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International Workshop on HIV & Aging 2022

13 – 14 October 2022
Virtual Meeting

Abstracts
Oral Presentations

1

Early Interruptions in Treatment Among PLHIV Over 50 Years of Age Starting Antiretroviral Therapy in PEPFAR-Supported Low and Middle-Income Countries

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Background: PLHIV over 50 years of age represent a large and growing population in low and middle-income countries. As of the end of March 2022, this age group represented 21.8% of PLHIV currently on treatment in PEPFAR-supported programs. People over the age of 50 are at risk of acquisition of HIV, as demonstrated by continued identification of new positive cases in this age group.

Materials and Methods: Programmatic data from 48 PEPFAR-supported countries with direct service delivery support was reviewed in aggregate for the period spanning January – March 2022. Data from one country was excluded due to data quality concerns. HIV positive case identification, treatment initiation, and interruptions in treatment (IIT), defined as a missed appointment more than 28 days since a client's last expected clinic appointment or medication pick-up date, were analyzed for PLHIV over 50 years of age (50+). IIT was also analyzed by duration of time on ART before the occurrence of the interruption.

Results: PLHIV over 50 years old accounted for 8.9% of positive HIV tests and 9.3% of new treatment initiations (January-March 2022). Fourteen percent (14.0%, 56,721/403,842) of all IIT occurred in people in this age group during the analysis period. ¬¬¬The overall percent of IIT was lowest (1.7%, 56,721/3,329,008) for the 50+ age band on ART compared to other age bands on ART (ranging from 2.0% to 3.9%). However, the percent of IIT among people 50+ years old and on treatment for less than three months was more than 5 times higher at 8.7% (2,807/32,400) compared to overall ITT. The comparatively high early interruption rate is consistent across all age groups (ranging from 8.1 to 9.1%).

Conclusions: People over fifty years of age continue to be at risk of acquiring HIV. Once identified and stabilized on therapy, people over fifty tend to have good continuity of treatment. However, this population experiences high rates of early interruption in their first months on ART. Keeping this group in care and ensuring that they stay in treatment past the first three months may call for attention to other needed services. A person-centered differentiated service delivery model for this age group could include screening for and treatment of medical comorbidities associated with aging such as diabetes and cardiovascular disease, as well as address other aging issues such as frailty and neurocognitive decline. These models could also include similar-aged peer support and early access to multi-month dispensing for both ART and other required medications. Reporting and analysis of finer age bands among clients over 50 years old are planned which will assist in identifying subpopulations most at risk for adverse outcomes and potential areas of intervention.

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Persistent CD38 Expression on CD8+ T Lymphocytes Contributes to Chronic Inflammation in People With HIV, Despite ART

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Background: Antiretroviral treatment (ART) has increased the life expectancy of people with HIV (PWH), however, comorbidities are higher in PWH than HIV-negative individuals. This is partly due to accelerated cellular aging, a consequence of chronic inflammation secondary to the overactivation of CD4+ and CD8+ T lymphocytes. A hallmark of this immune hyperactivation is the increased expression of CD38, which has been shown to cause cellular dysfunction. However, the contribution of CD38 expression in the context of chronic HIV inflammation is not completely understood. Therefore, we sought to assess the effects of CD38 on cytokine production in CD8+ T lymphocytes in PWH.

Methods: The proportion of cytotoxic CD38+ CD8+ T lymphocytes from peripheral blood mononuclear cells (PBMCs) of PWH and HIV negative-individuals was measured, and mean CD38 expression (by flow cytometry) was compared using Kruskal-Wallis test with post hoc-analysis. Next, after HIV Gag-specific peptide stimulation for 5 days, we measured Interferon-gamma (IFN) and Tumor Necrosis Factor-alpha (TNF) production (by flow cytometry) from CD38+CD8+ and CD38+HLADR+ (hyperactivated) T lymphocytes in a subset of PWH on ART. Last, to further verify CD38's role in cytokine production by stimulating CD8+ T lymphocytes with HIV Gag-specific peptide in the presence or absence of the CD38 inhibitor, 78c. Differences in cytokine production before and after gag-peptide stimulation and 78c culture were compared using paired t-test.

Results: The mean frequency of CD38 expression on CD8+ T lymphocytes among HIV-negative (n=119), PWH on ART (n=291), and PWH not on ART (n= 485) was significantly higher among PWH compared to HIV-negative individuals ($p<0.0001$). CD38 expression decreased in PWH with the use of ART ($p<0.0001$) but did not normalize to that of HIV-negative individuals ($p<0.0001$).
The frequency of hyperactivated (CD38+HLADR+) CD8+ T cells was significantly higher among PWH on ART compared to HIV-negative individuals ($p<0.005$). Gag-peptide stimulation significantly augmented CD38+HLADR+ expression on CD8+ T cells ($p<0.0005$) and IFN and TNF production. IFN- and TNF-producing CD8+ T cells also had significantly higher CD38 expression compared to CD8+ T cells that did not produce these cytokines.
Gag-stimulated cells cultured in the presence of 78c had significantly lower CD38 expression compared to cells cultured in the absence of 78c ($p<0.0001$). The frequency of hyperactive CD38+HLADR+ cells ($p<0.0005$) and the frequency of IFN+, TNF+ and IFN+ TNF+ CD8+ T cells ($p<0.05$) was also substantially reduced in Gag-stimulated cells cultured in the presence of 78c compared to cells cultured in the absence of 78c.

Conclusions: Our results show that the CD38 expression which persists in PWH despite viral suppression by ART may be one of the driving factors for a chronic, inflammatory state, ultimately increasing the risk for comorbidities and end organ damage. Functional inhibition of CD38 improves the effect of hyperactivated CD8+ T cells by reducing the proinflammatory response, suggesting that CD38 may play a direct role in cytokine production by virus-specific cells. Therefore, CD38 is a potential therapeutic target for mitigating the chronic inflammation that drives cellular aging and comorbidities in PWH.

3

Tenofovir Alafenamide Is Associated With Shorter Telomere Length in People With HIV

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People with HIV (PWH) are at high risk of aging-related diseases even while receiving ART. Premature aging might be reflected by telomere length, which is maintained by telomerase, a reverse transcriptase (RT) that can be inhibited in vitro by RT inhibitors, including tenofovir. To determine the influence of antiretroviral therapy (ART) on change in telomere length in people with HIV, we analyzed blood telomere length and specific cART drugs in 121 PWH on ART between 2003 and 2007 after a median 12.4 years in the CHARTER project. Median T/S ratio was 0.96 (IQR 0.84, 1.08) at the first visit and declined at the second visit (median -0.082, IQR (-0.02)-(-0.19), p<10-16). The most commonly used ART drugs at the second visit were emtricitabine (FTC, 65.3%), TAF (38.8%), dolutegravir (35.5%), lamivudine (25.6%), abacavir (24.8%), and darunavir (20.7%). The T/S ratio of PWH who used tenofovir, either tenofovir disoproxil fumarate (TDF, n=111 of 242 visits [45.9%]) or tenofovir alafenamide (TAF, n=47 at the second visit only), declined more over time than of those who did not use tenofovir (p=0.049). Additional analysis identified that TAF (p=0.002) but not TDF (p=0.69) was associated with greater T/S ratio decline (see Figure), even after multivariable adjustment (p=0.028). The only other ART drug that was associated with T/S ratio change was emtricitabine (p=0.040) but the p value weakened (p=0.38) after adjusting for TAF use. Adjusting for use of FTC or other ART drugs did not substantially weaken the relationship between TAF and T/S ratio. As combination therapies containing TAF have replaced those containing TDF as leading PREP and HIV medications, it is important to continue investigations of new formulations.

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Increasing Neuroinflammation Relates to Increasing Neurodegeneration in PWH

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Background: In vitro models of HIV neuropathogenesis show that HIV infection causes neuroinflammation and immune activation (NIIA) and systemic inflammation and immune activation (SIIA), which in turn drive neurodegeneration (ND). Cross-sectional studies of people with HIV (PWH) confirm that higher levels of biomarkers of NIIA correlate with increased biomarkers of ND. A more convincing confirmation would be a longitudinal demonstration that as NIIA and SIIA increase, ND does so as well. We evaluated this hypothesis in a cohort of PWH with repeated sampling over 12 years.

Methods: PWH in the US multisite CHARTER Aging project were assessed at a baseline visit and again after 12 years using standardized evaluations. Participants with severely confounding medical and neuropsychiatric conditions were excluded. We measured a panel of 14 biomarkers of NIIA, SIIA, and ND in plasma and CSF at two-time points and calculated the changes in each of these biomarkers from baseline to the 12-year visit. We then used factor analysis to construct simplified indices of NIIA, SIIA, and ND and tested for correlations between these factors.

Results: Participants were 108 ART-treated PWH, all virally suppressed at follow-up, mean (SD) baseline age years 56 (-/+8), 17 (15.7%) female, 54 (51.0%) non-white, median (IQR) current CD4+ T-cells 576 (368, 860), CD4+ nadir 96 (21, 200). The CSF NIAA factor analysis yielded two factors: Factor1, loading on soluble tumor necrosis factor type 2 and neopterin, and Factor2, loading on monocyte chemoattractant protein type 1 and soluble CD14. The SIIA factor analysis yielded a single factor loading on plasma C-reactive protein and d-dimer. NIAA Factor1, but not Factor2, correlated with increases in CSF NFL (r=0.370, p=0.0002). Increases in SIAA Factor1 correlated with increases in NIIA Factor2 (r=0.215, p=0.0327).

Conclusions: Increases in biomarkers of NIIA and SIIA in PWH were associated with corresponding increases in biomarkers of ND, supporting the hypothesis that neuroinflammation and systemic inflammation drive neurodegeneration. These results raise the possibility that reducing neuroinflammation and systemic inflammation will slow or reverse neurodegeneration, a possibility that can be evaluated in clinical trials.

5

Individual and Community Measures of Depression and Risk of Non-communicable Disease Among Adults With HIV

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Background: Mood disorders (including major depressive and bipolar active disorders) have been associated with higher risk of non-communicable disease (NCD) in people with HIV (PWH). Depression and HIV infection also co-occur with social determinants of health which can cause and perpetuate NCD disparities. Whether community mental distress (CMD) impacts individual NCD risk in PWH has not been evaluated.

Materials & Methods: We analyzed cross-sectional associations of depression diagnosis, CMD, and number of prevalent NCDs among the Vanderbilt Comprehensive Care Clinic cohort of adult PWH followed between January 2009-December 2019. CMD was measured by the closest (±2 years) Behavioral Risk Factor Surveillance System estimate for average monthly number of mentally unwell days among residents in the county. Prevalent depression included all mood disorder diagnoses ±6 months from baseline. Prevalent NCDs included cardiovascular disease (hypertension, coronary artery peripheral vascular, or cerebrovascular disease), liver disease (cirrhosis, chronic liver disease, steatosis), metabolic disease (diabetes or dyslipidemia), chronic kidney disease (stage ≥3), and non-AIDS defining cancers. We examined the association of depression with CMD using multivariable logistic regression; we then assessed the association of number of NCDs with individual depression and CMD using multivariable proportional odds models. Both models adjusted for pertinent confounders selected a priori including age, gender, race/ethnicity, HIV acquisition risk factor, substance use, antiretroviral therapy, year, hepatitis C virus coinfection, time since HIV diagnosis, CD4 cell count, HIV RNA, and body mass index (BMI).

Results: Of the 4798 PWH included, 1342 (28%) had prevalent depression. Compared to PWH without depression, PWH with depression were older (median age 42 vs. 40 years, p<0.001), disproportionately non-Hispanic White (64% vs. 45%, p<0.001), cis-gender women (26% vs. 19%, p<0.001), had a longer time since HIV diagnosis (median 6.95 vs. 4.45 years), higher BMI (median 26.5 vs. 25.8, p<0.001), and were more likely to have ≥2 NCDs (22% vs. 17%, p<0.001). Median monthly mentally unwell days for county of residence was the same for PWH with and without depression (3.00, p=0.4). After adjusting for confounders, CMD was not associated with depression (Wald statistic for adjusted OR [aOR] p=0.22). In multivariable proportional odds models, depression was strongly associated with higher number of NCDs (aOR = 1.21, 95% Confidence Interval [CI]: 1.11-1.31, p<0.001). Higher average days of CMD was associated with higher number of NCDs, but not statistically significantly (aOR comparing 25th to 75th percentiles, 4.2 vs. 2.9 days = 1.09, 95% CI: 0.96-1.24, p=0.076). The relationship between CMD and NCD prevalence was modified by race in adjusted analysis (p-value for interaction <0.0001). Higher CMD was associated with a higher risk of NCDs among non-Hispanic White and Black individuals, but with a lower risk of NCDs among Hispanic individuals.

Conclusions: Individual depression diagnosis was strongly and independently associated with higher NCD burden in PWH. We observed a potential association between CMD and NCD burden which may differ by race/ethnicity. In addition to individual risk factors, studies of NCD multimorbidity need to explore effects by and best measurements of social and community factors driving health disparities in PWH.

6

Social and Co-morbid Determinants of Brain Aging in Persons With and Without HIV

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Background: Aging persons with HIV (PWH) undergo pathological changes to cerebral structure, detectable on T1-weighted MRI. Such changes may represent accelerated aging, which can be quantified using the brain age gap (BAG), the difference between chronological and brain-predicted age. Brain-predicted age is derived by applying machine learning to neuroimaging data to build a normative age model, which is then tested on previously unseen individuals to obtain out-of-sample residuals, i.e. years of brain-predicted age above or below chronological participant ages.

Previous work has linked increased BAG (i.e. older-appearing neural phenotypes) with uncontrolled viral load; however, subtler increases are also present in older PWH with viral suppression on combination antiretroviral therapy. We hypothesized that beyond the effects of age and viral load, residual BAG variability can be explained by social determinants of health (SDOH) and co-morbid conditions prevalent among PWH. We also hypothesized that correlates of brain aging would differ between PWH and HIV-negative controls.

Methods: Participants and imaging: 358 PWH (age=44.0±15.4 yr.; 78% male; 68% African-American; 74% virally suppressed) and 226 HIV-negative controls (age=36.74±16.8 yr.; 51% male; 59% African-American) provided informed consent and were imaged at a single site between 2009 and 2020. MRI was performed on two 3.0-Tesla Siemens scanners (TR/TE=2400/3.2ms, resolution=1x1x1mm).

The following clinical predictors were assessed: current and nadir CD4+ lymphocytes, hepatitis C infection, body-mass index, 10-year Framingham cardiovascular risk score, and lifetime substance use (alcohol, tobacco, cocaine, and opioids from Kreek-McHugh-Schluger-Kellogg [KMSK] scale). SDOH included years of formal education, wide-ranging achievement test (WRAT-III), census tract-derived area deprivation index, and neighborhood atmospheric pollution (2.5µm particulate matter).

Machine learning and statistics: DeepBrainNet, a publicly available deep neural network, was applied to estimate BAG. To test the hypothesis that co-morbidities and SDOH account for BAG variability, we performed two analyses. First, individual co-variates were tested for linear association with BAG across all participants while controlling for HIV, age, and sex. To test the hypothesis that predictors of brain aging differ by serostatus, multiple linear regression with exhaustive 'best-subsets' model selection was performed separately for PWH and HIV-negative controls, using adjusted R2 to identify the best-fit model while penalizing models with numerous predictors.

Results: DeepBrainNet predicted age in study participants with a mean absolute error of 5.3 years (R2=0.82). BAG estimates did not vary by race (p=0.33). Examining predictors individually across all participants, BAG was positively associated with area deprivation index (p=0.03), alcohol use (p=0.02), Framingham risk score (p=0.01), and Hepatitis C positivity (p=0.01). BAG was negatively associated with WRAT-III, but only in HIV-negative controls (interaction p=0.02). For PWH, best-subsets selection identified a model with three predictors: Framingham score, alcohol use, and Hepatitis C.

Conclusions: Aging with HIV presents a unique gerontological challenge even with viral suppression, as PWH are at risk for increased brain pathology due to SDOH and chronic co-morbidities. In this study, we found that substance use, cardiovascular health, and co-infection are important predictors of neurological health in PWH. We also identified socioeconomic status (area deprivation index) as a brain aging correlate. In contrast, educational attainment was a key predictor in HIV-negative controls, potentially indicating a greater impact of cognitive reserve. Future research and clinical assessments of neural health in PWH should consider the effects of modifiable non-HIV risk factors.

7

The Impending African Challenge: Gaps in 95-95-95 Performance Herald an Emerging Double-Disease Burden of Ageing and HIV in Two High Burden Metropolitan Health Districts in South Africa

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Background: Among older persons (≥50 years of age) the HIV prevalence is 13% in South Africa and is expected to rise to 24% by 2030. Non-communicable diseases (NCDs) associated with ageing have a high prevalence in South Africa, and as the numbers of older people living with HIV (OPLHIV) on ART continue to grow, HIV will increasingly become comorbid with other chronic diseases. We questioned whether programme reorientation is needed to optimize 95-95-95 for OPLHIV, while also integrating planning for the "fourth 95": maintaining quality of life while managing the associated challenges of ageing with HIV. To profile the potential scale of the challenge, we analysed 95-95-95 programme performance data for two high HIV burden urban metropolitan districts in Gauteng, South Africa.

Materials and Methods: Wits RHI receives funding from the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) to support routine HIV program implementation in two metropolitan health districts. OPLHIV is defined as PLHIV 50 years of age and older for the purposes of this abstract. Age- and gender-disaggregated for OPLHIV were extracted from routine programme data reported to PEPFAR for the period of October 2021 to March 2022 for the two health districts. Data were collated and analysed, according to current PEPFAR Monitoring, Evaluation and Reporting indicator definitions (MER version 2.6). We report on indicators measuring 95-95-95 performance among OPLHIV: HIV case finding, anti-retroviral treatment (ART) initiation, retention in care within 28 days of the last scheduled appointment, treatment interruptions and returns to care per quarter, mortality, viral load (VL) coverage (at least one VL test conducted within a rolling 12-month period for patients on ART >6 months) and VL suppression (<1000 copies/ml).

Results: Within the 6-month period, 45327/760146 HIV tests done (6%) were conducted for people ≥50 years, with 3344 new HIV-positive diagnoses among those tested (7% positivity). Only 2737 OPLHIV (82%) were initiated on ART. At the end of March 2022, 125173/539418 (23%) of PLHIV in care were ≥50 years, with the majority (74%) aged 50-60 years old. The cohort of OPLHIV grew by 6772 (6%) between December 2021 and March 2022, including clients newly initiated on ART, patients ageing in, returns to care and transfers from other districts. Dynamic movement was seen into and out of the cohort: 5522 patients interrupted treatment between October to December 2021 and 2996 between January and March 2022, with 2341 and 3600 returns to care, respectively. There were 300 reported deaths among OPLHIV during the 6-month period of interest. While 121829 OPLHIV were eligible for VL monitoring, only 101246 (83%) had a VL done. Of those with a VL done, 96% had a suppressed VL.

Conclusions: This analysis found clear gaps in the HIV treatment cascade for OPLHIV. Among OPLHIV retained in care, most were 50-60 years old, with the potential for increasingly complex healthcare needs as their age increases. The need for tailored programmatic planning for this population is apparent, as is the need for more research to guide targeted interventions for OPLHIV in this context.

8

Aging and HIV: What Is the Gap Between Clinical Practice and Guideline Recommendations?

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Background: European AIDS Clinical Society (EACS 11.0, 2021) and Società Italiana di Malattie Infettive e Tropicali (SIMIT 2017) guidelines on HIV treatment provide specific statements regarding models of care for older people living with HIV (OPLWH). The objective of the study was to explore unmet needs of OPLWH regarding the compliance of Italian HIV clinics to the national and international recommendations on HIV aging care.

Methods: Part 1: EACS and SIMIT guidelines were compared regarding specific statements addressing OPLWH care needs. These included items such as co-morbidities, multimorbidity, polypharmacy, frailty and falls. A synoptic table was built to summarize key statements and agreements between guidelines. These statements were used to build a survey exploring aging model of care and unmet clinical needs.
Part 2: This was a cross sectional country wide survey offered to all HIV clinics and their attendees aged>50 years in Italy in the week including World AIDS day (1st December 2021). The survey was composed of two parts: the first was referred to health care workers containing questions related to model of care for OPLWH, while the second was referred to OPLWH addressing health domains including: frailty through Frailty scale (FS), resilience through CD-RISC-2, functional capacity by self-reported Duke Activity Status Instrument (DASI), health-related quality of life (HRQoL) through EQ-5D-5L questionnaire. Other collected geriatric syndromes included falls and polypharmacy. Questions regarding stigma, isolation, loneliness, sex life, social support, and relationships were also included.

Results: EACS and SIMIT guidelines resulted concordant in highlighting OPLWV health needs. Both quote HRQoL as the ultimate goal of clinical care but neither the two specify how to integrate it in the in a person-centered approach. Of the 35 HIV clinics that answered, 27 (77%) declared that there were no dedicated care models for OPLWH and 28 (80%) reported that geriatric consultation was not available at the clinic. Nevertheless, 29 (82.2%) HIV clinics provided health information on aging to their patients, and 23 (66.6%) facilitated access to treatment and care for OPLWH through telemedicine. A total of 66 OPLWH were interviewed, mean age was 61 years, 51 (77%) were males, median duration since HIV diagnosis was 21 years, median nadir CD4 cell count was 208 c/microL and 64 (96.4%) had undetectable HIV RNA. Screening for frailty assessed by FS showed that 27 (41%) required geriatric evaluation, 12 (18.1%) reported falls in the last year and 14 (21.1%) polypharmacy. Functional capacity assessed by DASI questionnaire was impaired in 71% of OPLWH, while 58% presented both poor resilience and suboptimal HRQoL.

