Abstracts presented at the 21st International Workshop on Co-morbidities and Adverse Drug Reactions in HIV
Basel, Switzerland, 5–6 November 2019
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**Pulmonary disease**

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ORAL PRESENTATIONS
Patterns of inflammation and comorbidity in human immunodeficiency virus (HIV) infection: a clustering analysis from the CARDAMONE study

S Zebachi¹, S Hüe¹,4, L Boyer¹,5, S Gallien²,4, M Surenaud²,4, J-L Lopez Zaragoza²,4, J-D Lelièvre²,4, E Audureau¹

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Objectives: Since the advent of antiretroviral therapy (ART), the occurrence of AIDS-related events has steadily decreased in HIV-infected individuals. Associated with increasing life expectancy, a rise in the incidence of comorbidities such as cardiovascular diseases and metabolic complications has been reported in this population. While the role of key inflammatory markers such as interleukin-6 (IL-6), IL1-β, tumor necrosis factor α (TNF-α) and sST2 has been discussed, less is known regarding their combinations and their complex interactions with age and other risk factors such as smoking. Therefore, we aim to better characterize and understand the associations between chronic inflammation and the occurrence of comorbidities in people living with HIV, here, through machine learning methods. Methods: Data were drawn from the CARDAMONE study, including 241 HIV-1-infected participants under ART with comprehensive clinical, biological and functional phenotyping. With a view to identify specific patients’ profiles with similar inflammation patterns and their association with comorbidity occurrence, unsupervised clustering analyses were performed using Self-Organizing Map (SOM) artificial neural network approach, allowing two-dimensional mapping of patients and grouping those with similar inflammation features in clusters. Other clinic-biological characteristics and comorbidities prevalences were analysed as illustrative features. Results: 4 clusters were identified: (1) gathered the heaviest smokers developing an elevated global inflammatory reaction (MCP-1, hsCRP, IL-6, IL1-β, TNF-α, sST2), (2) comprised younger subjects, mainly women, with globally low inflammatory response, (3) included younger subjects with a moderate and highly specific inflammatory response (sST2, hsCRP) despite the lowest smoking frequency but with the lowest CD4 and CD8 values, (4) grouped the oldest patients with a moderate inflammatory response. See Figure 1. Conclusions: Clustering analysis identified contrasted inflammation profiles with distinct associations with age, smoking and HIV-related end points. Our results confirm what has already been shown in the literature. We find here a cluster composed of smokers with a high degree of inflammation and a cluster of older people developing a different type of inflammation. The novelty here is the identification of a cluster of relatively young subjects, non-smokers, but developing a particular inflammatory profile. Our findings support the interest of unsupervised machine-learning approaches for improving our knowledge of the complex role of inflammation in HIV-infected individuals.
Colonic microbiota exhibits disparate associations with HIV infection and sexual practices

Objective: Effective antiretroviral therapy (ART) has prolonged survival and shifted the morbidity spectrum for people living with HIV (PLWH) from AIDS-associated opportunistic infections and malignancies towards age-associated non-communicable comorbidities (AANCCs), with these being more prevalent in PLWH compared with age-matched HIV-uninfected individuals. A key contributor to the current disease spectrum includes HIV-associated inflammation and immune activation, the aetiology of which in PLWH remains incompletely defined. Gut microbial dysbiosis is thought to be a potential important contributor, but data thus far are conflicting regarding the role that lifestyle factors, including sexual orientation and behaviour, and HIV-infection itself have on gut microbial dysbiosis.

Methods: Using 16S rRNA gene sequencing, we profiled the microbiota from fecal samples of PLWH with suppressed viraemia on ART and HIV-uninfected controls participating in the AGEhIV Cohort Study. PLWH were selected to include 40 men having sex with men (MSM), 20 men having sex with women (MSW) and 20 females (F) matched 1:1 by age, sex, sexual orientation, BMI, birth country and smoking status with HIV-uninfected controls.

