factors may identify those at risk for falls and opportunities for fall risk reduction.

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Frailty and its associations in an aging, multimorbid HIV cohort

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Background: Frailty measures have been developed to better understand the health and functional status of aging individuals. The Fried Frailty Index (FFI) has been used to assess a variety of aging HIV populations for both prevalence and predictive factors of frailty; as the populations have been heterogeneous, so have the outcomes of these analyses.

Materials and methods: We utilized the FFI in an aging HIV population enriched for medical illness to determine the factors associated with frailty. 139 participants in the Manhattan HIV Brain Bank (MHBB) underwent a comprehensive neuromedical, cognitive, and laboratory assessment as per the protocols of the National NeuroAIDS Tissue Consortium (NNTC). Bivariate analyses identified factors associated with frailty; those significant at $p < 0.100$ were entered into logistic regression.

Results: 47% of subjects in this sample were frail (2 or more FFI criteria); 33% pre-frail (1 FFI criterion); and 20% not frail (no criteria). The mean age was 59.5 +/- 7.5 years (range 39.4 to 77.7 years); 50% were women; 39% African American, 31% Hispanic, 20% Caucasian; 91% virally suppressed (plasma load <500 copies/ml); median CD4 count was 574 cells/mm³ IQR [822, 342]; median nadir CD4 90 cells/mm³ IQR [200, 12]; and 66 % had 2 or more HIV-associated non-AIDS medical disorders (multimorbidity; assessed for hypertension, diabetes, hyperlipidemia, hepatitis, cardiac disease, chronic renal disease, stroke, COPD, cancer). Factors with significance at the $p < 0.100$ level for frailty status in bivariate analysis included: gender ($p=0.019$), multimorbidity ($p=0.057$), diabetes ($p=0.088$), cardiac disease ($p=0.021$), COPD ($p=0.007$), cancer ($p=0.105$), smoking ($p=0.037$), global T score ($p=0.027$) and motor T score ($p<0.001$). These, as well as age ($p=0.814$; age did not predict frailty in this sample), were advanced to logistic regression. Factors with significance in logistic regression included: female gender (confidence interval (CI) -1.28, -0.18), cardiac disease (CI 0.25, 1.76), smoking (CI 0.10, 1.21), and motor T score (CI 0.01, 0.12).

Conclusions: Age was not a predictor for frailty status, similar to what has been reported for other, less multimorbid HIV samples. In this sample, women, active smokers, and those with cardiac disease were more likely to be frail, while metabolic factors were not associated with frailty. Motor deficits as assessed in the NNTC cognitive battery were better predictors of frailty than global cognition, perhaps unsurprising in the light of the three FFI components (walking speed, metabolic activity, grasp strength) that directly assess motor function.

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Apathy is distinct from poor cognition and depression, and may negatively impact adherence to interventions aimed at improving cognition: evidence from the Positive Brain Health Now cohort study

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Background: Apathy, a reduction of self-generated voluntary and purposeful behaviors which can be partially reversed under strong solicitation from the environment, is a common neuropsychiatric symptom associated with HIV. It has been associated with depression and with cognitive impairment, suggesting that there may be significant overlap in constructs. Apathy has been associated with greater functional impairment but its salience as a determinant of adherence to behaviour interventions to improve cognition remains to be clarified.

This study aims to 1. estimate the extent to which cognitive, motivational and affective symptoms cluster among people with HIV, and 2. estimate the extent to which apathy predicts adherence to 3 behavioural interventions aimed at improving cognition.

Material & Methods: The data came from the Positive Brain Health Now study, a Canadian cohort of people with HIV (≥ 35 years). Cognition was assessed using a computerized cognitive test (B-CAM); depression was measured with the Mental Health Index of the SF-36 and apathy was measured using a shortened version of Starkstein's Apathy Scale. The symptom constructs were transformed into binary variables using published or distribution cut-points (B-CAM: mean - 1SD; MHI ≤ 60 ; apathy: 25%ile) and subjected to a cluster analysis. Selected cohort participants with cognitive difficulties were invited to join one of 3 interventions aimed at improving cognition: 2 group-based (Goal-Management

Training [GMT] N=30 and structured exercise N=27); and one on-line (computerized cognitive training, N=35). Measure of good adherence was intervention specific. For GMT, it was defined as attendance at 8 or more of the 9 sessions and completion of $\frac{1}{2}$ of the homework assignments; for exercise, attendance at 80% of the 36 sessions; for cognitive training, any engagement was counted as adherent. Logistic regression was used to test whether apathy measured at study entry explained adherence.

Results: Data from 669 participants were available for the cluster analysis. Impaired B-CAM in isolation was found in N=89 (13.3%), with depression only in N=50 (7.5%), with apathy only in N=36 (5.4%) and with apathy + depression in N=42 (6.3%). Good adherence to interventions was as follows: GMT: 21/30 (70%); exercise 23/27 (85%); cognitive training: 0/52. Apathy was not associated with poor adherence to any of the interventions.

Conclusions: Among individuals with HIV, poor cognition, depression and apathy are distinct but overlapping constructs. Among those with cognitive difficulties, greater apathy, at least as we measured it, did not predict poor adherence to the interventions to improve cognition. Adherence to the on-line computerized cognitive training program was extremely poor. In contrast, adherence to the face-to-face interventions was very good, irrespective of the measured level of apathy. Potential explanations for our findings are that, among people with cognitive difficulties, apathy is not particularly relevant to adherence to cognitive interventions, or that the potential negative impact of apathy on adherence was offset by participation in a group. In the context where effective interventions for impaired cognition in HIV are lacking, we propose that a better understanding of the role of apathy on the ability to engage in such interventions is required.