Conclusions: Our findings revealed relevant gaps between guidelines recommendations and clinical practice. This calls for action and urges the need for a multidisciplinary person-centered approach, coupled with comprehensive geriatric assessment and screening tools to assess comorbidities, frailty and geriatric syndromes, using HRQoL as a key outcome measure in OPLWH.

9

Needs and Involvement of HIV Specialists and Geriatricians in the Care of Older Adults with HIV. A National Survey

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Introduction: Half of the people with HIV are currently older adults. Comorbidity, frailty, and geriatric syndromes are prevalent and appear at an early age. Our aim is to test the knowledge and involvement of geriatricians in the management of older adults with HIV and the HIV specialists' attitude towards a joint approach to these patients.

Methods: We developed a survey with 12 specific questions for geriatricians and another for HIV specialists. The surveys were distributed through the National Scientific Societies during the last week of March 2022. They were completed anonymously and voluntarily.

Results: 94 geriatricians (G) and 63 HIV specialists (H) answered. 71,2% of the geriatricians would feel uncomfortable if they had to evaluate a patient with HIV. 86.1% have seen one or no older patients with HIV in the last year. 79.3% of the HIV specialists believed that geriatricians should be involved in the management of older adults with HIV. Both groups agreed that the approach to these patients should be multidisciplinary (G91.9% vs H79,3%), that specific training is needed (G91.4% vs H80,9%) and that the criteria to refer an older adult with HIV for a comprehensive geriatric assessment should be the presence of frailty and/or other geriatric syndromes rather than the chronological age (G82,9% vs H87,3%).
Conclusions: Geriatricians have a lack of knowledge about older adults with HIV and are no involved in their management yet. HIV specialists are open to co-management of older HIV patients. Specific training is needed to ensure the best approach to them.

10

New York State AIDS Institute Initiatives to Improve Care For Older People With HIV and Long-Term Survivors: An Example of a Government-Academic-Community Partnership

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Background: The New York State Department of Health AIDS Institute (AI), founded in 1983, has always included improving health and wellbeing of persons living with HIV in its mission. Nearly 1% of New Yorkers 55 years and older have HIV. Of those with HIV, 60% are at least 50 years of age and more than one quarter are at least 60. There are more than 2400 people who were perinatally diagnosed with HIV in NYS, and most of these people are now adults. To respond to this need, the AI has created a multifaceted HIV and Aging program.

Methods: The AI Consumer Advisory and Clinical Quality Advisory Committees created a joint consumer/provider subcommittee on HIV and Aging, Long Term Survivors, and Perinatally Diagnosed (HALP) in 2020; this subcommittee, which has encouraged expansion of the AI's activities to directly address needs of older people with HIV (OPH) and LTS, held town halls and promoted a Syracuse University-sponsored statewide survey of barriers and recommendations to quality care.

Results: The New York State AIDS Institute has responded to demographic changes by initiating a number of programs:

- Its Clinical Guidelines Program has published a Guidance for Addressing the Needs of Older Patients in HIV Care.

- It has approved a functional screening tool modified from the WHO ICOPE model and is assisting sites in piloting the tool, with plan for statewide dissemination and implementation.

- Its Certified Peer Worker training program is committed to training peer workers on the use of the screen.

- It is funding a $4 million statewide People Aging with HIV (PAWH) RFP to create HIV-Aging programs that focus on community linkages and use of certified peer workers. This RFP is designed to ensure each region of the state is engaged.

- It has established a new Project Director of HIV and Aging (within the Bureau of Community Support Services) to oversee the PAWH initiative, foster coordination around all HIV and Aging activities across the AIDS Institute, and facilitate collaboration with non-NYS DOH entities (i.e., New York City Department of Health and Mental Hygiene, NYC Ryan White Planning Council, and New York State Office for the Aging) to streamline and support communication statewide.

- Its Center for Quality Improvement and Innovation has been competitively funded by the Federal Health Resources and Services Administration (HRSA) to create the aging+hiv Initiative, which will support a national learning collaborative with 10 demonstration sites and disseminate resources to the larger Ryan White community.

Conclusions: Government agencies can and must promote quality care for OPH and LTS by partnering with consumers and providers. Agencies have the resources and authority to ensure that programs of all sizes and regions can participate, and that that all consumers can benefit from these quality-of-care initiatives. The NYS AIDS Institute has established both intra- and extramural initiatives that can promote highest quality of care throughout the state and disseminate best practices across the country.

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Frailty and Physical Performance Assessments as Part of a Comprehensive Geriatric Care Model in an Urban HIV Clinic

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Background: Frailty is an increasingly recognized important condition in people living with HIV(PLWH) despite viral suppression with antiretroviral therapy (ART). In PLWH, frailty can occur up to two decades earlier compared to non-HIV infected people, with a prevalence of 5-30% among PLWH around age 40. Frailty is a syndrome where there is a decline in a person's physical and functional reserve to handle or endure usual life stressors which results in disability, falls, and death. Frailty among PLWH has been attributed to a combination of factors including systemic immune activation from HIV replication, chronic inflammation, co-infections, multimorbidity, polypharmacy, and ART toxicity. The Fried frailty phenotype (FP) is a tool for diagnosing frailty that has been validated in PLWH. The short performance physical battery (SPPB) is another tool that has been used to screen for frailty among people both with and without HIV infection. In this study, assessments using FP and SPPB were used as part of a comprehensive geriatric screening model in an urban HIV clinic.

Methods: The Strengthening Therapeutic Resources in Older adults aging with HIV (STRONG) Study, at the University of Maryland, Baltimore aims to create a geriatric care model by incorporating standardized geriatric assessments into an urban ambulatory care center. PLWH aged ≥50 years were invited to participate. FP and SPPB were assessed by trained study staff. FP scores of 0, 1-2, and ≥3 out of 5 criteria represented non-frail (robust), pre-frail and frail respectively, while SPPB score of ≤9 out of 12 indicated a positive screen for potential frailty.

Results: Of the 184 participants enrolled from November 2019 to February 2022, 165 patients completed the assessments. Participants were 56% male, 94% black, and the median age was 59 years (IQR 55-63). Most (78%) were virally suppressed (HIV viral load ≤40) and median CD4 count was 606 cells/µl (IQR 393-873). Using FP, 62% were prefrail, 11% frail, and 27% robust. The most frequently occurring frailty components were weakness (51%), low walk speed (31%), shrinkage (21%), and low physical activity (17%). Exhaustion occurred in <5% of participants. Using SPPB, majority (n=104, 63%) had low physical functioning (SPPB ≤9). Of these, 70 (67%) were pre-frail and 17% frail, using FP. All the FP frail patients had SPPB ≤9, which had a 100% sensitivity, 41% specificity, and 17% positive predictive value for FP frailty. In unadjusted analyses, polypharmacy (>5 pills), Montreal Cognitive Assessment (MoCA) score ≤18, Patient Health Questionnaire depression (PHQ-9) ≥5 and Generalized Anxiety Disorder (GAD-7) scores 5-9 and ≥10 were associated with frailty. In multivariate analyses, polypharmacy (OR 7.8, p=0.005), GAD ≥ 10 (OR 16.4, p=0.03) and MoCA≤18 (OR 24.3, p=0.03) remained statistically significant.

Conclusion: The majority of our HIV cohort were pre-frail and frail, with a positive SPPB frailty screening in two thirds. SPPB ≤9 identified all patients with frailty. Interventions targeting physical function, weight loss, polypharmacy, GAD and cognition may be strategies that could mitigate and prevent frailty in our aging PLWH.

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Evaluation of an Electronic Health Record-Based Frailty Index in People With and Without HIV in a Primary Care Setting

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Background: Compared with the general population, people with HIV (PWH) are at higher risk of becoming frail and are more likely to become frail at younger ages. Frailty risk scores calculated from electronic health record (EHR) data have been developed to efficiently identify frail patients in general primary care, but less is known about their utility in PWH.

Methods: We conducted a study among PWH and demographically-similar people without HIV (PWoH) at Kaiser Permanente Northern California, an integrated healthcare system in the U.S. Study participants were patients with health plan memberships between July 2013 and December 2019. Frailty risk scores were calculated at study baseline using a frailty index based on ICD and procedure codes recorded in the EHR. Participants were categorized as non-frail, pre-frail, or frail according to pre-defined numeric cutoffs determined based on prior study of the index in the general patient population. The association of baseline frailty status with risk of subsequent emergency department (ED) visit or hospitalization was evaluated separately for PWH and PWoH using Cox proportional hazards models.

Results: The study included 6,323 PWH and 120,893 PWoH (90.9% men; 62.5% White, 15.4% Black, 12.6% Hispanic, 9.5% Other race/ethnicity). The mean age at baseline was 56.4±6.6 years for PWH and 57.9±8.9 years for PWoH. Frailty was more common among PWH compared with PWoH (21.2% vs. 15.9%, p<0.001). During study follow-up, 3,515 PWH (55.6%) and 58,732 (48.6%) PWoH had an ED visit, and 1,626 (25.7%) PWH and 23,932 (19.8%) PWoH were hospitalized. The association of frailty with ED visits was stronger in frail PWoH (hazard ratio [HR] 4.33, 4.23-4.42) than in frail PWH (HR= 3.75, 3.39-4.13). The association of frailty with hospitalization was also stronger in frail PWoH (HR=10.32, 9.92-10.73) than frail PWH (HR=6.74, 5.73-7.92).

Conclusions: We evaluated an EHR-based frailty index which may be useful for identifying frailty among PWH in primary care. Further refinement of the frailty index by addition of HIV-specific variables may improve its ability to predict frailty-related clinical events in PWH.

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Risk Factors for Frailty in a Geriatric Cohort on Long Term Antiretroviral Treatment in Uganda

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Background: Antiretroviral treatment (ART) scale-up has led to a generation aging with HIV in sub-Saharan Africa (SSA). Frailty, an age-related syndrome heightened by HIV infection, is marked by diminished physiologic reserve and vulnerability to stress, and is predictive of adverse clinical outcomes. We determined the prevalence and risk factors of frailty in a geriatric cohort in Kampala, Uganda.

Methods: We determined frailty prevalence and predictors in an aging cohort (≥60 years) enrolled between December 2020 and December 2021. Frailty was defined by criteria proposed by Fried and colleagues: 1)

unintentional weight loss, 2) exhaustion, 3) weakness 4) slow walking, and 5) low physical activity. We performed logistic regression controlling for: gender, age, BMI, pre-ART and current CD4 count, WHO stage, years on ART, co-morbidities (NCDs), household income, depression, and cognitive status.

Results: Of 500 participants, 51.2 % were male, median age was 64 (IQR:62-68) years, and median time on ART was 15 (IQR:10-17) years. Twenty-eight (5.6%) were underweight, and 154 (31.2%) had an income lower than 1 USD/day. CD4 count at the ART start and at the time of enrolment were 159 cells (IQR:74-235) µL and 645 (IQR:450-805) µL, respectively. Two had a viral load >1,000 copies/ml, 151(30.2%) >1 NCD, 72.8% some degree of cognitive impairment, and 10.2% depression. Forty-five (9%) were frail, 229(45.8%) pre-frail, and 226(45.2%) robust. CD4 count and WHO stage were similar across the three groups.
Men (AOR 0.30, CI: 0.11-0.77, p-value: 0.012), those with normal BMI (AOR 0.06, CI:0.01-0.3, p-value: 0.03), and those overweight (AOR 0.08, CI 0.01-0.48, p-value: 0.005) were less likely to be frail. Participants who were below the poverty line (AOR 2.60, CI: 1.13-6.01, p-value: 0.025), cognitively impaired (AOR 5.70, CI:1.49-21.71, p-value 0.011) and depressed (AOR 20.68, CI:6.46-66.37 p-value: 0.000) were more likely to be frail.

Conclusion: Despite the exceptional rates of viral suppression and robust CD4 count recovery, more than half of the patients with HIV infection were frail or pre-frail in our cohort, highlighting the clinical relevance of this condition. The assessment of frailty may pave the way for interventions for preventive/multidisciplinary interventions in nutrition, mental health, and lifestyle.

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Physical Frailty Among Older HIV-Positive and HIV-Negative Women in Mombasa, Kenya: A Cross-Sectional Study

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Background: Physical frailty may reduce quality of life and longevity among older persons. It is not clear how physical frailty affects HIV-positive Kenyan women as they age, and whether they are more frail than their HIV-negative peers. Our objective was to investigate the associations between HIV status and three measures of physical frailty (grip strength, physical performance and Rockwood clinical frailty score) among older Kenyan women with and without HIV infection.

Material and Methods: A cross-sectional study was conducted among 150 HIV-positive women and 150 HIV-negative women aged 40 years and older in an ambulatory setting in Mombasa, Kenya. Sociodemographic factors, vital signs and anthropometric measurements, grip strength, a short physical performance battery (SPPB), and Rockwood clinical frailty score were assessed by trained research staff. Descriptive statistics were calculated for women in the overall study population and each HIV status category. For each of the three continuous physical frailty outcomes assessed (i.e., grip strength, SPPB score, clinical frailty score), linear regression was used to evaluate HIV status as the primary predictor, after adjustment for potential confounders including age, marital status, hypertension, smoking status, alcohol use, and body mass index. Grip strength was log2-transformed to approximate normality.
Results: Mean age was 52.6 years and did not differ by HIV status (p=0.78). HIV-positive women were more likely to be single and have less education than their HIV-negative

counterparts. Overall, HIV-positive women had stronger grip strength (14.2 vs. 10.7 kg, p<0.0001), similar SPPB score (8.1 vs. 8.2, p=0.47), and higher clinical frailty score (2.8 vs. 2.4, p<0.0001), compared to their HIV-negative counterparts. Most (74.7%) HIV-positive women were rated as "managing well" and most (62.7%) HIV-negative women as "well." In multivariable analysis of the grip strength outcome, HIV was a significant predictor of grip strength (adjusted beta 0.43 log2 kg for HIV-positive women, 95% confidence interval [CI] 0.26, 0.59 log2 kg) as were older age (adjusted beta -0.02, 95% CI -0.03, -0.01 log2 kg per year) and marital status (single women had higher grip strength compared with married, separated/divorced, or widowed women, overall p=0.002, details not shown). In multivariable analysis of SPPB score, there was no difference by HIV status (adjusted beta -0.15, 95% CI -0.51, 0.20) but older age was a significant predictor of lower performance (adjusted beta -0.06, 95% CI -0.08, -0.34 per year). Finally, in multivariable analysis of clinical frailty score, HIV remained a significant predictor (adjusted beta 0.46, 95% CI 0.31, 0.61), as did older age (adjusted beta 0.03, 95% CI 0.02, 0.04 per year).

Conclusions: Older women with HIV had a stronger grip strength and similar physical performance but were judged to be more clinically frail than HIV-negative women, largely based on their managed disease. The finding on grip strength was unexpected, and merits further investigation. Older age was associated with weaker grip strength, worse physical performance and increased clinical frailty. Prospective studies are needed to further elucidate the effects of HIV on physical frailty and aging.

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Assessing the Impact of HIV Status and Menstrual Abnormalities on Longitudinal Bone Density Loss in Women Living With and Without HIV

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Background: Preserving bone density is critical to promoting healthy aging in women. However, cross-sectional Canadian data indicate that women living with HIV (WLWH) have lower bone mineral density (BMD) and more fractures compared to HIV-negative women. Menstrual abnormalities may mediate this relationship, as WLWH are more likely to have prolonged amenorrhea (absent menses for ≥1 year) compared to HIV-negative women, and this has been associated with lower hip BMD in cross-sectional analyses. Here, we compare the rate of change in BMD per year (ΔBMD/year) in WLWH compared to HIV-negative women and assess whether this is impacted by history of menstrual abnormalities.

Methods: WLWH from the Children and Women: AntiRetrovirals and Markers of Aging (CARMA) cohort were matched 1:3 within 5 years of age with women from the Canadian Multicentre Osteoporosis Study (CaMos). BMD was assessed by dual-energy X-ray absorptiometry scan at two timepoints (3-5

years apart). History of menstrual abnormalities was defined as no menstrual periods for ≥1 year (not due to pregnancy/breastfeeding, surgery, or contraceptive use), or natural menopause before age 45. Demographic data were compared between groups using Chi-square, Mann-Whitney U, and t-tests. ΔBMD/year was calculated and compared between groups at the total hip and lumbar spine, controlling for age, income, ethnicity, education, body mass index (BMI), current/past smoking, weight cycling (ever gained/lost ±10 lbs), alcohol consumption, parity, menopause status, and age at menarche.

Results: Ninety-two WLWH and 278 controls were included in this analysis. The median [IQR] age was 49.5 [41.6 to 54.1] and 49.0 [43.0 to 55.0] years for WLWH and controls, respectively. WLWH were more likely to have <high school education, income <$20,000 CAD/year, unemployment, past/present smoking history, and be non-White. WLWH were more likley to have past/present menstrual abnormalities (21.7% vs. 4.3%; p<0.001). Participants were similar with respect to BMI, alcohol consumption, age at menarche, parity, and history of weight cycling. Most WLWH (79.3%) had undetectable viral loads (<40 copies/ml). In adjusted analyses, HIV status (β=-0.004 (95%CI -0.007 to -0.0008) g/cm2/year; p=0.015) and being menopausal (β=-0.007 (-0.01 to -0.005) g/cm2/year; p<0.0001) were independently associated with losing total hip BMD, whereas non-White ethnicity (β=0.004 (0.0009 to 0.007) g/cm2/year; p=0.011) and higher BMI (β=0.0003 (0.000 to 0.0004) g/cm2/year; p=0.005) were associated with gaining hip BMD. At the spine, menopause status was the only variable associated with losing BMD (β=-0.01 (-0.01 to -0.006) g/cm2/year; p<0.0001). Menstrual abnormalities were not associated with ΔBMD/year at either the hip or spine.

Conclusions: After adjustment for confounders, HIV status negatively influenced ΔBMD/year at the total hip, but there was no association between ΔBMD/year and history of menstrual abnormalities at either the hip or spine. This is in contrast with cross-sectional data, perhaps because participants with amenorrhea have since resumed menses and normalized their rates of bone loss. Our data underscore the importance of monitoring BMD in women living with HIV as they age, particularly in those who are menopausal. Finally, our analysis identified BMI as a key factor affecting ΔBMD/year, emphasizing the importance of nutrition in preserving bone health.

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Hormonal Intervention Combined with Allopregnanolone Alleviates Premature Age-Related Comorbidities in Female Mice Exposed to Ovarian Failure and HIV-1 Tat

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Background: In the U.S, over 50% of people living with HIV (PLWH) are aged 50 or older. However, age-related comorbidities occur frequently among PLWH compared to age-matched seronegative people. Women with HIV experience an earlier transition to post-menopause that is associated with a higher incidence of age-related comorbidities. Despite antiretroviral therapy, neurotoxic HIV proteins such as the trans-activator of transcription (Tat) persist within the central nervous system and may contribute to age-related comorbidities. We find that Tat is sufficient to dysregulate aspects of the neuroendocrine system in mice. However, the benefit of hormonal replacement therapy (HT) in HIV is unclear.

Material and Methods: We use 4-vinylcyclohexene diepoxide to achieve an ovary-intact peri- and post-menopause model in Tat-transgenic mice. We hypothesized that conditional Tat expression [Tat(+)] would exacerbate age-related comorbidities compared to age-matched controls [Tat(-)]. We anticipated HT would attenuate Tat/age-related comorbidities to a greater degree when intervention occurred in the peri-estropausal stage, as opposed to the post-

estropausal stage. We also assessed the effects of the most commonly-prescribed HT, Prempro® (conjugated equine estrogens and medroxyprogesterone acetate), alone or in combination with a neuroprotective progesterone metabolite (allopregnanolone; AlloP). Behavioral data were analyzed using three-way ANOVA.

Results: Overall, post-estropausal mice demonstrated greater anxiety- and depression-like behavior than did peri-estropausal mice. When exposure to Tat occurred in the peri-estropausal stage, mice exhibited little initial change in nociceptive sensitivity or neuromuscular function; however, as Tat exposure continued throughout the post-estropausal transition, mechanical nociceptive thresholds were increased. Neuromuscular function generally declined. These findings are consistent with a reduction in mechano-sensitivity and muscle strength as exposure to Tat becomes chronic. Notably, if Tat exposure first occurred in the post-estropausal stage, mechanical pain responses were much greater. The anti-anxiety-like benefits of Prempro® were only observed when HT was initiated in the peri-estropausal stage. At this time, the inclusion of AlloP potentiated the benefits of Prempro®, but only among Tat(-) controls and Tat(+) post-estropausal mice. Tat-induced cognitive deficits were not observed until mice transitioned to post-estropause. Prempro® alone did not improve cognition in Tat(+) mice, but did so when combined with AlloP. Similarly, co-administration with AlloP improved antiociception in post-estropause.

Conclusion: Tat and endocrine aging exhibited independent and interactive effects to accelerate age-related comorbidities in female mice. Hormonal replacement therapy, including combined Pempro® and AlloP, provided the greatest benefit to post-estropausal mice exposed to HIV Tat. Including a neurosteroid, such as AlloP, in HT may benefit for older women living with HIV.