Results: HIV-infection was associated with alterations in the gut microbiota including an enrichment in Enterobacteriaceae and Desulfovibrionaceae members and a depletion of short chain fatty acids-producing bacteria such as Lachnospiraceae and Ruminococcaceae. Furthermore, comparisons between MSM and non-MSM males revealed a unique MSM-associated microbiome signature characterized by an enrichment particularly in Prevotellaceae members (Figure 1), which was independent of HIV-infection. Finally, practicing receptive anal intercourse, regardless of condom use, was linked to a specific bacterial community variance independently of sex, which may explain the Prevotella-rich microbiome in MSM.

Conclusions: Our data provide unique evidence that colonic microbiota exhibit disparate associations with HIV-infection and sexual practices.
ABSTRACT 003
Antiviral Therapy 2019; 24 Suppl 1:A5

Higher anti-CMV IgG concentrations are not associated with longitudinal brain injury in virally suppressed people with HIV

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Objectives: People with HIV (PWH) have a higher CMV seroprevalence than HIV-negative individuals. Higher CMV IgG concentrations have been associated with poorer cognitive function in cross-sectional studies of PWH. We compared the longitudinal relationships between CMV, cognitive function and neuroimaging biomarkers in PWH and demographically-matched HIV-negative controls.

Methods: CMV-seropositive, virally-suppressed PWH and HIV-negative controls from the COBRA study were included. The relationship between anti-CMV IgG and high avidity anti-CMV IgG titres with cognitive function (standardized T-scores measured with a six-domain battery) and MRI biomarkers (volumetric, diffusion and a machine-learning derived prediction of apparent ‘brain age’), measured at baseline and after 2 years, were determined using rank regression adjusted for potential confounders.

Results: 130 PWH and 61 HIV-negative controls were included. Across the whole cohort cross-sectionally, higher anti-CMV IgG titres were associated with poorer global cognitive function and in the domains of processing speed, executive and motor function. This was only observed in PWH (largest effect size motor function: rho adj = -0.25 [-0.41, -0.09]; P < 0.01) although there were no statistically significant interactions between HIV status and anti-CMV IgG titres.

Relationships between anti-CMV IgG titres and neuroimaging biomarkers were generally weak across the cohort (rho adj < 0.15 for all; Table 1) aside from an association with increased brain-predicted age in PWH (rho adj = 0.24 [0.08, 0.40]; P < 0.01; HIV-status interaction P = 0.02). Relationships between baseline anti-CMV IgG titres, and longitudinal cognitive function and neuroimaging biomarkers were weak (rho adj < 0.15 for all; Table 1) with some associations being in the opposite direction.

Table 1. (Abstract 003)
to those found cross-sectionally for executive function and brain-PAD.

**Conclusions:** Higher anti-CMV IgG titres were not associated with short-term progressive brain injury in virally suppressed PWH. These findings and the lack of associations in HIV-negative controls suggest that the cross-sectional associations in PWH may represent type 1 errors or that CMV-associated brain injury is a static phenomenon in virally suppressed PWH.
ABSTRACT O04

Antiviral Therapy 2019; 24 Suppl 1:A7

Bone mineral density changes in young African women on tenofovir disoproxil fumarate antiretroviral therapy and non-hormonal contraception

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Aim: There are limited prospective data on bone mineral density (BMD) changes in HIV-infected young women in low-income countries initiating tenofovir disoproxil fumarate (TDF) containing antiretroviral therapy (ART). The NIH funded BONE: CARE study (R01AI118332) enrolled HIV infected depot medroxyprogesterone acetate (DMPA), or non-hormonal contraceptive users initiating TDF-based ART, as well as an HIV, DMPA unexposed control group. We compare longitudinal data on BMD changes 2 years post TDF initiation among infected non-hormonal users compared with uninfected controls.