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HIV-Related Stigma Hinders Cognition and Everyday Function in Older Men Living with HIV : Evidence for “social neurotoxicity”

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Background: Stigma remains an important aspect of the experience of living with HIV. There is ample evidence that stigma bears directly on mental health. We hypothesized that it might have an impact on brain health more generally, affecting cognition as well as mood, with potential for downstream effects on function. The specific objective of this study was to identify direct and indirect relationships among stigma, cognition, anxiety, depression and everyday function in a population of older HIV+ individuals living in Canada.

Material & Methods: The analysis was restricted to Caucasian men to avoid the confounding effects of gender and race on stigma. 512 older Caucasian men living with HIV were drawn from the Positive Brain Health Now Canadian cohort (age ≥35 years, HIV+ for at least 1 year, mean duration of HIV infection: 17.4 years (SD 8)). We estimated the impact of HIV-related stigma on brain health and everyday functioning using the International Classification of Functioning, Disability and Health as an a priori comprehensive framework to integrate biopsychosocial perspectives. Measures were chosen for their pertinence to key constructs related to HIV-related stigma and brain health, including cognitive performance and mood. Stigma was measured using a single item from the WHOQOL-HIV BREF questionnaire (“To what extent are you bothered by people blaming you for your HIV status?”). Structural equation modelling (SEM) was used to estimate the relationships between these variables. A model was built including personal, environmental, biological factors, and measures of mental and cognitive health, activity limitations, and participation restrictions.

Results: Over one third of the sample indicated that they were bothered by stigma. Stigma was influenced by HIV-related variables (duration of infection and HIV-specific signs and symptoms) and contributed to lower cognitive test performance and worse mental health. Individuals expressing stigma had significantly worse performance on cognitive testing, over and above the effects of mental health, controlling for age, sex and education. In turn, stigma had widespread downstream effects, through cognitive performance, anxiety and depression, to physical function, cognitive function and engagement in meaningful activities, in turn affecting social role and life space mobility. Stigma was most highly associated with anxiety, with cognitive test performance the second strongest association.

Conclusions: The results provide evidence that HIV-related stigma is a threat to cognitive health as well as mental health, with a negative impact on everyday function in Caucasian men aging with HIV. This is in line with findings that social experience changes the brain and argues for direct, mechanistic links between the psychosocial and biological impacts of HIV at the level of the brain, bringing together two major areas of research emphasis that to date have been largely studied in parallel. The environment in which people live with HIV contributes to mental health, but also to cognitive performance. Interventions focused on stigma reduction may offer novel routes to addressing cognitive impairment in this population.

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Association between cognitive reserve and cognitive performance in people with HIV: a systematic review and meta-analysis

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Objectives: Cognitive reserve is a potential explanation for the disparity between brain pathology and its clinical manifestations. Individuals with higher cognitive reserve are better shielded against cognitive decline than those with lower reserve. Education, occupation, physical activity and leisure activities are often viewed as contributors to cognitive reserve. Milder forms of HIV-associated neurologic disorders predominate despite revolutionized treatments. Although cognitive reserve has been studied in relation to cognitive ability in HIV, a quantitative synthesis has not been undertaken. This is deemed important as it could encourage development of rehabilitative interventions to offer neuroprotection in HIV. The main objective was to estimate, based on published studies, the strength of the association between cognitive reserve and cognitive performance in individuals with HIV.

Methods: A systematic literature search using Ovid MEDLINE, PsychINFO, and EMBASE was performed to identify studies published between 1990 -2016 that quantified the association between cognitive reserve and cognitive performance in HIV. A random-effects meta-analysis was used to compute a summary estimate (Cohen's d) with 95% confidence intervals (CI) and 95% prediction intervals (PI). The risk of bias and quality of reporting in the studies were indicated by the Appraisal tool for Cross-Sectional Studies (AXIS).

Results: 10 observational studies were deemed eligible. The pooled effect size was 0.9 0.9 (95% CI: 0.7 to 1.0; 95% PI: 0.4 to 1.4). with marked heterogeneity studies [Cochran's Q (df = 9) = 28.0, p =0.0009; I2 statistic=67.4%). Risk-of-bias appraisal showed that non-response bias was never addressed and the items associated with selection bias were only partially met.

Conclusions: The association between cognitive reserve and cognitive performance suggests that building

reserve through non-pharmacological interventions could be an effective way of combating cognitive impairment in people with HIV. Encouraging enriched leisure and recreational activities would be one logical recommendation which would not require substantial infrastructure as people could identify these activities in their community.

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The Impact of Structured Exercise on Brain Health in HIV Positive Individuals

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Background: Although exercise is shown to have impact on cardiometabolic and body composition outcomes in people with HIV, the effect of exercise has not been investigated on cognitive ability. We designed a pilot study to estimate the feasibility of a 12-week combined aerobic and resistance exercise program. Also, the extent to which the program impacted on cognitive ability and brain health outcomes of motivation, fatigue and motor performance were estimated.