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Plasma Extracellular Vesicles and Cell-Free Mitochondrial DNA Are Associated With Cognitive Dysfunction in Treated Older Adults With HIV

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Background: Extracellular vesicles (EVs) are small structures with a range of functions including cell-to-cell communication and inflammation. Neurons and microglia can secrete EVs that cross the blood brain barrier. Plasma cell-free mitochondrial DNA (cfmtDNA), a marker and potential inducer of inflammation, has been associated with cognitive dysfunction in older adults with HIV (OAH). Specific EVs also have been associated with inflammation in the setting of HIV and can provide diagnostic and predictive value for CNS injury in HIV. We hypothesized that plasma EVs would be associated with cognitive dysfunction in OAH.

Methods: A nested case-control study compared OAH age ≥55 with cognitive dysfunction (Montreal Cognitive Assessment [MoCA] score <23) to demographically similar OAH controls (MoCA >26). Frailty testing was conducted using the Fried Frailty Index. Participants with HIV-1 viral load >40 copies/ml were excluded. Plasma EVs were measured by flow cytometry and plasma/urine cfmtDNA by PCR for NADH dehydrogenase 1 gene. EVs measured included CD4, CD14, CD16, CD19, CX3CR1, WGA, CCR5, CD62p, CD41a, CD163, CCR2, CCR5, MAL-1, CD11b, CD200, Neurofilament, S100B, GFAP, MAP2, CD9, CD63, MHCII, GLUT-1, CD66b, CD73, and CD36. A support vector machine learning-based model using recursive feature elimination was employed for analyses and area under the curve of the receiver operating characteristic (AUC-ROC) assessed the

probability of discriminating cognitive function.

Results: Of 50 participants, median age 60 (IQR 57-65), 38% female, 53% Black and 25% Hispanic, with a median CD4 T-cell count of 596 (IQR: 479-859), and 65% met the criteria for pre-frail/frail. A model including 4-meter walk time, CCR5+ EVs, GLUT-1+ EVs and urine cfmtDNA classified cognitive status with an AUC-ROC of 0.86 (95% CI [70-100] and an AUC-precision recall curve of 0.97 [0.93, 0.99].

Conclusions: Our machine learning model predicted cognitive dysfunction with 86% certainty (±15%) using a combination of 4-meter walk time, CCR5+ EVs, GLUT-1+ EVs, and urine cfmtDNA. CCR5+ and GLUT-1+ EVs may mediate inflammatory and metabolic activity, respectively, in the CNS. Our findings suggest a role of EVs and cfmtDNA as potential biomarkers of cognitive dysfunction and warrant further investigation.

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Clinical Care Priorities and Service Needs Among Patients Aging with HIV in the Bronx, New York

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Background: As a result of widespread effective antiretroviral therapy, growing numbers of people with HIV are surviving into older age. New care models are necessary to address the increasing burden of age-associated comorbidities and geriatric syndromes experienced by the aging population with HIV. This project seeks to describe qualitative and quantitative data collected from older persons living with HIV (OPLWH) on clinical care priorities and service needs, to inform the development of an integrated geriatric-HIV model of care.

Material and Methods: Patient perspectives of PLWH age 60 years and above receiving care in an ambulatory HIV specialty clinic in the Bronx, New York were examined in Spanish and English via 84 telephone surveys, 27 in-depth individual interviews and 3 focus groups conducted online among priority groups of men who have sex with men (MSM), transgender women, cisgender women, people who inject drugs (PWID), and cisgender heterosexual (cis-het) men between 5/2021 to 2/2022 . Transcripts were analyzed using an adaptation of the 5M model, and use of analytic memos and framework analysis based on quantitative measures for an explanatory sequential model of data analysis.

Results: Median age was 63 years (IQR 62-66), 56% were Black, 33% Hispanic, 7% White, 6% other; participants included 13 MSM, 13 cis-gender women, 4 transgender women, 13 cis-gender heterosexual men, and 17 PWID. All OPLWH were taking ART, 71% were diagnosed with HIV over 20 years ago, and 72% reported that they had not expected to survive as long as they have. Using the Lawton IADL scale, 52% reported some degree of disability, including 30% with disability in one domain; 23% had disability in multiple domains, more commonly occurring among cisgender women, MSM, and PWID. Loneliness was reported by 25% (UCLA-3 score 6-9); 52% were considered socially isolated (Lubben Social Network Scale–6, LSNS-6 score <12), including 32% with marginal family ties (LSLS-6 subscale <6), and 63% with marginal friendship ties. Themes from individual interviews and focus groups emphasized concerns about functional decline, loss of independence, and memory impairment, as well as desire for greater connectedness. Highest priority services rated by OPLWH included evaluation and management of cognitive impairment, having an on-site geriatrician in the HIV clinic, enhanced provider education on aging, and increased access to aging-related social services. OPLWH also recommended offering support groups, additional mental health services, and increased engagement and input by OPLWH in program development for aging-related services.

Conclusions: Loneliness, social isolation, and cognitive and functional decline are key challenges facing OPLWH, many of whom had not expected to survive into older age. Models of care for aging PLWH must address these

particular challenges with the input of OPLWH to increase access to necessary services and support for the growing numbers of PLWH surviving into older age.

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Physical Functioning in Older People Living With HIV: STRONG Study

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Introduction: Older people living with HIV (oPLWH), 50 years and older, are at an increased risk for cardiovascular disease, cancer, diabetes, osteoporosis, and frailty even at an earlier age. oPLWH also struggle with depression, isolation, stigma, and cognitive impairment. In addition to chronic HIV, managing aging-related conditions with other comorbidities can affect health-related quality of life (HRQoL) and long-term survival. oPLWH experience a greater decline in physical functioning (PF) relative to the general population; PF can contribute towards other aging-related conditions and adverse events. Concerns regarding daily functioning and mobility highlight the need to incorporate geriatric and multimorbidity principles in HIV care for oPLWH. PF measures, like Short Physical Performance Battery (SPPB), timed up and go (TUG), and gait speed (GS) can be strong predictors of mobility, disability, cardiovascular health, and mortality. Different measures of PF were explored in this study to understand the physical functioning in oPLWH, and its association with HRQoL and daily functioning.

Methods: The Strengthening Therapeutic Resources in Older adults aging with HIV (STRONG) program was piloted at an outpatient HIV clinic from November 2019 to February 2022. PLWH ≥50 years of age completed standardized assessments, including Patient Health Questionnaire (PHQ-9), Fried Frailty Index (FFI), and activities of daily living (ADL) using Older American Resources and Services). For the PF measures, GS, SPPB, TUG, and grip strength scores were collected. Medical chart reviews were performed by clinicians for clinical and medication data. SPPB contains three components: balance, gait speed, and chair stand; each can be scored up to 4. Scores <50 on Patient-Reported Outcomes Measurement Information System reflected poor HRQoL, while >2 on OARS items indicated limited ADL. Using logistic regression, the estimated odds ratios (OR) with a 95% confidence interval (CI) for physical functioning with QoL and ADLs were reported.

Results: This study sample of 184 participants was predominantly male (56%), single (62%), virally suppressed (94%; VL<200), smokers (84.8%), and identified as Black (94%). On average, participants were 60 years of age and had been living with HIV for 24 years. Participants scored a median of 8/12 (IQR= 7-10) on SPPB, where 76.4% had reduced physical functioning (SPPB<10). Among the individual SPPB components, a lower percentage of participants scored 4 on the Chair stand (12.1%) relative to Balance (46.1%) and Gait (69.1%). Even with the increase in SPPB scores, oPLWH had lower odds of higher physical HRQoL (OR=0.78; 95%CI=0.64-0.95) after adjusting for sex, age, and depression. Among the ADLs, lower odds of independent functioning regarding walking, performing household chores, and traveling long distances were observed (OR=0.73; 95%CI=0.63-0.86, OR=0.82; 95%CI=0.69-0.96, OR=0.81; 95%CI=0.68-0.97, respectively); as physical performance scores increased, lower odds of oPLWH had urine control (OR=0.76; 95%CI=0.66-0.89).

Conclusion: These findings show that most of the STRONG participants have reduced physical performance, which was associated with poorer HRQoL and limited ADLs. Screening for physical functioning using SPPB in HIV clinics may be beneficial in supporting healthy aging in oPLWH by intervening earlier on those at elevated risk for adverse aging-related outcomes.

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Alzheimer-Type Cerebral Amyloidosis in the Context of HIV Infection: Implications for a Proposed New Treatment Approach

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Background: To evaluate the hypothesis that reverse transcriptase inhibitors (RTIs) protect against Alzheimer-type brain amyloidogenesis in the context of HIV infection.

Methods: This is a case series of participants from a prospective study of the neurological consequences of HIV infection at the HIV Neurobehavioral Research Program (HNRP) at UCSD who had serial neuropsychological and neurological assessments and on RTI. Two participants had gross and microscopic examination and immunohistochemistry of the brain at autopsy; one was assessed clinically for AD by cerebrospinal fluid (CSF) analysis of phosphorylated-Tau, Total-Tau and Aβ42. Additionally, a larger cohort of autopsied individuals was evaluated for presence of amyloid plaques, Tau, and related pathologies.

Results: Three older, virally suppressed individuals with HIV who had long-term treatment with RTIs were included in analyses. Two cases demonstrated substantial cerebral amyloid deposition at autopsy. The third case met clinical criteria for AD based on a typical clinical course and CSF biomarker profile. In the larger cohort of autopsied individuals, the prevalence of cerebral amyloidosis among PWH was greater for those on RTIs.

Conclusions: The amyloid ratings in those who took RTIs as part of their antiretroviral regimens (n=160, 58.6%; amyloid rating 0, 69.4%; amyloid rating 1, 20%; amyloid rating 2, 10.6%) did not differ from those who did not take NRTIs (amyloid rating 0, 72.6%; amyloid rating 1, 23.9%; amyloid rating 2, 3.54%; p=0.178). Therefore, long-term RTI therapy did not protect against Alzheimer-type brain amyloidogenesis in the context of HIV infection in these patients. Given the known toxicities of RTIs, it is premature to recommend them to individuals at risk or with Alzheimer's disease who do not have HIV infection.

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Fibroscan-AST (FAST) Score Predicts Liver-Related Outcomes in People Living With HIV at Risk for NAFLD

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Background and Aims: Non-alcoholic fatty liver disease (NAFLD) affects 35% of people living with HIV (PWH) in absence of viral hepatitis coinfection. About 15% of these PWH have also significant liver fibrosis. Natural history studies employing accurate non-invasive tools are lacking. The FibroScan-AST (FAST) score was developed to identify patients with histologic NASH with advanced fibrosis and elevated NAFLD activity score (NAS) associated with higher risk of end-stage liver disease. We estimated prevalence and evolution of severe NAFLD defined by FAST score in a large multicenter cohort of PWH.

Methods: FibroScan was performed in consecutive PWH without viral hepatitis coinfection from three prospective cohorts in Canada and Italy (LIVEHIV in Montreal; liver pathologies in HIV in Palermo; Modena HIV metabolic clinic) as part of a routine screening program for NAFLD. We compared prevalence of FAST>0.35 (90% sensitivity and 50% specificity for NASH with ≥F2 fibrosis and NAS≥4) and FAST≥0.67 (50% sensitivity, 90% specificity). Incidence of liver-related outcomes (ascites, encephalopathy, variceal bleeding, hepatocellular carcinoma) and extra-

hepatic events (cancer, cardiovascular disease) was evaluated by survival analysis.

Results: We included 1683 PWH (mean age 50.1 years, HIV duration 15.5 years, BMI 25.3 Kg/m2; 74.5% male, diabetes prevalence 32%). Prevalence of FAST>0.35 and FAST>0.67 was 8.1% and 1.5%, respectively. At baseline, on multivariable logistic regression higher BMI (adjusted odds ratio [aOR] 1.15, 95% CI 1.10-1.20), longer duration of HIV infection (aOR 1.05, 95% CI 1.02-1.07), lower CD4 cell count (aOR 0.99, 95% CI 0.99-0.99) and male sex (2.11, 95% CI 1.22-3.65) were associated with FAST >0.35. During a median follow-up period of 3.5 years, incidence of liver-related and extra-hepatic outcomes was 7% and 11.5%, respectively. Incidence of liver-related outcomes significantly increased according to FAST score category (p<0.001). There was no difference in extra-hepatic events by FAST score category. On multivariable Cox regression analysis, FAST score >0.35 was an independent predictor of liver-related outcomes (adjusted hazard ratio 4.44, 95% CI 1.66-11.9) after adjusting for sex, BMI, diabetes, duration of HIV infection, protease inhibitors exposure and CD4 cell count.

Conclusion: A significant proportion of PWH without viral hepatitis coinfection are at risk for severe NAFLD. FAST score predicts liver-related in this population. Non-invasive testing can help risk stratification and management in this population at risk for NASH and associated liver-fibrosis.

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Aging Accelerates Brain Metabolic Abnormalities in HIV Clade-C Infected Young Adults

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Background: HIV infection affects the metabolic balance of the brain due to persistent low-level inflammation and glial activation, leading to accelerated brain aging effect on adults living with HIV. While this has been reported in populations over 45 years of age, the brain aging process is less clear for young adults between 18 and 45, even though metabolic abnormalities are apparent in HIV patients of all ages. Additionally, no studies have examined brain aging with respect to HIV clade-C (HIV-C) specifically. In this study, we explore the effect of age on brain metabolite concentrations for a cohort of HIV-C infected and normal controls between the ages of 18 and 45. Metabolites were evaluated at multiple anatomical regions of interest (ROI) covering the whole-brain using a unique MR spectroscopic imaging (MRSI) approach.

Material and Methods: MRI Data were collected on a 3T scanner at the Post Graduate Institute of Medical Education & Research (PGIMER) in India from 108 HIV-C subjects (78/30 male/female; age: 31.1±7.1), and 108 age-matched controls (72/36 male/female; age: 31.6±6.3). The protocol included: T1-weighted MPRAGE image (TR/TE: 2300/2.42 ms; voxel dimension: 1.0×1.0×1.0 mm; 160 axial slices); whole-brain MRSI sequence using a 3-dimensional EPSI spin-echo sequence with: TR/TE/TI: 1,551/17.6/198 ms, matrix size of 50X50 with 18 slices, FOV = 280×280×180 mm. MRSI data were processed using the Metabolite Imaging and Data Analysis System software which can integrate spectra from voxels within a defined ROI to create a single integrated spectrum for an anatomical region. We evaluated levels of creatine (Cr), choline (Cho), N-acetylaspartate (NAA), and myo-inositol (m-Ins) at 65 ROIs selected from the JHU-MNI-SS-type2 atlas. Brain age analysis was done using a general linear regression model to define the relationship between age vs. each metabolite-by-ROI. Relations were also tested with Pearson correlations. Statistical analyses were performed using R (significance at p<0.05 uncorrected for multiple comparisons).

Results: Overall we observed diverging trends in the metabolic concentrations with respect to age between the two groups, with significant interactions between age and the grouping variable showing inhomogeneity of regression slopes at various regions of the brain. Cr levels were significantly decreasing with age for control subjects at 28 ROIs, while they increased with age for HIV-C at 20 ROIs.

Cho concentrations were relatively stable for controls with decreases only in 7 ROIs, whereas the HIV-C has a more remarked increase with age observed in 23 ROIs. Similarly, m-Ins remained stable among controls regardless of age with decreases seen in 4 ROIs, and HIV-C subjects showing significant increase with age in 32 ROIs. Conversely, NAA negatively correlated with age for controls in all but 2 regions, but was more stable for HIV-C patients with decreases in only 2 ROIs.

Conclusion: While m-Ins and Cho remained stable for controls, there was an increase among HIV-C subjects with with age throughout the brain, indicating increased low-level inflammation, neuronal functional disruption and glial activation with aging in HIV infected young adults. Concentrations of Cr between the two groups diverged with aging, the increase among HIV-C patients signifies higher cell energy output, possibly as more energy demand is needed to compensate in loss of neuronal function. Finally, we postulate that NAA concentrations are normalizing as they decrease with age for control subjects, whereas NAA in HIV-C subjects is lower overall but remains unchanged with increasing age.

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DTI and DKI Markers of Brain Microstructural Integrity Show Similar Aging Between HIV Clade-C Infected and Healthy Young Adults

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Background: HIV infection alters the microstructural integrity of the brain with damaged white matter and fiber connectivity, demyelination, and increased cellularity through glial activation. These processes contribute to an accelerated brain aging effect on adults living with HIV. While this has been reported in populations over 45 years of age, the brain aging process is less clear for young adults between 18 and 45, even though all HIV patients show similar signs of microstructural deteriorations irrespective of age. Additionally, no studies have examined brain aging with respect to HIV clade-C (HIV-C) specifically. In this study, we explore the effect of age on diffusion tensor imaging (DTI) and diffusion kurtosis imaging (DKI) derived markers of microstructural integrity for a cohort of HIV-C infected and normal controls between the ages of 18 and 45.

Material and Methods: MRI Data were collected at the Post Graduate Institute of Medical Education & Research (PGIMER) in India from 107 cART naïve HIV-C subjects (77/30 male/female; age: 30.9±7.1), and 110 age-matched controls (74/36 male/female; age: 31.7±6.4). Structural and diffusion-weighted MRI images were acquired on a 3T Siemens scanner, the protocol included: T1-weighted MPRAGE images (TR/TE: 2300/2.42 ms; voxel dimension: 0.5×0.5×3.0 mm); DW-images with dual-shell acquisition (b = 1000/2000 s/mm2) 30 gradient directions (TR/TE: 1150/98 ms; voxel dimension: 3.0×3.0×3.0 mm). Images were processed to obtain DTI and DKI metrics: fractional anisotropy (FA), mean, axial, and radial diffusivity (MD, AD, RD), kurtosis FA (kFA), and mean, axial, and radial kurtosis (MK, AK, RK). We evaluated these metrics at 65 ROIs selected from the JHU-MNI-SS-type2 atlas. Brain age analysis was done using a general linear regression model to define the relationship between age vs. each metric-by-ROI. Relations were also tested with Pearson correlations. Statistical analyses were performed using R (significance at $p<0.05$ uncorrected for multiple comparisons).

Results: Overall we observed significant decreases in FA/kFA and increases in all other metrics with respect to age. While homogeneity of regression slopes was maintained ($p>0.05$) between the two groups in all ROIs, some differences appear in the number of affected ROIs and the r and r2 values. For FA/kFA we see significant negative correlations with age in 37 and 38 ROIs for controls and HIV-C subjects respectively, however r values are much lower for HIV-C subjects with 13 ROIs showing moderate negative correlation ($r<-0.3$) with age and only

6 for controls. Conversely, the associations between the remaining metrics with respect to age were stronger for the control group with moderate positive correlations (r>3) seen in 25, 32, and 17 ROIs between age and MD/MK, AD/AK, and RD/RK respectively, while only 15, 9, and 8 ROIs were observed in HIV-C.

Conclusion: Decreasing FA/kFA with age points to deteriorating axonal integrity while increases in MD/MK, AD/AK, and RD/RK indicate more demyelination and glial activation. While the degree of change was different between the HIV-C and control groups in a few select ROIs, the overall trend was similar between the two groups and the HIV subjects did not show signs of accelerated aging.

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A Clinical Study of Non-Invasive Early Cardiovascular Disease Risk Assessment in the Hispanic Population Living with HIV.

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Background: HIV is a risk factor for accelerated cardiovascular disease (CVD). CVD is the leading cause of mortality among Hispanics. Hispanics in the US are disproportionately affected by the HIV epidemic, with higher rates of overall HIV-related morbidity and mortality. Therefore, HIV infection is likely to exacerbate adverse CVD outcomes among Hispanics.

Objective: This study aims to determine whether Hispanic men and women have greater vascular dysfunction. Also, seek to determine whether Hispanic men and women have greater epicardial adipose tissue (EAT) than other ethnicities.

Methodology: Of the 135 screened participants, data were collected from 99 eligible study participants, which included 53 Hispanics White, 38 Blacks, and 8 Non-Hispanic Whites. None did have CVD, metabolic, endocrine, or chronic renal conditions. Participants were on stable antiretroviral therapy (ART) for six months or more. Vascular assessments included epicardial adipose tissue thickness (EAT), flow-mediated dilation (FMD), aortic, radial, and femoral arterial stiffness (cAIx, crPWV, cfPWV). Traditional CVD risk measures included blood pressure, central adiposity, triglycerides (TG), total cholesterol (TC), low-density cholesterol (LDL), insulin resistance (HOMA-IR), and c-reactive protein (CRP). Statistical analyses were controlled for demographic variables (sex, hypertension, and statins medications)

Results: No significant differences were found in group composition based on age or education. However, there were significantly more women among Blacks than in the group of Hispanics. Of note, no significant group difference in BMI was observed, nor were differences in the proportion of the groups who were overweight or obese observed. Although, the BMI mean was higher at 39.6% in Hispanics compared with Black at 26.3%. Analysis showed group differences in mean arterial blood pressure (92.1±2.1 vs. 87.9±1.4), diastolic blood pressure (75.5±1.6 vs. 71.9±1.2), and heart rate (69.3± 1.7 vs. 64.9±1.4) became a trend with higher values in the Black group. Regarding prescribed medication use, there was no group difference in antihypertensive medications and statins among groups, and no one used fibrate medications. A large proportion was on three ART medications. In regard to the laboratory samples collected, the CRP became a significant trend; wherein the Black group displayed more elevated levels than the other groups (4.8±0.9 vs. 2.7 ±0.5). The analysis of lipid profile showed that, although no significant group differences were observed in TG, TC, and LDL; levels were greater in the

Black group relative to counterparts, with the exception of TG levels which were higher in the Hispanic group (122.7 ±7.6 vs.112.9±9.7); The analyses of the vascular function measures by FMD in both groups were non-significant. However, of the measures of arterial stiffness, significant group differences were found in crPWV and cfPWV; significantly higher crPWV was observed in the Black group ($p < .05$). A non-significant trend toward higher cAIx (22.3±2.1% vs 16.5±2.0%) was noted in the Black group. Aswell, EAT became a trend with higher values in the Hispanic group (3.7 ±0.2mm vs. 3.1±0.2mm).