Methods: Women were recruited from HIV care centres and general health facilities in and around Kampala, Uganda and classified into 4 groups: A) HIV+/DMPA+/TDF+, B) HIV+/DMPA+/TDF-, C) HIV+/DMPA-/TDF+ and D) HIV-/DMPA-/TDF-. All HIV-infected women were ART-naïve at baseline. BMD assessments of lumbar spine (LS), total hip (TH) and femoral neck (FN) were conducted using dual energy X-ray absorptiometry at semi-annual intervals. We used repeated measures analyses to compare the rate of change, calculated as the percent change in BMD per year between HIV-infected and uninfected women during the initial 2 years of ART initiation, adjusting for age, parity, education and baseline BMD.

Results: Between March 2015 and October 2017, we screened 549 women. Of the 529 women enrolled, 176 were non-hormonal contraceptive users; 109 HIV-infected and 69 uninfected. The median age was 25 (22–30) years. There was greater adjusted BMD percent decline among HIV-infected women than controls at the LS and NF compared with HIV-uninfected women (P=0.01 and 0.004 respectively) but not at the TH (P=0.716), see Table 1. Prior use of DMPA ≥2 years pre-ART initiation was not significantly associated with greater BMD loss among infected women.

Conclusions: HIV-infected non-hormonal users experienced significantly greater BMD loss at the LS and NF. Data from DMPA users in this cohort will establish the additional effect of DMPA use on BMD among women on TDF.

Table 1. (Abstract O04)

<table>
<thead>
<tr>
<th>Body site</th>
<th>Crude % difference in mean BMD change (95% CI)</th>
<th>P-value</th>
<th>Adjusted % difference in mean BMD change (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lumbar spine</td>
<td>-0.75 (-1.25 to -0.27)</td>
<td>0.002</td>
<td>-0.90 (-1.46 to -0.36)</td>
<td>0.001</td>
</tr>
<tr>
<td>Total hip</td>
<td>0.086 (-0.35 to 0.53)</td>
<td>0.703</td>
<td>-0.09 (-0.58 to 0.40)</td>
<td>0.716</td>
</tr>
<tr>
<td>Femur neck</td>
<td>-0.73 (-1.38 to -0.09)</td>
<td>0.026</td>
<td>-1.04 (-1.75 to -0.33)</td>
<td>0.004</td>
</tr>
</tbody>
</table>

Adjusted for age, BMI, education and baseline BMD
ABSTRACT 005

Antiviral Therapy 2019; 24 Suppl 1:A8

Association of current estradiol use with carotid intimal media thickness among transgender women: a cross-sectional study

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Background: Epidemiological studies suggest that transgender population has higher burden of cardiovascular (CV) risk factors and CV disease. It is uncertain whether the use of feminizing hormone such as estradiol (E2) or ethinylestradiol (EE) affects their risk. We aimed to assess CV risk and investigate the relationship between current use of E2 or EE and carotid intima-media thickness (cIMT) in transgender women (transwomen).

Methods: Cross-sectional evaluations of transwomen in the Transcendendo cohort in Rio de Janeiro, Brazil with a valid cIMT at baseline visit, from August 2015 to February 2017. cIMT was measured by ultrasonography, following the Mannheim protocol. Increased cIMT was defined as a measurement above the 75th percentile. We tested the association of E2, EE or both with cIMT. Covariables included traditional cardiovascular risk factors, HIV status, drug use and history of feminizing procedures. Framingham and ASCVD risk scores were calculated and compared with cIMT. Adjusted logistic regression models were fitted and odds ratios (OR) were used to assess the association of current use of the three hormone categories with cIMT.

Results: 308 transwomen were included; median age was 31 years (interquartile range [IQR]=25–38), 53.8% had HIV infection. Among current hormone users (40.8%), the most frequent were estradiol (26.53%), ethinylestradiol (5.15) or a combination of both (9.18%). Median cIMT was 0.57 mm (IQR=0.52–0.64). In participants with increased cIMT, 11 (3.97%) and 24 (8.66%) were classified as high risk by the Framingham equation and ASCVD, respectively. In the final adjusted model, age (OR=1.14, 95% CI=1.08, 1.20), systolic blood pressure (OR=1.05, 95% CI=1.01, 1.09) and estradiol use (OR=0.34, 95% CI=0.11, 0.92) were associated with cIMT.