Methods: The study was part of a larger project based on a cohort multiple randomized controlled design which resulted in three cohorts: exercise intervention cohort; refuser cohort and controls. Adults with sedentary lifestyle, 35 years old or above with HIV diagnosis for at least one year, without dementia and cardiovascular co-morbidities were eligible. 12-week exercise program consisted of high intensity interval training and resistance training three days per week. Cognitive ability was the primary outcome measure and was measured by Brief Cognitive Ability Measure (B-CAM) in all three cohorts. Cognitive deficits were measured using Perceived Deficits Questionnaire (PDQ). The standardized procedures for all physical performance measures as given in the Canadian Physical Activity, Fitness and Lifestyle Approach (CPAFLA) manual were followed. Aerobic capacity was measured by a three-minute step test. Functional walking capacity, leg power, grip strength, core strength, and gait speed were measured by 6 minute walk test, vertical jump test, hand dynamometer, push ups/curl ups, and GAITrite, respectively, in the exercise intervention group. Depression and anxiety was measured with RAND 36 Mental Health Index (MHI) and fatigue with Vitality sub-scale of RAND 36. Effect sizes for all physical performance measures were reported using standardized response mean (SRM). Responder status was computed for B-CAM and change in physical performance measures was estimated using paired t-test. Effect sizes for all physical performance measures

were reported using standardized response mean (SRM).

Results: 27 people completed the exercise program. 89% of the participants completed more than 80% of the total 36 exercise sessions, thus indicating good adherence. There was no change in B-CAM and PDQ pre-and post exercise training among the three cohorts. Dual task gait speed improved in 52% of the participants. Improvement was seen in all physical performance measures (SRM ranging from 0.3 to 1.0) except for maximal jump height in the exercise cohort.

Conclusion: The 12-week exercise program improved physical performance measures but it did not yield any gains in cognitive ability in HIV.

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Differences in emotional outcomes by LGBT and HIV status

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Background: Emotional well-being is an important component of health-related quality of life. The ability to positively regulate emotional responses to changing environments and maintain social relationships plays an important role in adapting to life challenges over the lifespan. This is particularly important among populations that experience stigma and disparities in mental and/or physical health, including people living with HIV (PLHIV) and LGBT individuals. LGBT PLHIV may experience compounding threats to emotional well-being. In this study, we investigated the separate and interactive associations of HIV serostatus and LGBT status with emotional health.

Methods: Three-hundred and seventy-five participants (206 HIV+/LGBT; 39 HIV-/LGBT; 53 HIV+/non-LGBT; 77 HIV-/non-LGBT) enrolled across multiple observational, cohort studies at the University of California San Diego HIV Neurobehavioral Research Program were included in the analyses. For the overall cohort: Age: M=52.6, SD=12.5; 76.5% were male, 55.5% were non-Hispanic White. Emotional health was assessed via the NIH Toolbox Emotion Battery (NIH TB-EB), which yields three composites: negative affect, social satisfaction, and psychological well-being. LGBT status was determined based on self-reported sexual orientation, sex at birth, and gender identity. Three separate linear regression models were fitted for each NIH TB-EB composite, with HIV status, LGBT/non-LGBT group and their interaction as predictors. Significant interactions were probed by examining the effect of LGBT/non-LGBT group within the HIV serostatus groups. Potential covariates included demographics, psychiatric characteristics (i.e., lifetime diagnosis of major depressive disorder and substance use disorder), and a summary score of global neurocognitive function. Covariates that were associated with emotional outcomes at $p \leq 0.10$ were included in final models. Additionally, we examined the association among LGBT group and emotional outcomes within the HIV

seropositive group only in order to adjust for significant HIV disease characteristics (e.g. nadir CD4, detectability of plasma viral load).

Results: There was a significant HIV serostatus by LGBT group interaction on negative affect ($B=6.40$, $SE=3.01$, $p=0.03$). Contrary to expectations, the interaction was driven by an association between HIV seropositivity and higher negative affect within the non-LGBT group ($B=-8.16$, $SE=2.43$, $p=0.001$) but not among LGBT individuals. The HIV serostatus by LGBT status interaction was not significant for social satisfaction and psychological well-being. There were also no main effects of HIV serostatus or LGBT status on either social satisfaction or psychological well-being. Among HIV seropositives, being in the non-LGBT group was associated with lower social satisfaction ($B=-5.38$, $SE=2.59$, $p=.04$) and psychological well-being ($B=-4.65$, $SE=2.28$, $p=.04$), after adjusting for HIV disease characteristics.

Conclusion: Our findings suggest that PLHIV who are LGBT may be less vulnerable to poor emotional well-being than PLHIV who are not LGBT. This might be explained by individual differences in adaptive coping behaviors and resilience. This may also be reflective of high levels of social support within the LGBT community. Efforts to improve emotional well-being of PLHIV should take into account the unique contexts and psychosocial strengths and challenges specific to sexual orientation and identity groups.

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Effect of Age on Efficacy and Safety of Elvitegravir, Cobicistat, Emtricitabine, and Tenofovir Alafenamide (E/C/F/TAF) in Virologically-Suppressed, HIV-1-Infected Participants Aged ≥ 65 Years: Pooled Analysis of Two Phase 3 Trials

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Background: As the HIV population ages, analyzing safety and efficacy data for antiretroviral (ARV) agents in older adults living with HIV is increasingly important. TAF is a tenofovir prodrug associated with 90% lower tenofovir plasma levels and greater renal and bone safety than tenofovir disoproxil fumarate (TDF). We evaluated the efficacy and safety of E/C/F/TAF in individuals < and ≥ 65 years of age.

Material and Methods: In two international, multicenter, Phase 3 trials, ARV-experienced participants with HIV RNA < 50 copies/mL were randomized 2:1 to receive:

- 1) E/C/F/TAF for 48 weeks or continued current abacavir/lamivudine (ABC/3TC)-based regimen for 24 weeks followed by a delayed switch to E/C/F/TAF for another 24 weeks (292-1823) or
- 2) E/C/F/TAF or continued TDF-based regimen for 48 weeks (292-1826, all subjects were ≥ 60 years).