Conclusion: This study suggests that there may be differences in some subclinical CVD measures among Hispanics with HIV, ethnicity needs to be taken into account when evaluating CVD risk.

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An Exploration of the Role of Intersectional Stigma and Discrimination on Cardiovascular Risk, Among Aging Women With HIV

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Introduction: Given expanded access to antiretroviral therapy (ART), 1.2 million people in the United States (US) are living with HIV, and more than a quarter are over the age of 55. Women aging with HIV (WHIV) are at a higher risk of CVD, compared to their male counterparts and have a 2- to 4-fold increased risk of myocardial infarction, heart failure, and stroke, compared to women without HIV. However, the relationship between HIV and CVD among women remains unclear. Mechanisms such as diminished immune function that alter innate protective mechanisms can play an important role. The Psychoneuroimmunology framework acknowledges the synergistic relationship between psychosocial factors (e.g., intersectional stigma) and immune function, which may contribute to the development of non-HIV-related co-morbid conditions. Because not all WHIV have CVD, resilience (i.e., bouncing back from negative experiences) may moderate this relationship. This study aims to examine the relationships between intersectional stigma, resilience, and CVD by life stages, among WHIV in the Southeastern US, where one of the highest incidences of HIV occurs.

Methods: University Institutional Review Board (IRB) approval was obtained. Participants were compensated for their participation. We enrolled N=31 WHIV, aged 35 and older; cross-sectional data were collected: standard clinical health indices, validated measures of stigma (Intersectional Discrimination Index: Anticipated, Day-to-day, Major Lifetime Discrimination subscales) and resilience (Connor-Davidson Resilience Scale), intravenous blood samples for cardiometabolic and inflammatory markers, anthropometrics, and coronary Computed Tomography Angiography (CTA). 10-year Atherosclerotic Cardiovascular Disease (ASCVD) Risk Scores were calculated. We then stratified the analyses by age group (<55 years of age, and >=55 years of age). Descriptive statistics characterized participants. Nonparametric Mann Whitney U and Chi-Square tests examined the relationships by age groups. Significance was determined at the $p<0.05$ level.

Results: 13 (42%) participants were below age 55 at enrollment, and 18 (58%) were 55 or older. 50% of participants in the younger group and 59% of participants in the older group were Black, non-Hispanic. Mean Major Lifetime Discrimination scores were significantly higher ($p=.044$) in the older group (3.2), compared to the younger group (1.6), although both were relatively low, given the range of possible scores (0-26). Resilience scores were similar between the groups (78.3

and 78.9, respectively), but relatively high, given the range of possible scores (0-100). Mean ASCVD risk scores were significantly higher (p<.001) in the older group (12.6), compared to the younger group (4.2). In terms of categorical risk (e.g., low, borderline, intermediate, and high) as assessed by the ASCVD risk score, age groups differed significantly (p=.006)—participants in the younger age group were categorized as low risk.

Conclusions: Older WHIV were at a significantly higher risk for CVD and endorsed significantly higher major lifetime discrimination. Both groups also endorsed high levels of resilience, which may act as a protective factor for CVD among WHIV. Further in-depth analysis is needed to understand the roles that age, stigma, and resilience factors have in predicting CVD risk in this population. Findings from our study will serve as preliminary data for the design of clinical interventions to improve the cardiovascular health of WHIV. Interventions to reduce CVD risk may need to consider other psychological factors such as HIV-related stigma and resilience in their design.

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Glucose Changes Among Aging Female PWH in Southeast United States

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Metabolic changes, such as altered glucose metabolism and insulin resistance, are common among persons with HIV (PWH). Advancing age, longer duration of HIV infection and certain ethnic backgrounds are also risk factors that contribute to the development of metabolic changes in PWH. In addition to these risk factors, certain classes of antiretrovirals, such as integrase strand transfer inhibitors (INSTIs) have reportedly been associated with weight gain and metabolic changes in PWH therefore changes in glucose were analyzed among female persons with HIV (PWH), ages 50 years and older, on current standard of care anti-retroviral therapy (ART) regimens, who were virally suppressed (HIV-1 RNA level less than 200 copies per milliliter) at Week 48, in a multi-clinic infectious disease organization in the southeast United States. A total of 39 cisgender females with HIV were included in this analysis. 35.9% had a history of Type 2 Diabetes Mellitus at baseline and 74.4% identified their race as Black. At 48 weeks post initiation of an INSTI based regimen, 79% of PWH maintained serum glucose levels less than 126 milligrams per deciliter. There was a median increase of serum glucose of 3 milligrams per deciliter over 48 weeks in the total sample population. In conclusion, as the median age of female PWH continues to increase in the United States, ART regimens that provide virologic suppression with minimal impact on co-morbid conditions is essential. In this patient population, aging female PWH, on current standard of care ART regimens, such as B/F/TAF and DTG/3TC, experienced small changes in serum glucose levels over 48 weeks therefore minimally impacting serum glucose in this patient population.

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In Support of Multidimensional Frailty: A Structural Equation Model From the Canadian Positive Brain Health Now Cohort

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Introduction: A large group of people is aging with HIV and face age-related conditions such as frailty. Frailty is a multifactorial syndrome with causes originating from morbidities,

genetics, lifestyle, and environment. Consequently, frailty manifests on physiological, physical, emotional, cognitive, and social dimensions of health. The interconnectedness between frailty constructs is of interest. Therefore, the objective of this study is to estimate the structure and relationships between and among physical, emotional, cognitive, and social frailty subdomains and their relationship with personal and HIV-related factors in people living with HIV.

Methods: First and second visit data from the Positive Brain Health Now Study (n=856) was used. The structural model included four non-hierarchical frailty subdomains: physical, emotional, cognitive, and social. Items covering areas that were too similar to each other's were excluded. All scales were standardized for ranging from 0 to 100 and for high scores to indicate better outcomes. Data from the second visit was used to estimate the internal validity of the model.

Results: A total of 514 persons' data (female=13.4%) from the first visit with complete data were analyzed. The mean age was 52.3 (8.1). The hypothesized 4-factor model showed adequate model fit. Correlations among frailty subdomains ranged from 0.40 to 0.82. Sex, nadir CD4-count, and diagnosis before 1997 didn't predict any frailty subdomains. On the other hand, age (β range: 0.10-0.24), number of symptoms (β range: -0.37 to -0.59), and measured cognition (β range: 0.09 to 0.24) directly predicted all frailty subdomains. Current CD4 predicted only social (β=0.09) and CRP predicted only cognitive frailty (β=-0.15). The model remained the same using the second visit data.

Conclusion: This is the first time that a multidimensional model of frailty is tested in HIV. Measures used here are connected to evidence-based interventions that could improve the lives of people living with frailty.

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Prevalence of Geriatric Syndromes, Frailty and Comorbidities and their Association with Quality of Life in Older Adults with HIV in the Spanish FUNCFRAIL Cohort.

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Introduction: More than half of people living with HIV are older adults. Our aim was to know the prevalence and impact of frailty, geriatric syndromes, and comorbidity on mortality and quality of life in older adults with HIV (OAWH).

Methods: cross-sectional study of the FUNCFRAIL Spanish multicenter cohort. OAWH, 50 years or over, were recruited. We recorded sociodemographic data, HIV infection-related data, comorbidity, frailty, geriatric syndromes (depression, cognitive impairment, falls and malnutrition), quality of life and estimate risk of all-cause mortality by VACS Index. Association of frailty with other geriatric syndromes and comorbidity was evaluated using the Cochran-Mantel-Haenszel (CMH) test.

Results: 796 patients were included. 24.7% were women, mean age was 58.2 (6.3) years. 14.7% were 65 or over. 517 (65%) patients had ≥ 3 comorbidities, ≥1 geriatric syndrome and/or frailty. There were significant differences in 5-year estimate risk of all-cause mortality by VACS Index (frailty 10.8% vs ≥3 comorbidities 8.2% vs ≥1 geriatric syndrome

8.2% vs nothing 6.2%; p=0.001) and in the prevalence of fair or poor quality of life (frailty 71.7% vs ≥ 3 comorbidities 52% vs ≥ 1 geriatric syndrome 58.4% vs nothing 51%; p=0.001). Cognitive impairment was significantly associated with mortality (MOCA <20, 8.7% vs MOCA ≥20, 6.2%; p=0.02) and depression with poor quality of life (GDS-SF ≥6, 76.5% vs GDS-SF < 6, 50%; p=0.001).

Conclusions: Frailty, geriatric syndromes, and comorbidity negatively impact mortality and quality of life in OAWH, with the impact of frailty being significantly greater than the rest.

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Psychometric Properties of a Frailty Phenotype used among People with HIV: An Item Response Theory Analysis

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Background: Frailty among people with HIV (PWH) is in many cases assessed using phenotype definitions, such as Fried's, which enumerate the presence of 4-5 frailty elements. Individual items are dichotomized and then summed with equal weights (i.e., each present component receives a score of 1). There are other scoring options, such as item response theory (IRT), that do not require dichotomizing each indicator and leverage the correlation structure across indicators to determine parameter weights for scoring, which can increase precision in the frailty phenotype measure. We used single IRT approaches to evaluate a frailty phenotype definition.

Methods: We conducted IRT analyses on our frailty phenotype among PWH engaged in care at four Centers for AIDS Research Network of Integrated Clinical Systems (CNICS) sites. The frailty phenotype definition included 4 self-reported items: fatigue, unintentional weight loss, physical activity, and mobility. Each item was considered based on its original Likert scale. Fatigue and weight loss were collected via the HIV Symptom Index, physical activity was collected using the Lipid Research Clinics questionnaire, and mobility was collected in the EuroQOL Health Related Quality of Life questionnaire (EQ-5D) but was collapsed into 2 levels due to sparseness in response categories. We used graded response IRT models to estimate discrimination and difficulty parameters for each ordinal indicator while simultaneously estimated overall frailty severity.

Results: Among 522 PWH, mean age was 52 years (median: 54), 112 (21%) were female, and half (268, 51%) self-reported Black race. The IRT estimated frailty phenotype levels ranged in our sample from -1.3 (least frail) to +2.1 (most frail).
Difficulty levels, which can be thought of as how likely the item response represents the frailty phenotype, varied substantially across indicators. The threshold between none and mild physical activity limitations was -2.4, and the threshold between the second greatest to the greatest physical activity limitations was +1.2. Thresholds for fatigue ranged from -0.4 to +2.0. The single threshold for mobility was at 1.3. Thresholds for weight loss ranged from +1.8 to 4.5. Discrimination parameters were 0.7 for weight loss, 1.1 for physical activity, 1.3 for mobility, and 1.8 for fatigue (i.e., weight loss was the least and fatigue the most discriminative).

Conclusions: Our results suggest notable differences between and within individual items in the frailty phenotype, suggesting the potential need for item weighting and rescaling using methods such as IRT in order to more accurately assign frailty scores among PWH. Future IRT analyses of frailty phenotypes comparing PWH and those without HIV should be conducted to understand if our observations are unique to PWH or are more generalizable; and could elucidate implications of applying frailty and other measures designed within the general population to

PWH. Additionally, this abstract highlights the importance of collecting patient reported outcomes and measures for identifying frailty phenotype and other measures for elucidating risk factors, prevent and treatment to support healthy aging among PWH.

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Role of Maraviroc and Rapamycin in the Cerebral Inflammatory State on a Murine Frailty Model

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Background: Frailty is a common geriatric syndrome that encompasses a large number of pathologies that include, among others, weakness and low physical activity, as well as neuroinflammatory and degenerative changes in the central nervous system. Ageing is associated with an increased risk of developing frailty syndrome. This is associated with a low-grade systemic inflammatory state. The identification of therapeutic interventions to ameliorate the frailty síndrome is essential need. RAPA, a macrolide antibiotic with antiproliferative properties and a specific inhibitor of the mTOR pathway, not only appears to prolong life in murine models, but has also shown benefits in some age-related conditions, could be an interesting option. Another therapeutic target could be Maraviroc (MVC), a CCR5 antagonist, as frailty is associated with increased expression of T lymphocytes with CCR5 correceptor and MVC blocks these cellular receptors.
We hypothesised that the administration of CCR5 antagonists, such as MVC and/or RAPA, could help to reduce the levels of inflammatory mediators in the brain.

Material and Methods: Male IL-10 deficient mice were randomised into 4 groups: (i) the IL-10KO group received a standard rodent diet and water; (ii) the MVC group received the same diet as the IL-10KO group and received MVC (Pfizer, New York, NY) in their drinking water (300 mg/L); (iii) the RAPA group received the same diet as the IL-10KO group and in addition received RAPA in their drinking water (1.5 mg/kg/day); and iv) the MVC/RAPA group received the same diet as the IL-10KO group and in addition MVC and RAPA in their drinking water at the doses previously discussed.
47 mice were studied. For the analysis of gene expression values, the means of the TC of each group were calculated and corrected using the values obtained with housekeeping. Subsequently, the means of the treatment groups were compared with the control group and with each other using an ANOVA test.

Results: After the necropsies of the animals, the brains were weighed and no differences were observed when comparing the groups. CCR5 levels were significantly lower in the group treated with MVC/RAPA ($p = 0.002$). Contrary to expectations, we did not observe differences when analysing CCL5. As for inflammatory cytokines, a decrease in IL-1β was only observed in the MVC-treated group ($p = 0.02$). No differences in IL-6 and IL-18 expression levels were observed. Senescence was measured by p16 and p21 expression and no differences were observed. After studying the expression levels of mTOR and Klotho, no differences were observed between groups However, a significant increase in β-galactosidase levels was observed in the RAPA-treated group ($p=0.0004$) and the MVC/RAPA-treated group ($p<0.0001$).

Conclusions: This could be related to a low diffusion of these drugs at the haematoencephalic membrane level.
The increase we observed in the expression of β-galactosidase needs further study, although it could not appear to be related to cellular senescence. Therefore, at the brain level, it would not be a suitable biomarker to quantify senescence.

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HIV, Social Networks, and Loneliness among Older-Aged People in Uganda

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Background: Data from the US indicate that 70% of PWH live by themselves, with a high prevalence of loneliness which varies geographically 1,2. Loneliness is associated with poor health outcomes, including death, particularly for older-age adults. In 2020, 70% of the 37 million people with HIV (PWH) worldwide lived in sub-Saharan Africa, and more than 50% were over 50 years of age3. Yet, little is known about social networks, and loneliness differ for people with HIV (PWH) compared with their HIV-negative counterparts in this region.

Methods: We analyzed baseline data on 600 participants from the Quality of Life and Ageing with HIV in Rural Uganda cohort study. This cohort includes older PWH in ambulatory care (mean age, 58 years; range, 49-88 years) and a sex-similar group of people without HIV (PWOH), recruited from the same catchment area. The outcome was the 3-item UCLA loneliness scale, with loneliness defined as "sometimes" or "often" feeling a lack of companionship, being left out of community meetings or events, or being isolated from others. The primary explanatory variable was HIV serostatus. The network variables included the number of people living in the household, types, and sources of physical and financial support, and social integration (defined as participation in 10 different community groups). We used logistic regression models to estimate the associations between HIV and loneliness and between HIV and social networks, adjusted for sociodemographic covariates (age, sex, education, alcohol consumption, and comorbidities).

Results: Of the 298 PWH, 7.1% (n=21) lived alone, versus 1.3% (n=4) of the 302 PWOH. The mean total loneliness score was 3.93 (SD=1.37, range 3-9). A substantial proportion of participants experienced different aspects of loneliness: lack of companionship (179 [29.83%]), feeling left out of community meetings (158 [26.33%]), and/or feeling isolated from others (118 [19.67%]); and 256 (42.67%) experienced at least one of those aspects of loneliness. Compared with PWOH, PWH were more likely to feel lonely (AOR, 1.49; 95% CI, 1.06-2.09). This difference was potentially explained by differences in social networks, as PWH had a smaller household size (3.46 vs. 3.91; P <.01), less physical support (2.27 vs. 2.35; P <.0001), less financial support (0.88 vs. 1.27; P<.01), and less social integration (2.84 vs. 3.77; P<.0001). Loneliness was inversely associated with household size (AOR, 0.89; 95% CI, 0.82 0.97) and social integration (AOR, 0.86; 95% CI, 0.81-0.91) but not with physical or financial support.

Conclusions: Older-age PWH were more lonely and had more limited social networks compared with HIV-negative persons. In rural Uganda, interventions to strengthen the social networks of older-age PWH may reduce loneliness in this high-risk population.

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The Last Mile for the First 95: The Imperative to Address Case Finding in Older People in South Africa

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Background: South Africa's HIV burden is the largest in the world. Progress towards 95-95-95 is ongoing, with available estimates indicating that the first 95 will be imminently achieved. Targeted testing is a priority within the national HIV programme to close the remaining gap. Despite estimates of over 20 000 incident HIV infections per year, older persons (≥50 years) are often perceived to be at lower risk of being HIV-positive and thus overlooked. To demonstrate the potential for targeted case finding for older people living with HIV (OPLHIV) in South Africa, we profile HIV testing services (HTS) among older persons in two high HIV burden metropolitan districts in Gauteng, South Africa.

Materials and Methods: Routine HIV case finding activities are implemented within the 2 districts in alignment with South African National Department of Health guidelines for HTS. This includes facility and community HIV testing, index contact testing and HIV self-screening (HIVSS), among other approaches. We collated and analysed age- and gender-disaggregated routine HTS program data reported to the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) from October 2021 to March 2022, using PEPFAR Monitoring, Evaluation and Reporting (MER version 2.6) indicators for HIV case finding for OPLHIV (≥50 years) . We report on the number of HIV tests conducted, HIV positivity, and testing entry streams (including tuberculosis (TB) services, antenatal and prevention of mother-to-child (PMTCT) services, community HTS and routine HTS within health facilities). We also examine the linkage of HIV-positive OPLHIV to anti-retroviral (ART) care.

Results: Between October 2021 to March 2022, 6.0% (45327/ 760146) of HIV tests were conducted for persons aged ≥50 years. Of those tested, 3344 OPLHIV were newly diagnosed with HIV (7.4% positivity) contributing 11.0% of new HIV diagnoses across the two districts. More women than men accessed HTS (55.0% versus 45.0%) however 52.0% (1738/3344) of new HIV diagnoses were among men. The positivity rate for men (8.5%) was also higher compared to women (6.4%). HIV testing services were accessed predominantly through facility-based care (44479/45327, 98.1% of tests, yield 7.4%). Community testing identified 53 OPLHIV out of 848 tested (6.3% positivity). Targeted testing through high priority streams identified few OPLHIV: 3.7% positivity through index testing (110/3003 tested); 0% positivity through TB services (0/1536 tested) and 5.8% positivity through PMTCT (8/137 tested). Of newly diagnosed OPLHIV, 2737 were initiated on ART (linkage to care of 81.8%) within the reporting period, with less men successfully linked to care than women (1371/1738, 79.0% versus 1366/1606, 85.0%).

Conclusions: Routine HIV case finding activities achieved high positivity in people ≥50 years, with suboptimal linkage to ART. Men accessed HTS less frequently but had higher positivity and poorer linkage to HIV care than women. Limited HTS uptake and positivity seen through testing modalities such as index and community testing, may indicate suboptimal implementation in this population. Differentiated case finding approaches which are both contextually sensitive and acceptable to older patients will help to address case finding gaps for OPLHIV in this context, as will additional research to inform effective programmatic interventions.

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The Contribution of Tcell Derived IL-1a to HIV Associated Hypertension

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Although the onset of combination antiretroviral therapy (cART) has extended the lifetimes of people living with HIV (PLWH), the affected population experiences increased rates of hypertension and cardiovascular disease (CVD) with increasing age. Despite these clinical observations, the etiology and individual contributions of cART and repressed viral infection towards hypertension remain largely undefined. While cART treatment has prevented viral replication, viral proteins are still detectable in circulation leading us to hypothesize that HIV-associated hypertension is largely in response to an immune response to the aforementioned viral proteins. To

assess the individual contributions of immune containing viral proteins to chronic inflammation and hypertension we took advantage of a transgenic mouse model expressing 7/9 viral proteins (Tg26) upon which we performed a bone marrow transplant to produce two groups: WT->WT and Tg26->WT. Systolic blood pressure measurements via tail cuff showed an increase in systolic blood pressure in Tg26->WT BMT as compared with the WT->WT control (WT->WT: 141.6; Tg26->WT 160.3; P<0.05). In addition, these mice have impaired endothelial vasorelaxation to acetylcholine (P<0.05), a precursor to hypertension. In order to determine which immune cell subtype was responsible for the observed CVD thoracic aortas were isolated and incubated in the media of either WT or Tg26 CD3+ Tcells and endothelial function was tested. Vessels incubated in Tg26 media showed impaired vasorelaxation as compared to WT media (P<0.05). Tg26 mice treated with a Tcell activator inhibitor, Abatacept, also showed improved vasorelaxation as well as a decrease in blood pressure. Upon further experimentation, cytokine panel revealed the Tg26 media had increased IL-1a levels when compared to WT (P<0.05). IL-1a levels were also increased in the plasma of Tg26->WT mice as compared to WT->WT (P<0.1). Additionally, vasorelaxation was restored upon the addition of anti-IL-1a to the Tg26 media. Mice treated with Abatacept also displayed a significant decrease in plasma IL-1a levels providing evidence of a link between Tcell derived IL-1a and our observed endothelial dysfunction and increased blood pressure. Further investigation into the cause of endothelial dysfunction led us to reactive oxygen species (ROS) which are commonly produced by NADPH oxidases. RT-qPCR of abdominal aortas showed a significant increase in NOX1, NOXO1, and NOXA1. While not showing changes in NOXO1 and NOXA1, abdominal aortas incubated in Tg26 Tcell media had a modest increase in NOX1 levels suggesting a role of Tcell derived IL-1a to HIV associated hypertension. To elucidate the effect of IL-1a on endothelial dysfunction and NOX expression human microvascular endothelial cells (hMVEC) were treated with varying concentrations of IL-1a for 24 hours. Again, we found increases in NOX1 along with NOXO1 and NOX4. In conclusion, we found evidence that hypertension in a virally repressed model is partially due to Tcell derived IL-1a increasing NOX1 and ROS levels in the endothelium and ultimately an increase in blood pressure.

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Effects of the COVID-19 Pandemic on Quality of Life: Cross-Sectional Study of Older-Age People With and Without HIV in Rural Uganda

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Background: COVID-19 related lockdowns and other public health measures may have differentially affected quality of life (QOL) for older people with and without HIV in rural Uganda.

Methods: The Quality of Life and Aging with HIV in Rural Uganda study enrolled people with and without HIV aged 49+ from 10/2020-10/2021. We conducted interviews to collect data on COVID-19-related stressors (behavior changes, concerns, interruptions in healthcare, income, and food), and quality of life. We used linear regression models to estimate the associations between COVID-19-related stressors and quality of life, adjusting for demographic characteristics, mental and physical health, and time before versus after 6/10/2021 (the start of the second COVID-19 wave in Uganda). Interaction between HIV and COVID-19-related stressors evaluated effect modification.

Findings: We analyzed complete data from 563 participants. Mean age was 58 (standard deviation [sd] 7); 265 (47%) were female, 387 (69%) were married, 283 (50%) had HIV and 401 (71%) were farmers. Those making 5+ COVID-related behavior changes relative to those making <3 had worse general QOL (b: -5.59, 95%CI [-7.51, -3.67]) and health-related QOL (b:-5.63, 95%CI [-9.79, -1.48]). Having access to sufficient food after the start of the COVID-19 pandemic (b:3.85, 95%CI [2.23, 5.48]) and being interviewed after 6/10/2021 (b: 3.14, 95%CI [1.58, 4.70]) was associated with better general QOL. HIV did not modify the COVID-19-related stressors and general QOL association.

Conclusions: In the context of the COVID pandemic in an HIV-endemic, low-resource setting, older Ugandans making multiple COVID-19 related behavioral changes had reduced QOL. Nonetheless, sustained general QOL during the second COVID-19 wave suggests resilience among older Ugandans. More research is needed to better understand resilience during pandemic crises.

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Mortality Among Adult PLHIV in All PEPFAR-Supported Countries—, October 2019—September 2021

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Background: As many countries in low and middle-income countries reach HIV epidemic control, there is a growing population of adults in treatment who are older than 50 years. Resources and interventions need to be focused on improving life expectancy and quality of life in this cohort of People Living with HIV (PLHIV). In 2019, the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) began collecting mortality data for PLHIV receiving antiretroviral (ARV) treatment (ART) that are lost to follow-up, in PEPFAR-supported programs. We reviewed mortality trends in PLHIV ages 50+ years on ART and assessed the impact of viral load coverage (VLC), viral suppression (VLS), and interruptions in treatment (IIT) on mortality.

Material and Methods: PEPFAR-supported programs submit aggregate data quarterly using standardized indicators disaggregated by age and sex. Relevant indicators, including TX_ML (captures information on interruptions in treatment and mortality), VLC, and VLS (HIV RNA <1000 copies/mL) were analyzed to assess deaths reported for all 15-49 and 50+ year old PLHIV on ART from October 2019 to September 2021 for PEPFAR-supported countries and regions (n=28). VLC was calculated quarterly as number of PLHIV on ART with a VL result documented in the medical or laboratory records within the past 12 months divided by the number of PLHIV on ART from 6 months prior. Proportion died was calculated quarterly as number of reported deaths in the current reporting quarter divided by the sum of the number of PLHIV on ART in the previous reporting quarter and the number of PLHIV newly initiated on ART in the current reporting quarter. We defined %IIT as proportion of PLHIV on ART that had no clinical visit or ARV pick up for at least 28 days after the last scheduled appointment, and are not known to have died, stopped treatment, or transferred to another facility.

Results: The median proportion died across all countries quarterly was 0.22% (range: 0.18–0.26) and was higher in the 50+ age group compared to the 15-49 group (0.34%; range: 0.29–0.44 versus 0.18%; range: 0.17–0.22). Among the 50+ group, the median proportion died was higher among men than women (0.42%; range: 0.37–0.55; versus 0.27%; range: 0.23–0.36). Over the same period, the median VLC and VLS were greater among 50+ group (VLC: 83.0%; range: 82–83; VLS 95.5%; range: 94–97) than among 15-49 group (VLC 74.8%; range: 73–77; VLS 92.6%; range: 91–95). Median %IIT was lower in the 50+ group (2.1%; range: 1.8–2.8) compared to 15-49 group (3.4%; range: 2.8–4.2). Among the 50+ group, median %IIT was higher among men than women (2.3%; range: 2.0–2.8 versus 2.0%; range: 1.6–2.7).

Conclusions: PLHIV are reaching older ages with lifesaving ART and those 50+ years have high VLC, high VLS, and low %IIT in PEPFAR-supported countries. Some of these deaths among the 50+ group may be expected due to the aging cohort. However, reducing mortality may require investigation beyond these HIV-associated factors, focusing on other modifiable causes of death such as COVID-19, comorbid noncommunicable diseases, and advanced HIV disease to inform future PEPFAR program resource allocation.

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36. A.

The Effect of an Electronic Alert in the Medical File to Improve the Screening of Osteoporosis in HIV Positive Patients Who Are Followed in a Community Clinic

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The effect of an electronic alert in the medical file to improve the screening of osteoporosis in HIV positive patients who are followed in a community clinic?

Introduction: Osteopenia and osteoporosis are frequent and occur at an earlier age in HIV disease as a consequence of chronic inflammation or HIV treatments. WHO and other guidelines recommend screening of these conditions after 50 years of age in HIV+ patients by measuring is Bone Mass Density (BMD) and/or by calculation of the FRAX-score. Screening for osteoporosis/osteopenia is an important part of clinical practice for preventing bone fractures. Following Canadian guideline, BMD should be repeated every five years as screening for people having normal BMD and every two years for osteopenic patients.

Objectives: To evaluate the impact of introducing an electronic alert in the patient's charts as a reminder for physician for prescribing measurement of BMD as indicated.

Material and methods: HIV patients aged 50+ followed at CMUQL were included. Their charts were reviewed and the information regarding BMD screening was added to the clinic's HIV database. When BMD was not measured timely according to the Canadian guidelines, an electronic alert was generated t in the chart to remind physician to prescribe BMD test at the next visit. Data related to the BMD measurements were collected prospectively every 3 months and included in the HIV database.
Statistical analyzes were performed on SPSS, comparing the proportions with BMD performed before and after the intervention.

Results: Out of 2371 patients actively followed at the CMUQL, 1422 patients (60%) were aged over 50 years and included in this study. At baseline only 444 patients (31%) had BMD in the past 5 years. 33 patients did not need screening for BMD, and 945 were overdue for their timely screening of bone mineral density. At the end of the project, BMD measurement was prescribed for 666 patients (70%), and 6 months later 579 patients (61%) have had their BMD measured.
95% of our patients were male, their mean age at BMD test was 58y (IQR: 53-62), they were infected since 23y (IQR: 17-29) and on antiretroviral since 18y (IQR: 12-23). Result of BMD indicated that, 18% had osteopenia and 15% osteoporosis.

Conclusion: Screening and prevention of comorbidities is an important aspect of HIV care. Bone health may be neglected by healthcare providers due to lack of awareness or time constraints. Through this project, awareness on bone issues was increased and a better application of screening recommendations was accomplished. At the end, more than a third of the patients had significant bone loss and needed intervention to supply this lost. An alert in the electronic medical chart could be very useful for the physician and guarantee a better bone health for the patients.

36. B.

Could Electronic Alert Improve the Screening of Osteoporose in HIV Positive Patients Who Are Followed in a Community Clinic?

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Introduction: Osteoporosis is a generalized skeletal disorder in which an individual's bone mass is reduced and their architecture deteriorated. Fragile bones increase the risk of fracture and facilitate other chronic morbidities. HIV has been associated with bone density loss either by the infection and inflammation caused by HIV or thru long-term use of some ARVs. WHO suggests Bone Mass Density (BMD) test and/or calculation of the FRAX-score in all PLHIV over 50y. Screening for osteoporosis/osteopenia is an important part of clinical practice and for preventing bone fractures. Following Canadian guideline, BMD should be repeated every five years as screening for people having normal BMD and every two years for osteopenic patients.

Objectives: To evaluate the impact of introducing an electronic alert in the patient's chart as a reminder for physician for prescribing BMD as indicated.

Material and methods: HIV patients aged 50+ followed at CMUQL were included. They chart were reviewed and the information regarding BMD screening was added to the clinic's HIV database. When bone screening was not done according to the Canadian guideline, an electronic alert was put in the chart to remind physician to prescribe BMD test. Each 3 months we had a follow up in the patient's chart, and data related to the BMD were collected prospectively.
Statistical analyzes were performed on SPSS, comparing the proportions with BMD before and after the intervention.

Results: Out of 2371 patients actively followed at the CMUQL, 1422 patients (60%) were aged over 50 years and included in this study. At baseline only 444 patients (31%) had recent BMD. 33 patients did not need BMD, so we put an alert in the chart of the 945 other without recent bone evaluation.
At the end of the project, BMD was prescribed for 666 patients (70%), and 6 months later 579 patients (61%) have had their BMO done. 95% of our patients were male, their mean age at BMD test was 58y (IQR: 53-62), they were infected since 23y (IQR: 17-29) and on antiretroviral since 18y (IQR: 12-23). Result of BMD indicated that 31% had a good bone health, 36% had a light loss of bone density, 18% had osteopenia and 15% osteoporosis.

Conclusion: Through this project patients received special attention for their bone health and doctors have been made aware of the importance of bone health for their over 50 HIV infected patients. The proportion of patients with recent BMD has doubled after the intervention. More than a third of the patients had significant bone loss and needed intervention to supply this lost.
The effort put into this project has been considerable because we introduce the alert manually in each patient's chart, but an alert computed automatically by the electronic medical chart could be very useful for the physician and guarantee a better bone health for the patients.

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Frailty Transitions in People With Post-Acute COVID Syndrome

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Background: Frailty has been an important predictor of clinical outcomes in the acute phase of COVID-19, but the impact of frailty in the post-acute COVID syndrome (PACS) is largely unknown. The objective of the study is to describe longitudinal transitions of frailty phenotype (FP) states in relation to symptoms'

clusters and health-related quality of life (HRQoL) in people with PACS.

Methods: This was an observational single center study including patients followed at Modena PACS clinic (MPC) from July 2020 to May 2022. MPC is a referral center established after the first wave of the COVID-19 pandemic to screen patients for signs and symptoms of PACS along with comprehensive geriatric assessment including frailty. Patients with at least two follow-up visits were included in the study. The diagnosis of PACS was based on ≥1 cluster of symptoms: respiratory, neurocognitive, musculoskeletal, psychological, sensory, dermatological. HRQoL was evaluated with EQ-5D-5L questionnaire. Optimal quality of life was defined as score >89.7%. The outcome was frailty transition, assessed by Fried frailty phenotype criteria. In order to explore probability of frailty phenotype changes over time, mixed effect model for ordinal data was applied. Multivariable logistic regression models were used to explore the relationship among PACS symptoms, quality of life and frailty.

Results: We included 823 patients evaluated for PACS, 60.3% were males, with the mean age of 60.3 years. At baseline, overweight and obesity were present in 333 (40.5%) and 301 (36.6%), respectively. Frailty was diagnosed in 30.5% (203) of patients. Among PACS clusters, musculoskeletal cluster was present in 575 (72.5%), neurocognitive in 398 (50.7%), respiratory in 399 (49.7%), psychological in 374 (47.8%), sensory in 363 (47.5%), and metabolic in 202 (31.4%) One-hundred seventy (32.1%) patients had optimal quality of life (>89.7%), assessed by EQ-5D-5L. Musculoskeletal, neurocognitive, and sensory significantly decreased over time, while QoL did not substantially change Prevalence of frailty decreased over time: in the first 6 months after COVID-19 symptoms' onset, frailty was present in 220 (30.3%), from 6 to 12 months in 34 (23.6%), and >12 months in 10 (17.9%). The probability of frailty reduced over time (OR=0.98, p<0.001). In a multivariate logistic regression model, frailty but no prefrailty was associated with metabolic cluster (OR=2.96, 95%CI: 1.09, 8.06). After adjustment for age, musculoskeletal cluster was associated with time, male sex, frailty and QoL. In unadjusted model, the risk of being prefrail (OR=0.99, 95%CI: 0.98, 1.00) and frail (OR=0.98, 95%CI: 0.97, 0.99) was reduced over time. Higher delta BMI and higher SPPB scores resulted negatively associated with frailty.

Conclusions: This longitudinal study showed that trends of frailty decreased over time, indicating that frailty in COVID-19 survivors might be reversable. Burden of musculoskeletal, neurocognitive, and sensory PACS clusters reduced over time, but without changes in other PACS clusters and overall QoL. However, both frailty and QoL were strongly associated with musculoskeletal, neurocognitive, and respiratory PACS, suggesting that self-reported PACS symptoms were indicative of overall vulnerability and well-being in COVID-19 survivors.

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The abstract was withdrawn.

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Vaccine Antibody Responses in Aging-PLWH: Lessons From the Non-human Primate Model

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Background: Despite virologic suppression, aging PLWH often manifest impaired immune responses to seasonal flu vaccination, underscoring the need for interventions to augment immunity. Our studies in aging rhesus macaques (RM) infected with simian immunodeficiency virus (SIV) showed that like humans, flu vaccine antibody (Ab) responses were impaired and were enhanced by administration of the cytokine interleukin (IL)-21, a regulator of CD4 T follicular helper cells (Tfh) and B cell function. In the present study, we investigated the mechanisms of action of

IL-21 by evaluating immune cells in draining lymph nodes (LN).

Materials and Methods: SIV infected old RM (n = 12, average age 21 years, range: 18 - 25 years) were divided into two groups-one treated with IL-21 (n=8) using IL-21-IgFc and the other untreated controls (n=4). All animals were SIV infected with 200 TCID50 SIVmac239-nef-stop by i.v. route and treated with ART at 12 weeks post-infection. Three months after ART initiation, all animals were vaccinated with the trivalent seasonal flu vaccination in a prime/boost/boost strategy at 3-month intervals. IL-21 treated animals were given 50 µg/kg body weight IL-21-IgFc in three s.c injections on day –2, day of, and 7 days post-vaccination for each of the three vaccine doses. Draining LN cells were collected at 14 days after each vaccine dose and subjected for the immune phenotype, flu antigen specific T cells and single cell (sc)RNA-seq for transcriptional analysis. Data compared between groups using two-tailed Mann-Whitney U tests, correlation analysis by two-tailed Spearman correlation and Ingenuity Pathway Analysis for transcriptional studies.

Results: Injection of IL-21 resulted in significant enhancement of flu Ab responses in this animal model of aging, with enhanced flu Ab on day 14 post-vaccine boost 1 ($p = 0.015$) and day 84 post-boost 2 ($p = 0.017$) compared to animals who were not given IL-21. LN cells exhibited proliferation (Ki67+) of flu-specific CD4 memory T cells ($p = 0.032$) and expansion of IL-21 receptor+ B cells ($p = 0.042$) on day 14 post-boost 1 and correlated with the flu Ab response. Tfh cells co-expressing T cell immunoreceptor with Ig and ITIM domains (TIGIT) and DNAX accessory molecule (DNAM-1) underwent expansion and correlated with the flu Ab response. Co-expression analysis of DNAM and TIGIT on flu-specific Tfh revealed enrichment of IL-21R+ DNAM-TIGIT+ and DNAM+TIGIT+ subsets. In scRNA-seq, pathways associated with B cell development and antigen presentation were enhanced with IL-21-treatment, while interferon signaling pathways in germinal center (GC) Tfh and B cells were inhibited, providing insight into mechanisms of IL-21 immunomodulation in LN at the inductive site of the flu vaccine response.

Conclusion: The cytokine IL-21 modulates LN germinal center activity, potentially reversing SIV-associated LN Tfh and B cell dysfunctional interaction, resulting from deleterious interferon signaling. IL-21 immunotherapy represents a strategy to enhance vaccine response in an aging HIV+ population that is worthy of further exploration and optimization.

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Selecting a Virtual Platform to Attenuate Social Isolation Among Older People Living With HIV: Lessons Learned From Community-Engaged Consultation

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Background: Some older people living with HIV (OPLWH) experience physical, psychosocial, and systemic barriers to aging in place. The COVID-19 pandemic exacerbated these barriers by severely limiting access to vital medical and social support systems. Inspired by a community call-to-action and the Village Movement to support aging-in-place, this study sought to identify an acceptable and feasible platform to pilot test a Virtual Village intervention with platform-naïve OPLWH.

Materials and Methods: We first identified the attributes that OPLWH wanted in the Virtual Village; these included text and verbal chat features, low- or no-cost to use, ability to create interest-based communities and share health resources, and a user registration requirement to protect privacy. Next, we systematically assessed the ease of implementing these attributes on existing

virtual platforms including Discord, Slack, Helpful Village, Facebook, Canvas, HeySpace, and WordPress. Discord emerged as most suitable.

Twelve Community Advisory Board (CAB) members from three study sites (Palm Springs, CA, Los Angeles, CA, and Tampa, FL) tested Discord. We assessed CAB members' training needs and perceptions of technological literacy and created written manuals and held virtual group and individual training sessions to familiarize CAB members with Discord. We assessed platform usability and acceptability over an eight-week trial period.

Results: Prior to the trial period, most (90%) CAB members planned to rely on desktop or laptop computers to engage with the Virtual Village. A third of CAB members reported feeling very uncomfortable learning new technologies, and most (70%) preferred recorded visual training that could be revisited after training sessions. We identified four lessons learned from the evaluation: Prepare for a diverse set of technology literacies. Despite efforts to develop a comprehensive training protocol, our CAB participants, many of whom were naïve Discord users, demonstrated disparate experiences with technology.

Expect to accommodate a variety of technological capacities. Disparate technological capacities (e.g., device availability) also complicated implementation of the Discord training protocol.

Novel technologies that support stakeholder preferences may still present significant barriers. Discord emerged as a leading platform to support the Virtual Village in part because it could accommodate all preferred attributes and because it is free to use and could be sustained beyond completion of our study.

Despite these strengths, many CAB participants required additional training on the platform which may have resulted in moderately positive perceptions of Discord usability and feasibility.

Regularly revisit study goals with community stakeholders. Frustrations emerged among some CAB participants about the lack of expediency and numerous steps involved in translating evaluation findings to intervention development. Revisiting study goals with CAB members emerged as an essential ongoing activity for the Virtual Village platform selection.

Conclusions: Incorporating insights from community stakeholders (representative of the target community) to select a virtual platform for a Virtual Village is an important and beneficial aspect of this community-engaged project, which seeks to mitigate the effects of social isolation in OPLWH. Planning for these "lessons learned" may help future virtual intervention research by reducing the barriers to participation, particularly for those with limited technology literacy or limited technology capacities.

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Rates of Vitamin D Supplementation and Barriers to Uptake Among Women Living With and Without HIV in Canada

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Background: Adequate vitamin D intake from diet and supplements is essential for women to maintain bone, prevent fracture, and promote overall health. Women living with HIV (WLWH) may be particularly vulnerable to its deficiency as they face unique challenges that may limit uptake and increase expenditure. Patterns of vitamin D intake are relatively unexplored amongst WLWH.

Here, we compare rates of vitamin D supplementation and dietary intake in WLWH at a specialized clinic versus HIV-negative controls and investigate socio-structural barriers to its uptake.

Methods: In this case-control study, WLWH in the Children and Women: AntiRetrovirals and Markers of Aging (CARMA) cohort in Vancouver, Canada were age-matched 1:3 within 5 years with HIV-negative women from the Canadian Multicentre Osteoporosis Study (CaMos). Participants reported on vitamin D supplementation, dose of supplement, and quantity of vitamin D consumed in fluid milk products. Demographic characteristics were compared by Chi-square, Mann-Whitney U or t-test, as appropriate. Univariable and multivariable models were constructed to assess factors associated with vitamin D intake, including HIV status, age, ethnicity, income, education, season of interview, smoking, history of osteoporosis, femoral neck bone density, and polypharmacy (number of current medications, excluding: antiretrovirals, vitamins/supplements, contraceptives, inhaled or topical medications, and over-the-counter medications). Models were constructed separately for supplementation (yes/no) and dietary intake (dichotomized at the median).