This pooled analysis of the E/C/F/TAF arms evaluated efficacy (HIV-1 RNA < 50 copies/mL, FDA snapshot analysis) and safety through Week 48 for participants categorized by age (< and ≥ 65 years). Randomization was not stratified by age.

Results: A total of 293 participants were included in this analysis. Of the 74 participants ≥ 65 years, median age was 69 (range 65-80), 81% were male, 89% were White, median CD4 was 608 cells/mm³ compared to 219

participants < 65 years with a median age 51 years (range 25-64), 88% male, 85% White, and median CD4 651 cells/mm³. Baseline regimens consisted of 2 NRTIs combined with an NNRTI 60% (175/293), INSTI 25% (73/293), or boosted PI 15% (45/293).

At W48, HIV RNA < 50 copies/mL was 89% in each age group. An HIV RNA ≥ 50 copies/mL was seen in 1 (0.5%) and 0 participants < 65 and ≥ 65 , respectively; no participant had virologic failure with resistance. W48 CD4 count was not significantly different between age groups. Adverse event (AE) profile was similar between both groups. Grades 2, 3 and 4 study drug-related AEs occurred 6.4% (14/219) and 5.4% (4/74) in the < 65 and ≥ 65 groups, respectively; all events except one in each group were grade 2. In the < 65 and ≥ 65 subgroups, AEs leading to study drug discontinuation occurred in 3.7% (8/219) and 5.4% (4/74); for the four subjects ≥ 65 the events consisted of 1) constipation, arthralgia, myalgia; 2) diarrhea; 3) flatulence; 4) hepatocellular injury. There were no study drug-related serious AEs nor any renal or bone AEs leading to E/C/F/TAF discontinuation. Median change from baseline in eGFR was -3.0 mL/min in the < 65 subgroup compared to -1.2 mL/min in the ≥ 65 . Urine albumin:creatinine, urine beta-2-microglobulin:creatinine, and urine retinol binding protein:creatinine ratios all improved more in the ≥ 65 than in younger participants.

Conclusion: Through W48, rates of virologic suppression were high and similar between participants < 65 and ≥ 65 years. AE, medication-related discontinuation, and tolerability were not significantly different between groups. Improved renal biomarkers were noted in those ≥ 65 . The W48 efficacy and safety data support the switch to E/C/F/TAF in HIV-infected, treatment experienced, HIV-1 RNA suppressed people ≥ 65 years old.

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Frailty index predicts quality of life in Chinese people living with HIV

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Background: With the aging population of people living with HIV, it is important to understand the impact of co-morbidities and frailty on quality of life in older HIV-infected individuals. Research in this area is particularly lacking in Asia. This study aims to determine the association of frailty and co-morbidities with quality of life in older Chinese HIV-infected individuals in Hong Kong.

Material and Methods: Adult Chinese HIV-infected individuals aged 50 or above who were followed up in an HIV Metabolic Clinic in a teaching hospital in Hong Kong were recruited into this study. Subjects completed a standardized interview, physical examination, questionnaires, and blood tests in a single visit. Multi-morbidity was defined as presence of two or more comorbid conditions. Polypharmacy was defined as use of more than 5 drugs. Depression was defined by the Center for Epidemiologic Studies Depression (CESD) Scale score ≥ 16 . Frailty index was composed of 37 age- and HIV-related health variables. Health-related quality of life was assessed by the EQ-VAS, a visual analog scale from 0 to 100 which recorded the subjects' self-rated health. Comparisons between continuous variables were performed using Spearman's rank correlation coefficient, and continuous variables were compared between categories using Mann Whitney U test. Multivariable linear regression analysis was performed to determine the variables that were independently associated with EQ-VAS.

Results: Fifty-two patients were included in this analysis. 88.5% were male, median age was 61.5 years (inter-quartile range 56-65). One or more co-morbidities were present in 84.6% (hypertension 50.0%, diabetes 48.1%, chronic kidney disease 15.4%, and hepatitis B 13.5%). Multi-morbidity and polypharmacy were present in 45.1% and 40.4% respectively. HIV was diagnosed for 13.3 ± 7.1 years. 38.5% had history of AIDS-defining illnesses. The latest CD4 count was 572 ± 270 cells/mm³. All patients had

HIV viral load less than 50 copies per mL. The mean frailty index was 0.31 ± 0.088 . The median EQ VAS score was 80 (interquartile range 70-90).

On univariate analysis, diabetes (median EQ VAS score 70 vs 80, $p=0.02$), multi-morbidity (median EQ-VAS score 70 vs 80, $p=0.003$), polypharmacy (median EQ-VAS score 70 vs 80, $p=0.006$), unintentional weight loss (median EQ-VAS 70 vs 80, $p=0.046$), depression (median EQ-VAS score 70 vs 80, $p=0.031$), and frailty index (correlation coefficient -0.427 , $p=0.002$) were associated with EQ-VAS. Multivariable linear regression model showed that frailty index ($\beta = -61.91$, $p=0.005$), diabetes ($\beta = -8.00$, $p=0.036$) and depression ($\beta = -8.66$, $p=0.03$) were independently associated with EQ-VAS.

Conclusions: Our study showed that in a cohort of Chinese older adults living with HIV and multiple co-morbidities, frailty index was associated with health-related quality of life.

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Youth born with HIV are in their mid-30's struggling to fit in the AIDS Long Term Survivors aging community.

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With no suitable drugs available for those born with HIV in the 1980s, around 50 per cent were dead by the time they were 10. However, some babies born with HIV have defied initial expectations: these babies are now youth in their mid 30's struggling to fit in the AIDS Long Term Survivors aging community.

As a 35-year old woman born with HIV, I conducted a qualitative research to find out other oldest youth born with HIV whereabouts. The goal was to find out how the youth born with HIV cope with HIV and how they integrate in the AIDS Long Term Survivors aging community.