Results: Ninety-five WLWH were age-matched with 284 controls. WLWH had lower rates of employment, household income, education, and bone mineral density, and were more likely to smoke cigarettes and be of non-White ~~ethnic~~city than controls. Vitamin D supplementation was higher in WLWH than controls (62.2% vs. 44.7%; p=0.03), but median [IQR] intake from food was lower (0.76 [0.20 to 2.58] vs 1.79 [0.62 to 3.93] mcg/day; p<0.001). After adjusting for confounders, WLWH had higher odds of supplementation (adjusted odds ratio (aOR) 3.44 [95%CI 1.16 to 11.00]; p=0.03) and lower odds of dietary intake above the median (1.51 mcg/day) than controls (aOR 0.29 [0.12 to 0.61]; p=0.002). Total median intake from both sources was not significantly different between groups (WLWH: 8.28 [0.48 to 20.57] vs. controls: 5.27 [1.43 to 11.61] mcg/day; p=0.33). Both groups had a total intake less than the recommended Canadian guidelines (15 mcg/day). Women who smoked had lower odds of supplementation (aOR 0.37 [0.15 to 0.84]; p=0.02), while non-White ethnicity (aOR 0.31 [0.14 to 0.65]; p=0.002) and low income (aOR 0.24 [0.09 to 0.59]; p=0.002) were associated with lower dietary intake.

Conclusion: WLWH had lower vitamin D intake from dietary sources compared to controls, particularly those with low income and of non-White ethnicity, but had higher rates of supplementation, suggesting that bone health is being considered and/or discussed by HIV care providers in this setting. Women with smoking histories were less likely to supplement for vitamin D even though they may especially benefit from its health effects given their likelihood for multimorbidity. These data highlight a preventable gap for groups of women who are particularly vulnerable to lower intake of vitamin D and inform targeted efforts to promote adequate intake for bone health.

42. A.

United Voices: Adaptation and Implementation of a Virtual Group-Singing Intervention for Older People with HIV during COVID-19

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Background: People with HIV (PWH) experience a wide spectrum of aging-related health conditions that compromise quality of life in later years. Loneliness and social isolation increase with age and compromise wellbeing. Group-singing interventions such as Community of Voices (CoV) are efficacious in improving psychosocial wellbeing among older people but require adaptation to PWH using community-engaged research. This study describes the adaptation of an evidence-based group-singing intervention for older PWH, United Voices, using community-engaged participatory method.

Methods: The research team comprised of 2.5 full-time staff and experts in community- engaged intervention development with PWH, HIV geriatrics, and music and

arts-based intervention research. Key stakeholders were invited to serve as members of the United Voices Community Advisory Council (CAC) that led the adaptation of CoV to develop United Voices. The CAC convened to discuss intervention core components, protocol, and procedures, which included identifying candidates for music directors and producers, music genre and repertoire, weekly intervention sessions (i.e., rehearsals), and music performance production (i.e., virtual final concert recording). The music and research teams met weekly prior to the start of the intervention to draft the syllabus, and throughout the trial period to check in and troubleshoot issues that arose at the previous intervention session. Adaptations to the CoV Manual were documented and guided by the ADAPT-ITT model.

Results: Based on CAC recommendations, two choir directors and two music producers were selected to reflect the diversity and experience of the local community of older PWH. Twelve weekly, 90-minute sessions were co-led by the two choir directors (30 minutes each) and included a 30-minute "check-in" led by the principal investigator to facilitate socializing opportunities among choir members via ice breakers, topic-based discussions (e.g., aging with HIV), and sharing personal stories. Virtual "drop-in helpdesk" sessions were hosted by the music producers as needed to support participants in recording their individual music videos that comprised the final concert recording. A study website (https://unitedvoices.ucsf.edu) allowed access to music rehearsal tracks, lyrics, syllabus, instructions, and other information. A final performance, a virtual concert recording (https://youtu.be/3zSB7uUdih0), was professionally produced using recordings from all participants.

Conclusions: The COVID-19 pandemic resulted in widespread lockdowns and physical distancing that exacerbated loneliness and social isolation. United Voices, conceptualized as an in-person group-singing intervention, pivoted to intervention adaptation and implementation in a virtual environment. This study manualized the United Voices intervention by adapting the CoV and implementing a virtual group-singing intervention for older PWH.

42. B.

United Voices: Feasibility and Acceptability of a Virtual Choir Intervention for Older People with HIV during COVID-19

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Background: People with HIV (PWH) experience a wide spectrum of aging-related health conditions that compromise quality of life in later years. Loneliness and social isolation increase with age and compromise wellbeing. Group-singing interventions are efficacious in improving psychosocial wellbeing among older people but require adaptation to PWH. We conducted a randomized, waitlist-controlled trial of the United Voices, an online, virtual group-singing intervention for older PWH, to evaluate the feasibility and acceptability of implementation and assessment procedures and protocols during COVID-19.

Methods: PWH 50 years of age and older were recruited remotely using community-engaged research methods: We garnered interest in the study by meeting with leaders and staff at community-based organizations serving older PWH, who disseminated study information virtually (e.g., social media posts, emails) within their social networks during pandemic lockdown. Interested individuals contacted the study staff and were screened for eligibility over the phone. There were 12 intervention sessions (i.e., rehearsals) held via Zoom during the pandemic. Feasibility and acceptability of intervention procedures and protocol were evaluated using metrics for recruitment and enrollment (number of participants enrolled per week), retention and attrition (retention rates and dropout), adherence to intervention (sessions attendance), follow-up assessment completion (proportion completed), and satisfaction. We conducted individual, semi-structured exit interviews (n=12).

Results: A total of 41 individuals were screened for eligibility over 13 weeks

(M=3.2/week). Of 40 eligible participants, 23 were randomized into the immediate-start intervention (n=13) or delayed-start control (n=10) arm, of whom 18 completed baseline assessment, and 16 completed follow-up assessments at 6- and 12-weeks. Attendance was high (M=10.9, SD=5.0): 88.9% attended one or more of the 12 sessions, and 77.8% attended six or more sessions. Satisfaction at 12 weeks (n=7) was moderately high to high (5/7), recommend to others (5/7), participate ~~after stud~~y end (4/7), satisfied with level of information (6/7), enjoyed being part of UV community (5/7), satisfied with level of staff support (7/7), website was helpful (6/7), and technical assistance for recording was helpful (4/7). Findings from exit interviews indicated that while participants would have preferred to singing in person, the virtual group singing experience was enjoyable, providing a social outlet during shelter-in-place. Participants expressed skepticism at the beginning regarding the online nature of the choir and appreciated getting to know and supporting each other over time. The final product, a professionally rendered virtual concert recording, was a source of pride.

Conclusions: To our knowledge, this was the first randomized, controlled pilot trial of an online group-singing intervention for older PWH. Overall, the thresholds for recruitment and enrollment, retention and completion of follow-up assessments, and adherence to intervention were reached. Participants were moderately to highly satisfied with the choir intervention and highly satisfied with the staff support, music director and producer knowledge and support, and technical assistance. Future research will examine the comparative efficacy of a virtual versus an in-person group-singing intervention for older PWH in a large randomized controlled trial.

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The Role of HIV-Derived Proteins to the Development of Pulmonary Arterial Hypertension (PAH)

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Pulmonary arterial hypertension (PAH) is a severe and progressive disease, a key feature of which is pulmonary vascular remodeling (PVR). People living with HIV (PLWH) are exposed to accelerated aging and have an elevated susceptibility to develop severe PAH. Despite significant effort to understand its pathophysiology, the underlying mechanisms of HIV-associated PAH are not yet established. The goal of this study is to investigate whether and how HIV-derived proteins contribute to the pathological processes of PAH and right ventricle (RV) hypertrophy, and to identify the pathways respectively altered in endothelial (EC) and smooth muscle cells (SMC) involved in HIV-associated PAH. We utilized three mouse model of HIV to answer these questions. We found that transgenic HIV-1 Tg26 mice, which mimics PLWH with low viremia and without progression to AIDS, exhibit PVR of PAH and RV hypertrophy. More importantly, transfer of bone marrow (BMT) from Tg26 to wild-type (WT) mice and chronic treatment with HIV-encoded Tat protein caused progression of PAH and RV hypertrophy in WT mice indicating that HIV-derived proteins contribute to the pathogenesis of PAH in mouse models of HIV. RNA sequencing and quantitative real-time PCR were performed in lung samples from control/Tg26 mice and BMT mice to explore signaling pathways involved in the HIV-related PAH. We found that the relative expression of proliferative markers were increased in the EC fraction of Tg26 lungs as well as the relative expression of contractile SMC phenotype markers were decreased and markers for synthetic SMC phenotype were upregulated in the flow through (FT) fraction of Tg26 lungs suggesting increased EC proliferation and SMC de-differentiation in Tg26 mice. Moreover, we

identified ten genes which relative expression were up/ downregulated in lung samples of Tg26 mice which can potentially contribute to the development of HIV-associated PAH. In conclusion, we have established a novel model of HIV, the BMT Tg26 to WT mice, to study the contribution of immune cell derived viral proteins to PAH and demonstrated that at least one viral protein is involved in the development of PVR of PAH and RV hypertrophy. Additional studies are needed to further elucidate the role of these signaling mechanisms in HIV-induced PAH in order to develop effective therapy for the prevention and treatment of this lung disorder.

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This abstract was withdrawn.

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Nutrition Intervention Programs in the Care and Treatment Continuum of People Aging With HIV – A Case of Aids Information Centre (AIC)

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Background: Poor nutritional status and malnutrition in the elderly population are important areas of concern. Malnutrition and unintentional weight loss contribute to progressive decline in health, reduced physical and cognitive functional status, increased utilization of health care services, premature institutionalization, and increased mortality. Nonetheless, many health care practitioners inadequately address the multifactorial issues that contribute to nutritional risk and to malnutrition. As people age, their nutritional needs change. This could be attributed to sensory changes that reduce taste and smell, teeth loss and gum diseases, digestive problems among others. This could be worse with People Living with HIV (PLHIV) as HIV can cause or worsen undernutrition by causing reduced food intake, increased energy requirements, and poor nutrient absorption. Nutrition care and support helps in maintaining and improving their nutritional status, boost their immune response, manage the frequency and severity of symptoms, and improve their response to antiretroviral therapy (ART).

Materials and methods: In February 2022, AIC started a nutrition clinic to help support malnourished clients in care by providing nutrition assessments, psychosocial support, therapeutic foods and referrals to livelihood strengthening programs. Of the 40 malnourished clients identified in the month, 12 (30%) were individuals aging with HIV and on ART for more than a year. Nutrition interventions using home visits were started and up to date statistics prove that atleast 23% of the newly identified malnourished clients are 50 years and above.

Results: Nutrition community facilitators conducted home visits on all the 12 clients and provided psychosocial support, ready-to-use therapeutic foods (RUTF), started nutritional gardens for 7 clients and atleast 3 women were successfully enrolled in livelihood programs. As of today, 10 clients have a normal Body Mass Index (BMI) between 18.5—24.9 and 2 are still on treatment.

Conclusions: Proper nutrition care and support helps to strengthen the immune system, alleviate symptoms, enhance the effectiveness of and adherence to medical treatment, and manages the negative effects of drug-food interactions on nutritional status and may slow disease progression for older PLHIV. However, at times some individuals require prolonged support which could not be provided by the facility and livelihood programmes are more focused on the strong abled or adolescents living the elderly behind with few support.
None the less, nutritional assessment and treatment should be a routine part of care for all elderly persons.

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Exploring Experiences With Exercise From the Perspectives of Women Living With HIV: A Qualitative Study

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Background: With HIV as a chronic illness characterized by episodic disability, there is an increasing role for rehabilitation, and specifically exercise as a rehabilitation intervention and self-management strategy with a potential to enhance health and well-being among those aging with HIV. Despite the benefits of exercise, a considerable number of women living with HIV do not meet the physical activity guidelines and few are represented in existing exercise literature.

Purpose: To explore experiences engaging in exercise among women living with HIV, specifically i) nature and extent of exercise, ii) components that characterize exercise experiences, iii) facilitators and barriers, and iv) strategies for uptake and sustainability.

Material and Methods: Qualitative descriptive study involving online semi-structured interviews with women living with HIV who may or may not engage in exercise, followed by a web-based demographic questionnaire. Descriptive thematic analysis informed by Braun and Clarke was used to identify themes and patterns within qualitative data. Responses from the demographic questionnaire were evaluated using descriptive analysis to describe the characteristics of the participants.

Results: Ten women characterized their exercise experiences with six intersecting components: culture, gender, HIV-related stigma, episodic nature of HIV, sense of belonging, and perceptions of exercise. Facilitators to exercise included: aspirations to achieve a healthy lifestyle, using exercise as a mental diversion, having an exercise companion, and receiving financial support from community-based organizations; and barriers to exercise included: limited resources, such as lack of mental-health support and fitness classes, financial limitations, time and gym restrictions, and the cold winter weather conditions. Finally, four strategies to facilitate the uptake and sustainability of exercise included: creating social interactions, provision of online classes, raising awareness and educating the population, and offering practical support.

Conclusions: Experiences with exercise were characterized by intersecting personal and environmental contextual components. Results may help to inform tailored implementation of exercise as a rehabilitation strategy among women living with HIV. This can increase the skills and capacities to enable women living with HIV to make informed choices to improve their health, and health care engagement.

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This abstract was withdrawn.

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Cancer Screening in HIV Geriatric Care Model: The STRONG Study

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Background: People living with HIV (PLWH) have elevated incidence of cancer diagnosis compared to the general population. HIV infection is associated with increased risk of

both AIDS-related and non-AIDS related cancers, as evidenced by increased rates of HPV-related cervical cancer in women and anal cancer in both men and women. Therefore, recommended screening for these cancers in PLWH is more frequent than the general population. Women living with HIV are recommended to have cervical Papanicolaou (Pap) smears annually for life, or every three years if Pap and HPV testing for 3 consecutive years are both negative. Current recommendations for anal cancer screening include anal cytology annually for PLWH ≥35 years old, but data on the benefit of screening are not yet definitive. Screening may be discontinued after 2 consecutive negative anal cytology results if not sexually active or when life expectancy is less than 10 years. Screening for colon and breast cancer in PLWH are based on general population guidelines. Cancer screening remains a mainstay of primary clinical care. Incorporating cancer screening guidelines into a geriatric HIV care model is an opportunity for reducing morbidity and mortality associated with malignancies. We examined the frequency of screening at an urban center targeting screening and assessment for those over the age of 50.

Methods: The Strengthening Therapeutic Resources in Older adults aging with HIV (STRONG) Study, aims to create a geriatric care model by incorporating standardized geriatric assessments and treatment perspectives into an urban HIV ambulatory care center. PLWH over the age of 50 were invited to participate and completed gerontological assessments. A systematic medical chart review was performed for age-related comorbidity screenings. We assessed cancer screening adherence, defined as being up to date based on clinical recommendations or guidelines. We followed USPSTF recommendations for colon cancer and breast cancer screening. Cervical cancer screening and anal PAP recommendations were from the Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV.

Results: Participants (n=184) were enrolled between November 6, 2019, and Feb 1, 2022. Median (IQR) age was 59 years (55 to 63), females were slightly less represented (45%), and majority were Black (94%). Participants had well controlled viremia (94% undetectable HIV RNA) and the median (IQR) CD4 was 617.5 cells/mm3 [396.5-888.0], with 94% of participants having a CD4 >200 cells/mm3. Majority of participants were not up to date for colon cancer screening (57%) and those meeting criteria for anal pap screening were not up to date (77%). Likewise, majority of female participants were not up to date on cervical pap screening (67%) or screening mammography (55%).

Conclusions: The STRONG Study identified an aging HIV population that is not meeting optimal cancer screening guidelines. To further address the gaps and delays in cancer screening, targeted screening approaches need to be integrated into clinical care model. Further preventive standardized screenings for lung and prostate cancer should be considered. Additional inquiry is needed to identify the barriers to completing routine screening and accessing screening procedures.

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Prevalence of Anal Human Papillomavirus and High-Grade Squamous Intraepithelial Lesions Among Older Men Who Have Sex (MSM) Living With HIV and HIV-Negative MSM Ages 50+

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Introduction: The incidence of anal cancer increases with age, particularly after age 50. Anal cancer also occurs most frequently among men who have sex with men (MSM) who are living with HIV (LWH); MSMLWH also have the highest risk of anal high-grade squamous intraepithelial lesions (HSIL), the precursor to anal cancer, and anal HPV infection, the cause of approximately 91% of all anal cancers. The population of persons LWH is aging; more than half are above the age of 50, and it is estimated that by 2030

more than 70% will be 50+. Little is known about anal HPV infection, anal HSIL, and HIV infection among MSM ages 50+. An understanding of the relationship among aging, HPV and HIV will be critical to development of HSIL screening and treatment guidelines.

Materials and Methods: This study presents the baseline cross-sectional results of a three-year prospective cohort study of MSM aged ≥50 years. We enrolled both MSMLWH and HIV-negative MSM. All participants completed an anal exam including high-resolution anoscopy (HRA), cytology, and HPV DNA testing. HPV genotyping was determined through Atila Biosystems Multiplex High Risk HPV fluorescent detection. HSIL diagnosis was confirmed on HRA-guided biopsy.

Results: 129 (54%) MSMLWH and 109 (46%) HIV-negative participants were studied; 54% of participants were ages 50-59, 36% were 60-69, and 10% were 70+ years. Sixty-six percent of men self-identified as non-Hispanic white, 10% as Black, 5% as Hispanic white, 7% Asian, and 13% as multiracial. Compared with the MSMLWH, the HIV-negative MSM reported higher full-time employment (36% vs. 15%, p<0.01) and annual household income ($84,000+, 53% vs. 34%, p<0.01), and a higher proportion reported having at least a bachelor's degree (71% vs. 56%, p<0.01).

Among MSMLWH, 47% (95% CI: 38-56%) had biopsy-confirmed anal HSIL. The prevalence of HSIL by age group (50-59, 60-69, 70+) was 47%, 45%, and 55%, respectively. Among all MSMLWH, 71% (62-79%) had at least one oncogenic anal HPV infection and 19% (95% CI: 13-27%) had HPV-16.

Among HIV-negative MSM, 37% (28-47%) had anal HSIL. The prevalence of HSIL by age group (50-59, 60-69,70+) was 34%, 44%, and 33%, respectively. Among all HIV-negative MSM, 57% (47-67%) had at least one oncogenic anal HPV type and 22% (15-32%) had HPV-16.

Although some patterns by age group were noted, increasing age was not statistically associated with prevalent HSIL, oncogenic HPV infection, or HPV-16 in either MSMLWH or HIV-negative participants. In separate models, both oncogenic HPV and HPV-16 increased the odds of HSIL (Oncogenic HPV OR: 7.5, 95% CI: 3.8-15; HPV-16 OR: 11.1, 4.8-25, p<001), both adjusted for age and HIV status.

Conclusions: The prevalence of oncogenic anal HPV infection, anal HPV type 16, and anal HSIL remain very high in both MSMLWH and HIV-negative MSM over the age of 50 years. With the recent evidence that screening and treating anal HSIL prevents anal cancer, both MSMLWH and HIV-negative MSM over the age of 50 should be strongly considered for anal cancer and HSIL screening.

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Telehealth Access and Experiences of Older Adults With HIV During COVID-19

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Background: Early in the COVID-19 pandemic, care interruptions for older adults and people with HIV (PWH) created additional medical and social needs for this vulnerable population. Despite the recent uptake in telehealth services, inequities in telehealth access for older adults and PWH exist due partly to resource limitations and digital literacy. Despite potential barriers to telehealth access, the experiences of older adults with HIV switching to virtual platforms have not been closely examined. This study aimed to assess the telehealth capability and experiences of older PWH at an urban safety net HIV clinic.

Methods and Materials: Participants were from Ward 86, a safety net HIV clinic in San Francisco. Between May and October 2020, community-dwelling adults 65 and older were contacted via telephone about current telehealth capabilities and other health-related needs, including access to the internet, telehealth-capable devices, and email. During this time, focus groups were conducted with people with HIV 50 and older participating in classes through the Golden Compass HIV and Aging program at Ward 86. Patients' perceived challenges and benefits of switching to a telehealth platform were assessed using a semi-structured interview guide. Focus group data were analyzed using brief content analysis, and descriptive statistics for all data were performed.

Results: Among the 179 community-dwelling adults 65 and older, 147 (82%) were contacted, and 80 answered the telehealth questions. Of those who answered the telehealth questions, the majority were male, 73 (91%), with a mean age of 69 (SD 3.0), and 44 (55%) were White. One-third (n=25) did not have internet access, and 2 (3%) had internet access but did not know how to use it. 30% (n= 24) did not have an email address on file, and 5% (n=4) had an email address but did not know how to use it. 52 (65%) had at least one telehealth-accessible device (e.g., smartphone, tablet, computer), and 7 (9%) did not. Among the 52 who reported having at least one telehealth-accessible device, 10 (12.5%) had a device but did not know how to use it. Thirteen patients 50 and older participated in the focus groups, and nine answered demographic questions. The mean age was 64 (SD 6.9); four (44%) were female, one third were White. Four major themes were identified in the switch to a virtual platform: technological barriers, convenience, and social and emotional impact. The most noted challenges were adoption, securing telehealth-capable devices, and internet connectivity. Participants preferred in-person classes but felt telehealth was a good alternative for mitigating isolation, especially for those with few social connections. Telehealth gave those with mobility and transportation issues more options for participation.

Conclusions: Our findings provide insight into telehealth accessibility and virtual platform experiences of older adults with HIV. Challenges identified included limited internet, device access, and knowledge of how to utilize virtual platforms. However, benefits also were found, including addressing social isolation and improving access for those with mobility limitations. Improving device access and training on usage will be critical to better serve those with transportation and mobility challenges and support hybrid healthcare models for older adults with HIV in the future.

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Examining the Association of Sleep Deficiency in People Living With HIV

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Background: Sleep deficiency is common in People Living with HIV (PLWH) and becomes more common with aging. However, the synergistic effects of age and HIV on sleep deficiency, or the association of sleep deficiency with HIV specific clinical factors is not well understood.

Materials and Methods: We leveraged the HARC (HIV Associated Reservoirs and Comorbidities) study at Yale, where participants donate paired blood and cerebrospinal fluid (CSF) and complete standardized surveys assessing for mood and substance use disorder. Clinical data were extracted from the medical record. We included PLWH with suppressed viral load, defined as <200 copies/mL, on combination antiretroviral therapy (cART) for >1 year and uninfected controls.

Sleep deficiency was assessed by a single item from the Center for Epidemiological Studies Depression (CES-D) survey. In preliminary analyses, we found this item to be highly correlated with the Insomnia Severity Index, a validated measure of sleep deficiency ($r=0.75$, $p<0.0001$). The item asks participants to rate how often, over the past week, they have felt "my sleep was restless", with scores of 0 (Rarely), 1 (Some), 2 (On occasion), and 3 (Most). Participants with scores of 1-3 on this item were considered to have sleep deficiency.

We assessed the bivariate association of HIV status with sleep deficiency for all participants. Among PLWH, we assessed the bivariate association of age, substance use disorder, CD4:CD8 ratio, CD4 nadir, comorbidity burden (defined as number of comorbidities in addition to HIV status), cART regimen, and polypharmacy (defined as number of drug classes not including cART) with sleep deficiency.

Results: This study includes 42 PLWH and 16 uninfected controls with median ages of 57 and 47.5 years, respectively. For both groups, over 80% of participants were male. For the entire study, 58.62% of participants were Black or African American, 27.59% were White, 1.72% were Asian, and 12.07% were of an unknown race. There were no significant differences among the PLWH and control participants in years of education, smoking status, alcohol use disorder, substance use disorder, depression, or anxiety status. PLWH were more likely to have a higher comorbidity burden and polypharmacy, even after excluding cART regimen (p values <0.03). HIV status was significantly associated with sleep deficiency (59.5% in PLWH vs 25% in controls; p<0.02). Among all participants, we found a trend toward a positive association between comorbidity burden and sleep deficiency (r = 0.23, p<0.08). Among PLWH, age, substance use, CD4 nadir, CD4:CD8 ratio, comorbidity burden, cART regimen, and polypharmacy were not significantly associated with sleep deficiency through bivariate analysis.

Conclusions: Despite similarities in demographics between PLWH and uninfected controls in our study, HIV status was associated with sleep deficiency. However, among PLWH, comorbidity burden, polypharmacy and HIV-specific clinical factors were not associated with sleep deficiency, suggesting that other factors may contribute to higher rates of sleep deficiency in PLWH. Future work will include examining CSF inflammatory profiles to assess whether sleep deficiency and age in PLWH may associate with higher rates of neuroinflammation, and multivariable analyses of sleep deficiency among PLWH and uninfected controls.

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The Patient Generated Index as an Early-Warning System for Predicting Brain Health Challenges: A Prospective Cohort Study for People Living With HIV

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Background: In research people are often asked to fill out questionnaires about their health and functioning and some of the questions refer to serious health concerns. Typically, these concerns are not identified until the statistician analyses the data. An alternative is to use an individualized measure where people are asked to self-nominate areas of concern which can then be dealt with in real-time. The relevance of this approach to identify brain health concerns has not been explored in people aging with HIV.

Objective: To estimate the extent to which self-nominated areas related to mood, anxiety and cognition on an individualized measure of quality of life (QOL), the Patient Generated Index (PGI) predict the presence or emergence of depression, anxiety, or cognitive impairment among people living with HIV at study entry and for successive assessments over 27-months.

Methods: The data comes from participants enrolled in the Positive Brain Health Now (BHN) cohort (n=856). The nominated areas were category coded to a sentiment framework. A longitudinal design was used to link self-nominated sentiments to presence or emergence of anxiety, depression, or low cognitive ability as assessed using standardized measures of these constructs. Logistic regressions were used to estimate the goodness of fit of each model using the c-statistic.

Results: The sentiments categorized as 'emotional' predicted all of the brain health

outcomes at all visits with adjusted odds ratios (OR) ranging from 1.61 to 2.00 and c-statistics >0.73 (good to excellent prediction). Nominating an anxiety sentiment was specific to predicting anxiety and mental health (OR: 1.65 & 1.52); nominating a cognitive concern was specific to predicting self-reported cognitive concerns (OR: 4.78). Positive sentiments were predictive of good cognitive function (OR: 0.36).

Conclusions: This study indicates the value of using this semi-qualitative approach as an early-warning system in predicting brain health outcomes from the spontaneously nominated life areas obtained by administering the PGI.

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Social Support Network Factors Linked to Neuropsychological Performance Among Disadvantaged Persons Living With HIV Who Use Drugs: Implications for Multi-Level Intervention on Cognitive Impairment Linked to HIV

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Background: Cognitive impairment has been linked to HIV and to reduced social support and isolation. Disadvantaged persons living with HIV (PLHIV) who use drugs are at especially high risk of cognitive impairment and challenges accessing quality support of family and friends in later life. We sought to identify social network factors associated with neuropsychological test performance of a high-risk group to further an understanding of unmet needs for community support among PLHIV with impaired cognitive function.

Materials and methods: Former or current injection drug using PLHIV enrolled in the BEACON study (n=383) completed the Controlled Oral Word Association test (COWAT) of verbal fluency and a social support network inventory. Latent class analysis with count variables was used to determine the number of distinct classes of PLHIV based on their social network characteristics.

Results: The majority of PLHIV were male (61.4%), African American (85.9%), and had a high school education or less (83.8%). Standardized COWAT scores (T-scores) were approximately normally distributed with a range of 18.8 to 75.6, a mean of 46.9, and a standard deviation of 9.3. Fewer support network members ($\beta = 6.25$, $p < 0.01$), greater frequency of negative interactions with support network members ($\beta = 6.67$, $p < 0.01$), and less frequent positive interactions with network members ($\beta = -6.67$, $p < 0.05$) were significantly associated with lower COWAT scores.

Conclusions: Given high rates of cognitive impairment among PLHIV, comprehensive screening of high-risk PLHIV and early intervention is important for addressing the social support needs for those with impaired function. The findings suggest the importance of interpersonal and network-level intervention for cognitively impaired PLHIV to ensure optimal quality and functioning of community support structures and avert potential social isolation.

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Frontostriatal White Matter Microstructure Alterations in HIV and Aging

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Background: Despite the advent of

combination antiretroviral therapy, the prevalence of HIV-associated neurocognitive disorders (HAND) remains high. While the neural mechanisms of HAND are unknown, prior studies point to dysfunction within the frontostriatal pathway in people with HIV (PWH). In this study, we tested the effects of aging and HIV disease on frontostriatal white matter microstructure as measured by diffusion tensor imaging.

Methods: Participants 41-70 years of age were recruited for this study from the greater Washington, D.C. metropolitan area between 2018 and 2021. Diffusion MRI (dMRI) data were acquired with 70 gradient directions using a 3T Siemens Prisma Fit scanner at Georgetown University. Whole-brain tractography was computed for each participant using the two-tensor unscented Kalman filter (UKF) method, as implemented in the open-source ukftractography package (https://github.com/pnlbwh/ukftractography). We performed tractography analysis and visualization in 3D Slicer (http://www.slicer.org) via the SlicerDMRI project (https://github.com/SlicerDMRI). Using the O'Donnell Research Group Atlas, the left and right frontostriatal tracts were identified in each participant. Three measures of white matter microstructure were calculated from the frontostriatal tracts: fractional anisotropy, mean diffusivity, and number of streamlines (i.e., the number of reconstructed fibers). We then entered these three dMRI measures as dependent variables in 6 ANCOVA models examining the main effects of HIV serostatus and age on left or right frontostriatal tract microstructure. Education, sex and race were additional covariates. The alpha level was set to 0.05 and p-values were corrected for multiple comparisons using the false discovery rate. Executive and motor function T-scores were compared between PWH and controls and correlated with frontostriatal dMRI measures.

Results: Participants were 66 PWH (mean (SD) age 57.3 (7.2) years, 27% female, 56% Black, education 14.4 (3) years, duration of HIV infection 25.2 (9.8) years, median (interquartile range) nadir and current CD4+ T-lymphocytes/uL 180 (302) and 617 (413), on ART 98.5%, 90% with undetectable plasma HIV RNA) and 20 demographically comparable controls (age 58 (4.9) years, 25% female, 60% Black, education 14.6 (2.7)). PWH had significantly worse motor performance compared to controls, F(5,80)=5.8, p=0.02, but there was no difference in executive function. Increased age was associated with higher left, F(5,80)=12.3, p=0.003, and right, F(5,80)=11.7, p=0.003, frontostriatal mean diffusivity and fewer left, F(5,80)=5.1, p=0.04, and right, F(5,80)=9.4, p=0.006, frontostriatal streamlines. Compared to controls, PWH had higher mean diffusivity in the left frontostriatal tract, F(5,80)=6.8, p=0.046, and fewer streamlines in the right frontostriatal tract, F(5,80)=6.1, p=0.046. There were no significant correlations between behavioral performance and frontostriatal dMRI measures.

Conclusions: Our results support the hypothesis that frontostriatal white matter microstructure is compromised in middle-to-advanced aged PWH compared to controls. Analysis of the main effects of age and HIV serostatus indicates that deterioration in the frontostriatal connections in PWH could be independently impacted by older age. Early identification of brain changes is often associated with neurocognitive impairment and could inform the development of diagnostic methods for HAND.

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Comparing a Novel Virtual Reality Assessment Device, Detect, to Best-Practices in Assessing HIV-Associated Cognitive Impairment and Mild Cognitive Impairment

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Background: Persons living with HIV (PLH) are at elevated risk of cognitive impairment. The cognitive impairment associated with HIV is usually relatively mild and non-progressive; however, older PLH have entered an age where they are at-risk for developing Alzheimer's disease (AD) and its precursor, mild cognitive impairment (MCI). Current best practices for assessing

cognitive function are time-intensive, expensive, and require experienced assessors. Self-administered, scalable tools to screen for MCI/AD and to differentiate it from HIV-associated cognitive impairment among older PLH are needed. This study compares a brief virtual reality automated screening tool (DETECT) to a gold- standard comprehensive neuropsychological battery in differentiating HAND, MCI, and normal cognition among individuals with and without HIV.

Materials and methods: One-hundred fifteen persons with and without HIV and with and without cognitive impairment (mean age = 68.63 [SD = 6.48]; 65% male; 70% PLH; 65% MCI) completed a standard neuropsychological battery as well as a brief virtual reality (VR) neuropsychological assessment battery using a Samsung Oculus device. HIV-Associated Neurocognitive Disorder (HAND) was diagnosed via a Global Deficit Score (GDS) >0.5. MCI was diagnosed using Jak/Bondi criteria. DETECT, which takes 15 minutes to complete, measures executive functions, recognition memory, processing speed, attention and working memory. To assess these domains, participants sequentially completed six modules using stimuli such as words, faces, shapes, and arrows. Within each of these modules, participants were either instructed to indicate if new stimuli were presented previously (such as in word recognition or face and shape similarities) or to differentially respond depending on the color and direction of arrows. A composite score was created reflecting the proportion of correct responses to the total number of trials (including trials without a response). We corrected for demographic differences in this composite score and then used Pearson's R to test for a correlation between VR composite scores and global composite demographically corrected t-scores from the NP battery. We used linear regression to examine between group differences on the VR tasks.

Results: The composite cognitive score derived from DETECT was correlated with the global cognitive composite score on the neuropsychological battery ($r = .41$; $t(99) = 4.48$, $p < .001$, 95% CI = .24 - .56). Controlling for demographic differences between groups, individuals with MCI performed worse on the VR tasks ($b = -0.06$, $t(94) = -2.16$, $p = .03$) as did individuals with HAND ($b = -0.06$ ($t(100) = -3.09$, $p < .01$), compared to persons without cognitive impairment.

Conclusions: The self-administered, brief DETECT cognitive battery was moderately correlated with a gold-standard neuropsychological battery and differentiated persons with and without HAND and MCI from persons without cognitive impairment. Although preliminary, these results suggest DETECT is a promising tool to reduce barriers to cognitive screening (e.g., cost, time, access).

Longitudinal work is ongoing to examine whether DETECT can identify cognitive decline over time in persons aging with HIV.

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Brief Evaluation of Cognitive Impairment and Iadl Among Art-Treated People With HIV in a Primary Care Setting

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Background: Cognitive impairments are common in people with HIV (PWH) and may increase problems with instrumental activities of daily living (IADL). We aimed to describe the prevalence of cognitive impairments and IADL difficulties among PWH engaged in care.

Methods: We conducted a study among PWH at Kaiser Permanente Northern California, an integrated healthcare system in the U.S. Study participants were recruited between March 2020 and June 2022 (with periodic suspension in recruitment efforts due to COVID-19). Participants were eligible for inclusion if they were ≥50 years old, taking antiretroviral therapy (ART; defined as ≥1 ART prescription fill in the past year), and had no prior clinical diagnosis of dementia. Research staff administered a brief cognitive screen (St. Louis

University Mental Status exam; SLUMS exam) and a questionnaire regarding self-reported difficulty in IADL (modified Lawton and Brody questionnaire). The SLUMS exam was scored on a scale from 1 to 30. Cognitive status was categorized as normal, mild cognitive impairment, and possible dementia, according to pre-defined numeric cut-offs which accounted for participants' self-report of high school completion (yes/no). IADLs included housekeeping, managing finances, buying groceries, cooking, transportation, using the telephone, doing laundry, taking medications, and working.

Results: Of 47 study participants (85.1% men, average age 59.7±7.0 years, 51.1% White race, 25.5% Black race, 97.9% with at least a high school education), 27 (57.5%) had normal cognition, 17 (36.2%) had mild cognitive impairment, and 3 (6.4%) had possible dementia. Of the 20 participants with any cognitive impairment (i.e., mild cognitive impairment or possible dementia), most (85.0%) were men, in their 50s or 60s, 45.0% were White, 40.0% were Black, and 30.0% reported difficulty in at least one IADL. Difficulty in IADLs were most frequently reported for housekeeping (20.0%), working (15.0%), buying groceries (10.0%), and doing laundry (10.0%).

Conclusions: Despite ART use, cognitive impairments are frequent in PWH and may be accompanied by difficulty in IADL. Additional efforts are needed to determine factors contributing to cognitive and IADL impairments among ART-treated PWH and explore ways to optimize identification of these issues among PWH in primary care.

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This abstract was withdrawn.

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"HIV Is a Steppingstone for Getting Yourself Better:" Exploring Narratives of Resilience Among U.S. Veterans Aging With HIV

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Background: People aging with HIV, especially military Veterans, have unique illness experiences related to growing health disparities and intersectional stigma. Intersecting stigmas occur when populations experience layered stigmas (age and HIV stigma). Our study aims to understand the experiences of U.S. Veterans aging with HIV and investigates risk and protective factors that do and do not contribute to resilience among our study sample.

Materials and Methods: This qualitative study uses secondary data from a larger multi-method study entitled, "Social Determinants of Health of Veterans Aging with HIV in Georgia." Participants included 25 Veterans (≥ age 50) participating in the Veterans Aging Cohort Study who were recruited from the Atlanta Veterans Affairs Medical Center between January 2015 and September 2015. Maximum variation sampling was used to select participants that varied in sociodemographic and health characteristics. We conducted semi-structured interviews and social network mapping as well as brief sociodemographic and health surveys. Qualitative domains included: life history and significant life events; current living arrangements; social support; daily routines; use of healthcare and long-term care; health

perceptions; and future expectations. We used a thematic analysis approach to analyze the data informed by the life course perspective to examine how events in each participant's life course contributed to coping trajectories.

Results: Participants ranged in age from 50 to 72, with a mean age of 59. Most (80%) were male, and more than half (60%) were African American. Close to half had annual incomes below $25,000. Qualitative findings showed that many participants experienced military sexual violence, childhood abuse, and non-military domestic violence, as well as harassment based on sexual identity. The cumulative effect of negative childhood and military events exacerbated the experience of additional negative live events, such as receiving an HIV diagnosis. The transition out of the military often caused life instability due to difficulty with employment, housing, and stable relationships. Receiving an HIV diagnosis was described as a "death sentence" and shocking experience by almost all participants. This resulted in one of two pathways: 1) maladaptive coping or 2) therapeutic coping. Some who experienced maladaptive coping experienced a subsequent turning point (e.g., imprisonment, turning to religion, outreach from others), which altered their trajectory to align with the therapeutic group. While others in this category continued along a maladaptive trajectory. Participants who experienced more maladaptive coping strategies than therapeutic had smaller social networks or engaged in social networks that encouraged maladaptive coping mechanisms such as substance abuse. Those with more therapeutic coping strategies described being able to connect with others, disclose their HIV status, and feel comfortable living with HIV despite their previous negative life experiences. Participants showing higher levels of resilience such as through therapeutic coping mechanisms also were more likely to be compliant with their medications and more likely to engage in health promotion activities.

Conclusions: In summary, U.S. Veterans living with HIV experienced cumulative life experiences that shaped their overall health status and resiliency. Major life events, such as receiving an HIV diagnosis, turning points, and subsequent coping ability shaped resilience trajectories.

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How Useful Is an Individualized Approach to Measuring Physical Health Challenges in HIV?

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Background: Physical health challenges are common among people living with HIV and are associated with greater fall risk, higher mortality, and reduced health-related quality of life (HRQOL). Other work has shown that individualized measures such as the patient generated index (PGI) provide unique information that is not captured by generic HRQOL measures.

Objective: The purpose of this study is to estimate the extent to which the PGI is interpretable in terms of known constructs from generic HRQOL measures.

Methods: The PGI, SF-36, WHOQOL, and EQ-5D were administered to participants from the Positive Brain Health Now study, a Canadian cohort of people living with HIV. Logistic regression and chi-square tests were used to determine factors associated with nomination of a physical health challenge, relationships between nomination of a physical health challenge and generic HRQOL items scores, and consequences to downstream HRQOL outcomes. Because of the large sample size, response distributions across HRQOL items were considered meaningful if there was a 10% difference between those who nominated a physical health challenge and those who did not.

Results: The sample comprised 866 participants (mean age: 53; years with HIV: 16.8; women: 15.7%). There were no differences in age, sex, education levels, years living with HIV, proportion living with AIDS, viral load, nadir CD4, or comorbidities between those who nominated a physical health challenge and those who did not. Mean PGI scores differed between groups by 5.6

points (95%CI 2.12 to 9.14). Participants who differed by 20 points in terms of lower pain (OR: .82, 95%CI: .73 to .92) and better vitality (OR: .71, 95%CI: .63 to .80), respectively, had lower odds of reporting a physical health challenge. Physical component summary (mean diff: 4.1, 95%CI 2.55 to 5.65, Cohen's d: .41) and physical functioning (mean diff: 4.7, 95%CI 1.45 to 7.90, Cohen's d: .22) scores on the SF-36 differed between groups. Limitations in vigorous activities from the SF-36 was the only item that met the 10% threshold, with 78% of participants who nominated a physical health challenge reporting difficulties with vigorous activities versus 63.2% among those who did not nominate a physical health challenge. Other items of potential discrimination included limitations in moderate activities (36.5% reported limitations in moderate activities versus 26.7% among those who did not nominate a physical health challenge), lifting or carrying groceries (33.6% versus 24% among those who did not nominate a physical health challenge), and climbing several flights of stairs (52.6% in comparison with 43.9% among those who did not nominate a physical health challenge). EQ-5D scores differed between groups (mean diff: .043, 95%CI .018 to .067, Cohen's d: .26).

Conclusions: The PGI may be a useful tool for identifying the unique physical challenges and rehabilitation needs of people living with HIV. The items participants nominated on the PGI reflected higher level physical functioning items on the SF-36, indicating that difficulties with vigorous and moderate activities, lifting and carrying groceries, and climbing several flights of stairs may be useful items for identifying those in need of rehabilitation.

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The Relationship Between Social Determinants of Health and Physical and Mental Function Among People With HIV Aged 50 and Over Enrolled in a Multi-Site Housing and Employment Intervention Project

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Background: Compared to the general population, people with HIV (PWH) are more likely to live in a context of social determinants that negatively influence health such as unstable of housing, inadequate income, or food. At the same time, because of improvements in clinical treatment, they are also living longer and require sustained support to overcome these disparities, which can help to assure mental and physical function into later life. We use data from a large federal initiative evaluating innovative housing and employment interventions for people with HIV to assess the relationship between social determinants of health (SDOH) and physical and mental function among PWH aged 50 and older participating in the initiative.