Narrative approach method was used. Twenty youth born with HIV were interviewed, and documents and researches on youth born with HIV were consulted, to form a cohesive story illustrating the larger story for other youth born with HIV.

The study found out that youth who grew up with HIV have usual youth problems like: school drama, financial literacy, finding jobs, dating, forming families, accessing sexual reproductive health and rights and services, procreation, coping with HIV and AIDS related rumors, stigma and discrimination. But they also experienced medical complications, medical intoxication, perceived increased rate of aging as well as get pill fatigue. Some of the youth born with HIV feel tired from taking pills. Some die because they stop taking Anti-Retroviral Treatment.

Also, youth born with HIV often find themselves isolated, unable to relate to other AIDS Long Term Survivors. Often AIDS Long Term Survivors scare youth born with HIV with what they should expect as they age

yet little is known about the aging process among those born with HIV.

When it comes to Sexual Reproductive Health, those born with HIV are often discouraged to have children. Many of the youth born with HIV are orphans and feel a great desire to have children. However, when they have children, AIDS long term survivors who are dealing with AIDS related trauma don't have a support system to mentor youth born with HIV throughout life events such as children bearing and raising. The aging process for youth born with HIV keep getting complicated as there is a complete disconnect between AIDS Long Term Survivors and youth born with HIV. On top of all these problems, youth born with HIV constitute one of the group of people affected by mental illnesses such as depression. Many find consolation in using drugs which lead to more complicated problems.

This qualitative study provided a glimpse on the state of youth born with HIV lives. Youth born with HIV have to be integrated in the AIDS long term survivors aging community dialogue. More researches on the aging processes among youth born with HIV needs to be conducted. AIDS long term survivors aging community should create a special space for youth born with HIV.

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Advance Directives and Medical Power of Attorney Assignment in Individuals with HIV

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Background: People living with HIV (PLWH) often have social isolation, loss of partners and close friends, and estranged relationships with family. Completion of an advanced directive (AD) or identification of an informal proxy or medical power of attorney (MPOA) are of particular importance, but we have previously shown low rates of both. Whether these rates are higher preceding death, or if rates differ by the ultimate cause of death among PLWH is unknown. This study aimed to examine the factors associated with AD completion or MPOA assignment prior to death in PLWH.

Material & Methods: Retrospective study of all deceased patients with HIV from a single clinic between 2013-2017. Demographic and selected clinical characteristics were collected. For categorical variables, n (%) were reported by AD and MPOA recorded prior to death; means (SD) were reported for age. Chi-square, Fisher's exact and T-tests were utilized, as appropriate.

Results: Of 86 total patients, 36(42%) completed the AD form and 64(74%) had a formal or informal MPOA assigned. Those with AD completed tended to be older(54.4[10.6] years vs 50.5[8.7] years, p=0.065), with higher rates of lower CD4 count(16[45%]<200, 13[36%]200-500, 7[19%] >500 cells/ μ L with AD vs 19[38%], 14[28%] and 17[34%] without AD, p=0.33), but did not differ significantly by race(28[77%] white with AD vs 34[70%] without AD, p-value=0.54), ethnicity(5[13.9%] Hispanic with AD vs 6[12%] without AD, p=0.76) or number of clinical visits in the preceding year(8[22%] with AD vs 5[10%] without AD with >6 visits, p=0.12). PLWH with AD completion tended to differ in cause of death: 31% died of AIDS-related causes, 61% non-AIDS causes and 8% unknown vs 22% AIDS-related, 50% non-AIDS causes, and 28% unknown among PLWH without AD (p=0.075). Among those that died of non-AIDS causes, those with an AD tended to have a higher cancer death rate (16[73%] vs 8[32%], p=0.11). Those with an assigned MPOA tended to be older(52.6[9.3] years vs 50.5[10.7] years, p=0.37) and

Hispanic(10[16%] Hispanic with MPOA and 1[5%] Hispanic PLWH without MPOA, p=0.04), with higher rates of lower CD4 count (29[45%] <200, 20[31%] 200-500, 15[24%] >500 cells/ μ L with MPOA, vs 6[27%], 7[32%] and 9[41%] without MPOA, p=0.21) but did not differ by race(44[69%] white with MPOA vs 18[86%] without an MPOA, p=0.31) or number of clinical visits in the preceding year(9[14%] with MPOA vs 4[18%] without MPOA with >6 visits, p=0.73). Of those with an MPOA, 33% died of AIDS-related causes, 55% non-AIDS causes and 12% unknown causes vs 5% AIDS-related, 54% non-AIDS causes, and 41% unknown causes among those without an MPOA (p=0.003). Among those that died of non-AIDS causes, those with an MPOA tended to have a higher cancer death rate (22[63%] vs 2[17%], p=0.002).

Conclusions: Rates of AD completion are low, even immediately preceding death among PLWH, with the lowest completion among those with an unknown cause of death (and presumably less terminal conditions). Even among participants who died of non-AIDS cancer, however, nearly 40% of these patients with a terminal condition were still without an AD or an MPOA. Interventions are needed to increase the proportion of AD completion.

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Prevalence of hypertension among elderly patients living with Human Immunodeficiency Virus

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Background: Hypertension is one of the common medical conditions observed among elderly people living with HIV (EPLWH) and to date no systematic review has estimated its global prevalence.

Purpose: To conduct a systematic review to estimate the global prevalence of hypertension among EPLWH.

Data Sources: PubMed/MEDLINE, EMBASE, the Cochrane Library, Scopus, and Google Scholar for relevant publications up till November 30th, 2017.

Study Selection: Observational studies (cohort or cross-sectional studies) that estimated the prevalence of hypertension among EPLWH.

Data Extraction: Required data were extracted independently by three reviewers and the main outcome was hypertension prevalence among EPLWH.

Data Synthesis: The 12 (n = 5428) eligible studies included were conducted in North America, Europe and Asia. A low level bias threat to the estimated hypertension prevalence rates was observed. The global prevalence of hypertension among EPLWH was estimated at 42.9% (95% CI 38.4% to 47.6%), I² = 86%. The sub-group analysis showed that North America has the highest prevalence of hypertension 48.1% (95% CI 41.0% to 55.2%) followed by Europe 38.3% (95% CI 31.7% to 45.3 %) and Asia 31.0% (95% CI 25.9% to 36.3%). We found the regions where the studies were conducted explaining a considerable part of variation in hypertension prevalence.

Limitations: No study conducted in sub-Saharan Africa was eligible for inclusion. Also, insufficient number of studies hindered sub-group analysis.

Conclusion: This study demonstrated that two out of five EPLWH are hypertensive. North America appears to have the highest prevalence of hypertension followed by Europe and Asia respectively. Findings from this study will serve as vital information that stakeholders in HIV program can utilize to integrate hypertension management to HIV management package.

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The Prevalence of Obesity among Elderly Patients Living with Human Immunodeficiency Virus in Nigeria

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Background: Over 3 million Elderly Patients are Living with the Human Immunodeficiency Virus (EPLHIV) in sub-Saharan Africa. Highly active antiretroviral therapy (HAART) is effective against the HIV but obesity – risk factor for cardio-metabolic disorders, is associated with HAART and there is limited information on its prevalence among EPLHIV in Nigeria.

Methods: EPLHIV aged 50 years and above, enrolled from 2004 to 2015 were included in the analyses. Baseline characteristics were reported as a percentage or means and standard deviation. Obesity was defined as having a Body Mass Index (BMI) of $\geq 30\text{Kg/m}^2$.

Results: Among the 6,714 EPLHIV enrolled, 55% were male, 65% were married, 22% had attained post-secondary education, 30% were employed. The prevalence of obesity among the EPLHIV was 11.5% higher than the national obesity prevalence of 9.7%. More women compared with men were obese (16.4% vs 7.1%).

Conclusion: The prevalence of obesity among EPLHIV was higher than the national prevalence. This study provides important information for policy makers and HIV program implementers in addressing the health needs of EPLHIV.

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Neopterin is Related to Depression in Older Persons Living with HIV on Suppressive Antiretroviral Therapy

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Background: Major depressive disorder (MDD) is prevalent among older persons living with HIV (PLHIV). Levels of neopterin, a monocyte activation marker, are associated with depressive symptoms in the general population. While suppressive antiretroviral therapy (ART) reduces neopterin levels in PLHIV, they often remain higher than in the general population. This study investigates the relationship between neopterin and MDD in older PLHIV on suppressive ART.

Material & Methods: This is a cross-sectional study of 70 PLHIV and 35 HIV-uninfected (HIV-) older (≥ 50 years of age) adults. The mean age of entire sample was 58.0 years, and participants were mostly non-Hispanic white (74.0%) men (79.0%). All participants were on suppressive ART with a mean estimated duration of HIV disease of 17.7 years and a median current CD4+ T cell count of 649/ μL . Plasma neopterin levels were measured by immunoassay (nmol/L; ALPCO, Salem, NH USA), and values were log transformed for analyses. A structured, computerized interview was conducted to assess for lifetime (LT) MDD and substance use disorders based on Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR). Group comparisons were performed with a two-tailed t-test. A series of logistic regression analyses were used to model categorical diagnosis of LT MDD as a function of HIV serostatus, neopterin, and HIV disease characteristics. A multivariable logistic regression model was conducted to examine the association between LT MDD and neopterin levels, controlling for factors related to LT MDD (LT alcohol use disorder and LT cannabis use disorder). Hedge's g (g) statistic for continuous variables and odds ratios (OR) for binary variables were used to generate effect sizes for group comparisons.

Results: PLHIV had higher levels of neopterin than HIV- participants [median 9.9 nmol/L vs. 6.3 nmol/L; $p < .0001$; $g = 1.2$]. PLHIV were also more likely to be diagnosed with LT MDD than those without HIV (55.7% vs. 28.6%; $p = .008$; OR = 3.1). Higher neopterin levels

were associated with LT MDD in the entire sample ($p = .004$; OR = 1.82 per standard deviation increase in log-transformed neopterin levels). Stratifying by HIV serostatus group, the association between neopterin levels and LT MDD was observed in the PLHIV group ($p = .01$) but not the HIV- group ($p = .73$). HIV disease characteristics (e.g., current CD4+ T cell count) were not significantly associated with neopterin levels or LT MDD (p 's $> .05$). In the entire sample, higher neopterin levels ($p = .02$; OR = 1.86 per standard deviation increase in log-transformed neopterin levels) were independently associated with LT MDD in a logistic regression model controlling for HIV serostatus and relevant covariates.

Conclusions: Older PLHIV adults with higher levels of neopterin had greater odds of meeting criteria for LT MDD. This cross-sectional analysis cannot determine causality. Whether cause or effect (or both), chronic immune activation and inflammation are common in older PLHIV and associates with MDD in the context of suppressive ART.