Material and Methods: We report patient demographics including age, race/ethnicity, gender, sexual orientation, and education attained for the sample. Self-reported measures of housing status, employment, food security, financial resources and unmet needs related to all social determinants were compiled into SDOH scores assessed at study entry and at 12-months post-enrollment. We assessed mental and physical function with 12 items each, scored and processed to reflect mental and physical composite scores that are standardized to have a mean of 50 and a standard deviation of 10 in the general adult population. We used generalized estimating

equations to explore the relationship between changes in SDOH and physical and mental health function, controlling for study site, demographics, years living with HIV, and client-level repeated measures.

Results: Participants (n=284) were on average 55 years old (min = 50, max = 73). Most participants were African American (49.8%) or Latino (29.5%). Most identified as male (80%). About half identified as heterosexual (53.1%). Participants had been, on average, living with known HIV for 9 years. Most had a high school diploma or more education (63%). In the analytic sample of participants who had both baseline and follow-up data (n=188), SDOH scores decreased after 12 months of study participation (-4.4, scale set at median 50 at 12-months, p=0.003), indicating fewer barriers. Changes in SDOH were mediated by mental health function, which improved as SDOH barriers decreased (p=0.03). Physical function was unrelated to changes in SDOH.

Conclusions: Interventions for older adults with HIV should account for the social context in which they live and work, and, in particular, how they experience SDOH, because this context may influence individual-level factors associated with function, particularly mental health. Future studies should be conducted to assess how SDOH and mental health influence care seeking among those aging with HIV because they may suggest targeted interventions for this group.

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Stigma and Social Isolation Impacts on Depression and Anxiety among Persons 50 and Older Living with HIV

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Background: Persons ages 50 and older living with HIV can have extensive health issues and may experience loneliness, poor social support, depression, and anxiety. In one study, approximately 70% of older adults living with HIV experience HIV-related stigma and 37% experience social isolation. Impacts of stigma and social isolation among those living with HIV may lead to poorer health-related quality of life, higher depressive symptoms, anxiety, isolation, functional impairment, and substance use. The goal of this project was to assess these associations in an urban, primarily Black/African American cohort of persons ages 50+ with HIV.

Methods: The Strengthening Therapeutic Resources in Older adults aging with HIV (STRONG) is an ongoing study incorporating gerontological assessment measures into an urban HIV clinic. Participants completed the GAD-7 and PHQ-9 surveys assessing anxiety and depression. Participants were asked, "Have you experienced stigma as a long-term survivor?" and "Do you feel isolated as a long-term survivor?" to gather information on stigma and social isolation.

Results: Of 184 participants, 95% identified as Black, 58% were high school graduates/earned a GED, and 55% were male. Mean age was 59.1 years old (SD=5.5). Moderate-to-severe depressive symptoms (PHQ-9>14) were reported by 50%; 41% had moderate-to-severe anxiety (GAD-7>10), and 46% felt lonely somewhat or very often. Most (90%) reported supportive responses when disclosing their status. Many participants (35%) reported stigma and 26% reported social isolation. Low education, non-black race, and loneliness were all associated with stigma ($p<0.05$ by Fisher's Exact test). Similarly, associations between social isolation with less education, non-black race, and feeling lonely were found ($p<0.05$ via Fisher's Exact Test). There was no association between stigma or social isolation with sex (p=0.33, p=0.46). Those who reported stigma were younger (mean=58.2, 95%CI= 56.9-59.5) than no stigma (mean=60.0, 95%CI:59.1-61.2). Similarly, those who felt socially isolated were younger mean=58.9, 95%CI=57.3-60.4) than those not isolated (mean=59.7, CI 95%=58.7-60.7). Overall, 27.8% of the participants who reported social isolation also reported

moderate-to-severe depression and 66.7% reported moderate-to-severe anxiety compared to those without social isolation (17.3% depression, 16.0% anxiety). Among those who reported stigma, 36.7% had moderate-to-severe depressive symptoms and 50.0% had moderate-to-severe anxiety compared to those without (50.0% depression, 29.2% anxiety). Among those who reported stigma, 47.4% reported social isolation.

Conclusion: Stigma and social isolation were common in this sample of urban, black persons age 50+ living with HIV. Those experiencing stigma and social isolation were younger, which may be impacted by how long they have lived with HIV. There was a strong association between stigma and social isolation, and both were associated with having more severe anxiety and depression symptoms. These findings suggest that exploring methods to reduce HIV-related stigma and social isolation could improve psychosocial factors for older adults living with HIV.

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Loneliness Among Older Gay and Bisexual Black Men and White Men Living With HIV

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Background: Loneliness is a concern among older people living with HIV (PLWH), especially given the ongoing COVID-19 pandemic. Currently, there is little research characterizing loneliness among PLWH in the LGBTQ community. To investigate how HIV impacts older (age 50+) PLWH in the US, a study called Aging with Dignity, Health, Optimism and Community (ADHOC) was launched. This study uses ADHOC data to compare loneliness between older Black and White men living with HIV who identify as gay or bisexual.

Methods: A cross-sectional analysis was performed. Loneliness was assessed using the Three-item Loneliness Scale, with higher scores indicating greater loneliness. Student's t-test compared loneliness between Black and White men. Multivariate linear regression was employed to explore the impact of race on loneliness while controlling for age, education, depression, anxiety, number of co-morbid conditions, being single, and income.

Results: Of 716 participants, the average age was 60 (SD 6.1) years, 89% (N=634) were White and 11% (N=82) were Black, and 95% identified as gay. In bivariate analyses, Black participants were less lonely than White participants (5.1 (1.8) vs 5.7 (2.1), P=.02). After multivariate adjustment, Black participants remained less lonely than White participants (β = -0.72, P<0.01, Adjusted R2=0.39; P<.01).

Conclusion: Black gay and bisexual men experienced less loneliness than gay and bisexual White men. Understanding the causes of these differences will allow for more effective design of support programs for older PLWH who identify as gay or bisexual, by addressing the unique needs of Black and White individuals.

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"Is It HIV or Just Old Age?" Uncertainties of Ageing With HIV

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Background: In Australia, around half of all people living with HIV (PLHIV) are now over 50, with many representing the first generation of people diagnosed in the pre-HAART (highly active antiretroviral treatment) era. Understanding the psychosocial experiences of ageing for PLHIV is of critical concern to ensure HIV communities, service providers and policy makers are well equipped to address these changing needs.

Methods: Living Positive in Queensland (LPQ), is a participatory qualitative longitudinal study, co-designed with community to examine

ageing and social isolation among people living long-term with HIV. LPQ, one of the largest research projects of its kind, commenced in data collection in 2013 with 73 participants. The study has involved four in-depth interviews, the most recent was conducted in 2020 during the first wave of COVID-19 in Australia. Inductive thematic analysis was used to draw themes from over 250 interviews. This presentation discusses participants' perceptions and experiences of ageing.

Results: Participants described uncertainty about ageing, expressing ambivalence in the face of debates surrounding adverse HIV ageing discourses and unknown futures. Alongside uncertainties about health and increasing comorbidities, participants described uncertainty about the social determinants of 'successful ageing'. Experiences of social isolation, loneliness and limited social support were discussed by many participants who described the loss of networks at critical points across the life course.
Older participants, particularly those from the Pre-HAART era, experienced cumulative disadvantage related to disrupted employment trajectories, limited resources, long-term welfare access and limited social support arising from service cuts and the corresponding fracturing of communities. Experiences of precarity were magnified during COVID-19 for those who were the most socially marginalised. During COVID-19, some older participants with complex physical and psychosocial needs had disconnected from health and social care.These issues continue to generate concerns about living and ageing in disadvantage.
Care for older people was often considered synonymous with residential aged care. Having experienced stigma and discrimination in healthcare settings, many were concerned about discrimination in aged-care settings and worried the aged-care sector would not respond to the needs of PLHIV. Fourth phase interviews included conversations with a small number of people who had progressed to aged care.

Conclusion: Ageing with HIV is biosocial, lived within diverse intersections of embodied experiences of HIV, generational, social, and locational contexts. 'Successful ageing', as it is currently portrayed in the broader ageing literature must move beyond individual actions and acknowledge the role of social determinants of health. HIV and ageing literacy; quality and culturally competent aged-care services; and coordination and partnership between the aged-care sector and HIV communities are urgently needed.
The presentation will consider how policy and program responses must integrate these elements in the development of services to move beyond the biomedical to address the social aspects of health and ageing for PLHIV.

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Physical Activity as a Means of Improving Quality of Life in Individuals with Chronic Pain

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Background: Chronic pain poses a significant burden on the healthcare system and is notoriously difficult to treat. The neurogenesis of pain and pathophysiology of chronic pain share inflammatory pathways, and individuals with chronic pain are more likely to experience mental health disorders. Understanding the shared biology and psychology of chronic pain and mental health disorders can elucidate commonalities that may serve as treatment targets, especially when analyzing the effects of exercise on these pathways. The purpose of this literature review is to explore the shared molecular and psychological mechanisms underlying chronic pain and mental health disorders by analyzing 1) classification of chronic pain types, 2) classification of chronic pain perception, 3) molecular markers correlated with pain onset, 4) molecular markers present in chronic pain syndromes, and 5) the relationship between chronic pain and mental health. The influence of exercise on each of these factors is analyzed to propose the use of physical activity as a means of improving quality of life in individuals experiencing chronic pain.

Methods: This literature review used PubMed as its primary database. Search terms included "chronic pain classification," "chronic pain

biology," "chronic pain etiology," "chronic pain cytokine," "chronic pain inflammation," "chronic pain endocannabinoid," "chronic pain exercise," "chronic pain mental health," "chronic pain quality of life," "exercise mental health," "exercise inflammation," and "exercise depression." Literature reviews, systematic reviews, randomized controlled trials, retrospective cohort studies, and basic science articles were included. Research design, primary outcomes, qualitative and qualitative data were extracted and analyzed qualitatively.

Results: Proinflammatory cytokines IL-1β, IL-6, and TNF-α, were involved in the development, perpetuation, and hypersensitization of chronic pain. Chronic pain had a strong association with mental health disorders like anxiety and depression, which can perpetuate pain perception and negatively impact coping mechanisms. Pain increase was a predictor of increase in depression, and, vice versa, change in depression severity predicted a proportional change in pain severity; this is potentially due to shared neural pathways and the shared role of norepinephrine and serotonin in pain perception and depression. The bidirectional relationship between chronic pain and mental health was seen in medical management, particularly in the use of tricyclic antidepressants and serotonin norepinephrine reuptake inhibitors, which may be prescribed for chronic pain in addition to mood disorders as they have been shown to decrease levels of proinflammatory, pain pathogenic cytokines IL-1β, IL-6, and TNF-α. Treatment of anxiety and depression was shown to reduce opioid consumption in patients with chronic pain, supporting a bidirectional relationship between pain and mental health. Physical activity reduced production of proinflammatory IL-1β, IL-6, and TNF-α and increased production of the anti-inflammatory IL-10 across a multitude of chronic pain conditions, suggesting that exercise could be a non-opioid intervention that can attenuate pain onset, perception, and hypersensitization. Varying forms of physical activity- including aerobic exercise, strength and resistance training, and yoga- were shown to improve pain, function, mood, and fatigue while decreasing depression and anxiety, thus improving quality of life.

Conclusion: Exercise is unique in its ability to positively impact both the molecular and psychological aspects of chronic pain. Its role in decreasing inflammation as well as improving mental health make it an excellent option for improving the quality of life in individuals experiencing chronic pain. Physicians should work with their patients to develop a safe, patient-centered exercise plan to manage chronic pain.

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Assessing the Measurement Properties of the Episodic Disability Questionnaire (EDQ) With Adults Aging With HIV in Canada, the United States, Ireland and the United Kingdom

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Purpose: Measuring disability is important for understanding the health related challenges experienced among adults aging with HIV and the impact of interventions. The Episodic Disability Questionnaire (EDQ) is a patient-reported outcome measure that assesses the presence, severity and episodic nature of disability across six domains: physical, cognitive, mental-emotional health challenges, difficulties with day-to-day activities, uncertainty about future health, and challenges to social inclusion. We assessed the measurement properties of the EDQ among adults aging with HIV in Canada, the United States (US), Ireland, and United Kingdom (UK).

Methods: We conducted a cross-sectional measurement study. We recruited participants from five clinical sites in Canada (Casey House), Ireland (St. James's Hospital), US (University of Colorado), and UK (Chelsea and Westminster NHS Foundation Trust, Brighton and Sussex University Hospital). We electronically administered the EDQ followed by three reference measures (World Health Organization Disability Assessment Schedule 2.0, Patient Health Questionnaire-8; MOS-Social Support Scale) and a demographic questionnaire. We administered the EDQ again 1 week later. We compared the following statistics with pre-determined acceptability thresholds: internal consistency reliability (Cronbach's alpha; >0.8 acceptable) and test-retest reliability (Intra Class Correlation Coefficient (ICC); >0.8 acceptable). We estimated required change in EDQ domain scores to be 95% certain that a change was not due to measurement error (Minimum Detectable Change (MDC) 95%). We evaluated construct validity by assessing 80 hypotheses of relationships between EDQ scores and scores on the three reference measures (>75% hypotheses confirmed indicated validity).

Results: 359 participants completed the baseline questionnaires at time point 1; 321 (89%) completed the second EDQ. The median age of participants was 51 years (25,75th percentile: 42, 59), most (83%) were men and white (81%), and the median number of concurrent health conditions in addition to HIV was 4. Cronbach's alpha ranged from 0.84 (social domain) to 0.91 (day-to-day activities domain) for the EDQ severity scale, and 0.72 (uncertainty domain) to 0.88 (day-to-day activities domain) for the EDQ presence scale, and 0.87 (physical, cognitive, mental-emotional domains) to 0.89 (uncertainty domain) for the EDQ episodic scale. ICCs ranged from 0.80 (physical, uncertainty domains) to 0.89 (day-to-day activities domain) for the EDQ severity scale and from 0.70 (uncertainty domain) to 0.85 (day-to-day activities domain) for the EDQ presence scale. MDC 95% ranged from 18 (day-to-day activities domain) to 24 (mental-emotional, uncertainty domain) in the severity scale, and MDC 95% ranged from 35 (physical domain) to 52 (cognitive domain) in the presence scale. Sixty-five of 80 (81%) construct validity hypotheses were confirmed.

Discussion: The EDQ possessed internal consistency reliability, construct validity, and test-retest reliability for EDQ severity scale domains, with limited precision when administered electronically with adults aging with HIV across five clinical settings in four countries. The EDQ may be used to measure presence, severity and episodic nature of disability among adults aging with HIV; however more research is required before the EDQ can be recommended as a method to measure change in disability.

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Over 50 and In Charge

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Background: People ageing with HIV face significant health concerns, such as high rates of depression and isolation, the comorbidities associated with early ageing, and the challenges of self-advocacy in the aged care system. Living Positive Victoria's Taking Charge project aims to provide opportunities for participants to have more control over their lives and address these issues.

Material and Methods: In 2017, Living Positive Victoria partnered with Thorne Harbour Health to deliver the Taking Charge Project.

One activity is the Positive Self-Management Program (PSMP). This Stanford University Chronic Disease Self-Management Program model supports the physical, mental health and well being of people with chronic conditions by providing skills and knowledge through peer education. The six-week HIV-focused program consisted of weekly 2.5 hour group sessions run twice a year both in person and online, covering areas such as HIV monitoring; making action plans; communicating effectively; nutrition/exercise; and developing support systems.

The other activity, our monthly Peer Support Network meetings also provided regular opportunities to connect and gain up-to-date information on issues such as treatments; legal; residential and supported aged care as

well as HIV & Ageing related conference updates.

For the self management program, The Connor-Davidson Resilience Scale was used to assess impact on participants' psychological resilience and quality of life measures relating to living with HIV (the PozQOL scale) was also used.. Pre- and post- workshop surveys were used to measure the impact of participation on engagement with peer support services, community and peer networks, healthcare systems and service providers.

Rating scales and feedback forms were also used to capture peer facilitator's observations and insights on peer interaction and engagement and the key issues that arose from discussions during workshops and support network meetings.

Results: The pre and post surveys showed a marginal but definite improvement in self-confidence, social connection, engagement with health professionals and resilience. The participants' comments also reflect the increased confidence gained. "Was great to share and receive others' opinions [and] ideas in a way that was open and non-judgemental." "Never give up. There is life after 50 even if you are HIV." In addition to their personal growth, the peer facilitators observed that many PSMP participants went on to engage with other peer-led programs offered by the two lead organisations.

Conclusions: The Taking Charge project with it's two activities is a highly participatory peer intervention, where mutual support during participation and the outcomes have been shown to build participants' confidence to self-manage their health and maintain active and fulfilling lives.

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Development of a Prototype for a Bilingual Patient-Reported Outcome Measure of the Important Health Aspects of Quality of Life in People Living With HIV

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Aims: A challenge with current measures of health-related quality of life (HRQL), generic or disease-specific, is that they are of the profile type, in that there are multiple domains each with multiple items leading to multiple scores. These are often burdensome to complete, they are rarely used clinically, and multiple scores complicates research application. Creating an index requires a weighting system for the domains. Increasingly, HRQL measures that produce one value across multiple dimensions are being developed. The preferences patients have for each health state are then used to weight the dimensions so that one value is produced. The aim of this project was to develop a short, HIV-specific, HRQL measure with a scoring system based on patient preferences for the different dimensions, the Preference Based HIV Index (PB-HIV).

Methods: The data from the Canadian Positive Brain Health Now (BHN) cohort (n=854 participants with HIV; mean age 53 years) that used the Wilson-Cleary model for the measurement framework included both standard format and individualized measures. The latter identified the important areas of life that are affected by HIV and items from the standard format measures were mapped to these areas and formed the domains. Rasch analysis was used to identify the best performing item to represent each dimension. To develop a prototype scoring system, each dimension was then regressed on self-rated health (scored 0 to 100) and the regression parameters were used as weights. To customize the dimensions, cognitive debriefing

and simultaneous translation in English and French was conducted with patients and healthcare professionals.

Results: Seven independent (item-to-item correlations: 0.16 to 0.55) dimensions with three declarative statements ordered as response options, formed the PB-HIV Index (pain, fatigue, memory/concentration, sleep, body image, depression, motivation). Regression parameters from a multivariable model yielded a measure with a scoring range from 0 (worst health) to 100 (perfect health).

Conclusions: Preference-based measures are optimal when cost- or comparative-effectiveness is of importance as the total score reflects gains in some dimensions balanced against losses in others. PB-HIV Index is the first HIV specific preference-based measure.

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Short-Form HIV Disability Questionnaire Sensibility, Utility and Considerations for Implementation in Community-Based Settings: A Mixed Methods Study

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Purpose: The Short-Form HIV Disability Questionnaire (SF-HDQ) is a patient-reported outcome measure that assesses the presence, severity and episodic nature of disability across six domains: physical, cognitive, mental-emotional health challenges, difficulties with day-to-day activities, uncertainty about future health, and challenges to social inclusion. Our aim was to assess the sensibility, utility and considerations for implementation of the Short-Form HIV Disability Questionnaire (SF-HDQ) in community-based settings to measure the presence, severity and episodic nature of health challenges experienced among adults living with HIV.

Methods: We conducted a mixed methods study with adults living with HIV and community health providers in seven community sites across three provinces in Canada (AIDS Vancouver; Dr. Peter Centre, Vancouver; Toronto PWA Foundation; AIDS Committee of Toronto; Alliance for South Asian AIDS Prevention, Toronto; AIDS Community Care Montreal; and St. Michael's Hospital Family Health Practice, Toronto). We electronically administered the SF-HDQ followed by a sensibility questionnaire (face and content validity, ease of usage, format) and conducted semi-structured interviews (exploring potential utility and implementation of the SF-HDQ in community settings). The SF-HDQ was sensible if median scores on the sensibility questionnaire were ≥5 out of 7 for adults living with HIV and ≥4 out of 7 for community health providers for at least 80% of the items. Qualitative interview data were analyzed using a team-based directed content analysis.

Results: Median sensibility scores were ≥5 for adults living with HIV (n=44) for 95% of items (18/19 items) and ≥4 for community health providers (n=10) for 100% of items. Interview data indicated that the SF-HDQ is comprehensive, represented the health-related challenges (disability) living with HIV and other health conditions; captured the episodic nature of disability; and was easy to complete. Community utility of the SF-HDQ included i) facilitating communication and fostering engagement with community; ii)

taking a 'snap shot' of disability and tracking changes in disability over time; iii) guiding referrals to services and supports; and iv) informing community organization programs and planning. Considerations for implementation included the importance of person-centered approaches for tailoring the mode of administration (familiarity and comfort with technology, literacy, other health challenges), offering flexibility for administration (format, location, timing, frequency, persons administering, level of facilitation and supports available), burden of administration (time, conundrum of identifying health challenges with limited resources or supports to address them, logistical issues of community setting space, accessibility and privacy), the importance of buy-in from the community to utilize the tool, and communicating scores based on personal preferences among persons living with HIV and community providers.

Discussion: The SF-HDQ possesses sensibility and utility for use in community-based settings with adults living with HIV and community health providers in Canada. Future research includes assessing the measurement properties of the tool in community settings.