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Improvement of Intrinsic Capacity in Older Adults Living with HIV through a health promotion resource

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Background: My Smart Age with HIV (MySAwH) is a multi-center prospective ongoing study designed to empower older adults living with HIV (OALWH) in achieving healthier life styles. It is based on collection of physical function data and patient-related outcomes through dedicated smart phone app. The aim of MySAwH is to detect health changes assessed with frailty index (FI), generated by health professionals, and with health index (HI) evaluating patient's Intrinsic Capacity (IC), generated by themselves. IC is consisted of 5 domains, comprising all the physical and mental capacities that an individual can draw in old age. It is built on residual health and patient empowerment. Given that IC is an innovative concept, there have not yet been validated tools to measure IC, but HI can be used as a potential instrument to assess it.

Objective: The aim of this study is to describe variations of FI and HI across time, after 9 months of follow-up.

Material and Methods: This study includes OALWH aged >50 years undergoing stable ART from Italy, Australia and Hong Kong recruitment sites who completed 9 months of follow-up. FI includes 37-item health variables where each variable is coded with a value of 1 when a deficit was present, and 0 when it was absent. FI > 0.3 was used to identify most frail individuals. HI includes 12-variables from 5 IC domains - Locomotion, Cognition, Vitality, Sensory, Psychosocial. After obtaining HI scores, IC is calculated with a 0-1 range score; the lower is the score, the better is IC evaluation.

Variables were collected through a fitness tracking wearable device (Garmin-Vivofit 2) and through

questionnaires provided via Ecological Momentary Assessment (EMA) using MySAwH App. HI was collected on a monthly base, while the FI was assessed on the baseline and follow-up visit.

ANOVA test was applied to identify statistical difference for the continuous variables with normal distribution, while Kruskal-Wallis test was used for those without normal distribution. χ^2 test was performed to assess the frequency of the categorical variables. P value cut off < 0.05 was chosen. Statistical analyses were performed in R software.

Results: 153 OALWH are included in this analysis. 96 (62.75%) from Modena-Italy, 45 (29.41%) from Sydney-Australia, 12 (7.84%) from Hong Kong - China. Median age is 57 years. 22 (14.38%) patients are women. Mean CD4 is 686.99 (324.14 SD) and 141 (92.76%) patients had undetectable HIV viral load. Median FI at baseline is 0.23 (0.2-0.32 IC) and at 9 months follow-up is 0.26 (0.2-0.31 IC) with no significant p-value 0.37. Median Intrinsic Capacity at baseline is 0.33 (0.25-0.4 IC) and at 9 months follow-up is 0.3 (0.2-0.36) with significant p-value 0.05. IC domains prevalence was calculated every month, but no domain shows a significant change after 9 months.

Conclusion: This study shows a continuous improvement in IC after 9 months of follow-up, but not decrease of FI. The presence of a Health Coach that provides information about HI variations and life style promotion can stimulate patients to be personally empowered to change their health measured by IC.

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Do frequency of bacterial infections and spectrum of pathogens vary by age among HIV-positive patients?

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Background: Despite introduction of cART and irrespective of immune reconstitution, bacterial infections remain common diseases among HIV-positive patients. Here we investigate spectrum of infections and pathogens in three age groups of HIV-positive patients routinely followed at the HIV Out-patient Clinic in Warsaw.

Methods: All symptomatic HIV-positive patients with at least one culture performed during routine follow-up were included into analyses. Patients were followed from the date of registration in the clinic until first positive culture or last clinical visit. We categorized patients according to age at registration in HIV clinic (<30, 30-40, >40). Groups were compared according to standard statistical methodology.

Results: In total 559 patients, with median 2.9 (IQR:0.81-5.17) years of follow-up, were included into analyses. 486 (86.9%) patients were men, 394 (70.5%) infected through MSM sexual contacts. Median age at registration was 31 (26.8-37.2) years, medial CD4+ count was: nadir 291 (179-380) and time updated 514 (384-673) cells/ μ l.

251 (44.9%) patients had positive culture, 117 (20.9%) from <30, 128 (22.9%) from 30-40 and 63 (11.3%) from >40 age group. Patients from >40 age group were more likely to have positive urine culture, while younger groups to have upper respiratory tract smears positive ($p=0.014$). Accordingly, *E. coli* was the most common pathogen for older and *S. aureus* for younger HIV-positive patients ($p=0.0692$).

Conclusions: Almost half of studied patients had bacterial infection identified, but its frequency decreased with age. The patterns of infections and most common pathogens reflect well the one observed in general population.

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Frailty Phenotype in Canadian Men and Women with HIV

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Background: Treatment success for HIV infection over the past two decades has resulted in a shift from a disease with a dire prognosis to a manageable condition. There is now a population of people aging with HIV, and they wish to age well. One impediment to active aging is the emergence of frailty^{1, 2}. Frailty has been defined as “a multidimensional syndrome characterized by decreased reserve and diminished resistance to stressors”, however, there is no agreed upon way of operationalizing frailty³. Age is considered a necessary condition for frailty but no cut-point is recognized; co-morbidity is also implicated³. HIV infection is considered to accelerate aging through chronic inflammation, immune system deterioration, depressive symptoms, and HIV-associated neurocognitive disorder⁴⁻⁶. Evidence for the importance of frailty in HIV is provided by the observation that there are over 719 reviews of this topic, 367 in the past 5 years.

Objective: The purpose of this study is to estimate the prevalence of frailty in a cohort of Canadians of middle or older age with HIV and identify contributors to prevalence. The data for this analysis came from the Positive Brain Health Now (BHN) cohort, an ongoing prospective study involving 872 persons living with HIV recruited between 2014 and 2016 from five clinics in Canada.

Methods: Fried’s criteria (≥ 3 of 5) for frailty was operationalized using items from the SF-36 indicating slow gait speed, weak grip strength, and exhaustion, and low Body Mass Index (< 21), and low physical activity.

Results: Out of the 729 men (mean age 53.3 years) and 139 women (mean age 50.5 years) with useable data, 55 (7.5%) of men and 17 women (12.2%) met Fried’s criterion for frailty, ≥ 3 of 5 criteria. Using a more global criterion, $< 45/100$ on the Physical Function Index (PFI) of the SF-36, the prevalence of frailty was 9.3% among men and 15.8% among women. The average values on the PFI for members of this cohort were 82/100 for men

and 77/100 for women, slightly lower than age-expected norms (89 and 87, for men and women, respectively). However, on other domains covered by the sub-scales of the SF-36, members of this cohort scored $\approx 1/3$ less than members of their peer group. In contrast to the low prevalence of frailty, over 40% met the cut-point for major depression ($\leq 60/100$) on the Mental Health Index (MHI). Results on neuropsychological testing indicated that 46% met criteria for severe cognitive impairment. The strongest contributor to frailty in this population was co-morbid arthritis.

Discussion: The estimate of frailty in the BHN cohort was lower than estimates from similar HIV populations. However, these estimates are similar to general population estimates but for people at least 10 years older. A striking feature of the BHN cohort is that members were physically quite robust, at least on self-reported indicators. However, indicators of emotional and cognitive frailty were more prevalent, over 40%, and these receive rather less attention in the literature.

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Immunosenescence in HIV-positive subjects on HAART: Can vanadium and glyburide be a treatment option?

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Background: HIV-infected individuals have immunosenescence which is a predictor of mortality in the general population. In spite of best combination and several years of ART the treatment has little to no effect on immunosenescence in HIV-1 virologically suppressed subjects. HIV patients tend to suffer early aging due to persistent chronic inflammation and residual immune activation. Early aging contributes to higher than expected risk of non-AIDS-morbidity, which includes cardiovascular, renal, liver, neurologic, and bone diseases, as well as cancer.

Material & Methods: In this retrospective chart analysis study 11 subject's data were included. All patient who took vanadyl sulfate, 60mg, OD and micronized glyburide 3mg in non-diabetic and 6mg in diabetic patients were included in this analysis. In this study, mean age was 52 years (range 24-63), 64% were male, all were white. HIV-RNA viral load was <20 to undetectable level in 8 patients in past 6 months and 7 patients had <20 to undetectable viral load level even before the treatment was initiated. One patient had 500-800 copies of HIV-RNA viral load and one patient had less than 100 and the last one was between 15000 to 18000 range which was partly because of non-compliance. HAART included most of the commonly prescribed drugs with two patients on Triumeq and Stribild. One patient was without any antiretroviral treatment by his/her decision.

Results: Vanadium based metallodrugs have shown promise as anti-inflammatory therapeutic agents targeting various diseases. In our coincidental finding where patient taking vanadium and glyburide for diabetes mellitus and HIV found to have improved cell count not only in CD4+ T cells but other cell lines including platelets, neutrophils and lymphocytes.

Average CD4+ T cell improvement was 32 cells/cubic cc for 3-month period and was 128 cells/cubic cc for a year period compared to their non-treatment past. The

cumulative effect is continuing even after their CD4+ cells have reached over 500 cells/cubic cc. Similar improvement was noticed with CD4+/CD8+ T cell ratios 0.014727 for 3 months and 0.06908 for a year treatment period. Other cell line improvement was about 10-30% compared to their baseline.

Three patients who started this treatment when their CD4+ T cell count was less than 50 have their cells recovering to above 400 CD4+ T cell and they showed remarkable improvement which resulted in reduced number of infections lessening the burden of antibiotics, antifungal and antiviral drugs. This recovery happened in shorter period of 4 -8 week to several months in these patients. 3 patients who had their platelets, neutrophils and absolute lymphocyte count below normal level were increased to normal levels. One patient had abdominal symptoms with diarrhea and cramping. 3 patient reported hypoglycemic symptoms.

Conclusions: In this preliminary analysis of short-term administration of vanadyl sulfate and glyburide on HIV infected subjects who are on standard of care treatment has shown improvement of CD4+ T cells and CD4+ T cell to CD8+ T cell ratios. We also noticed improvement in different cell lines. Overall patient had lesser frequency and severity of infections.

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HIV+ Women 50+ Stigmatized and Discriminated

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Introduction: HIV + Women who are 50+ are facing stigma and discrimination while disclosing their status to their family, friends, community and partners. GIPA/MIPA would require that HIV women are empowering and educating other HIV+ women so they too can become leaders in the community. The issues they are facing are stress, depression, isolation, and trauma (mental health issues). HIV disclosure is one of the important issues that these women are faced with and need support around how to disclose and when. This creates issues with adherence to medication, accessing services and education of HIV.

Method: Creating social groups in safe places for the women to come together to learn from other regarding

the issues they face being HIV+, a safe place where they can speak about relationships, medication, health issues, and accessing services and program. It is a place to empower and interact with each other and build each other's capacity and knowledge of HIV and its related issues. They gain a sense of family and connection through cooking, sewing, knitting, and other subjects that women can bond, engage and learn. Peers who run these groups would receive training in supporting each other as home based care providers and facilitators. This will help with those whose English is a second language. Women can take tours of the agencies and learn about services available to them. Results: Demographic of those attending the group 87% identify as female, 13% identify as transwomen. Age 45-50+ 28%, 50+ 72% attended group session.

Conclusion: The women who attended this group have come out of isolation and are now supporting and mentoring other women. Allowing the women to become activists and advocates for their community. They are seeking out more services and attending more training provided by their local agencies.

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