Conclusions: A negative association between cIMT and current estradiol use was found in transgender women. The ASCVD equation identified more participants as high risk among those with increased cIMT. While conflicting results exist in the literature about estrogen replacement therapy in women, these data suggest cardioprotective effects of estradiol use without medical supervision in younger transwomen. Follow-up studies are needed to confirm its safety and it might be considered as a choice of hormone for transwomen.
ABSTRACT O06

Antiviral Therapy 2019; 24 Suppl 1:A9

An analysis of HIV and comorbidity profiles for adults accessing health care in Khayelitsha, South Africa

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Aim: To explore the HIV comorbidities profile of patients accessing public health care at Khayelitsha.

Methods: A longitudinal dataset for all individuals who accessed public health facilities at Khayelitsha from January 2016 – December 2017 was obtained from the Western Cape Provincial Health Data Centre. Descriptive and inferential statistics explored demographics, HIV cases and comorbidities, and pairwise associations between comorbidities using Pearson’s product-moment correlation.

Results: Of 181,620 individuals (median age 37 years, IQR: 30–48) seeking health, 131,933 (72.6%) were females and 49,521 (27.4%) were males. Of 88,316 people living with HIV (PLHIV), 63,016 (71.4%) were female and 25,219 (28.6%) male. Males seeking health care were 1.15 (CI= 1.11, 1.16) times more likely to have HIV than females. Median age (IQR) of HIV ascertainment differed in females 35 (30–43) and males 40 (34–47), P<0.001. Tuberculosis (31.4%), hypertension (14%), mental health conditions (5.3%), diabetes (4.1%), cancers (1.81%) and chronic kidney disease (CKD; 1.7%) were the top 6 comorbidities identified, with correlations between hypertension and diabetes (r=0.24), hypertension and CKD (r=0.13) and diabetes and CKD (r=0.13); all P<0.001 in PLHIV. Whilst comorbidity clustering varied with age, median ages of ascertainment of comorbidities were younger in PLHIV than HIV-negative individuals except for tuberculosis (Table 1). Significant differences were also found between median ages of ascertainment for comorbidities in females and males with HIV.

Discussion: As HIV-related mortalities decline and life expectancy increases, PLHIV face increasing burden of chronic comorbidities. This burden, in addition to existing tuberculosis, in PLHIV seeking care in South Africa is rising. Differences between female and male demographics also reflect to some extent contraceptive/maternal care access by women in good health.

Conclusions: The emerging burden of chronic HIV comorbidities requires in-depth studies to inform adequate planning for all-encompassing health-care delivery.

Table 1. (Abstract O06)
ABSTRACT 007

*Antiviral Therapy 2019; 24 Suppl 1:A10*

Integrase inhibitors dolutegravir and raltegravir exert proadipogenic and profibrotic effects and induce insulin resistance in adipose tissue and adipocytes

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Objectives: There is growing evidence that integrase inhibitors (INSTI) dolutegravir and raltegravir promote peripheral and central adipose tissue/weight gain in HIV-infected individuals, but the mechanisms involved remain unknown. We aimed to assess the effect of these molecules on adipose tissue morphology, function and metabolism.

Methods: Morphology and function of subcutaneous (SCAT) and visceral adipose tissue (VAT) were studied in: HIV-infected patients from the ObeVIH study, at the time of bariatric surgery (BMI 41.8 kg/m²): 14 patients received INSTI (10 dolutegravir, 2 raltegravir, 2 elvitegravir) and 5 an INSTI-sparing regimen; and uninfected cynomolgus macaques treated or not 15 days with dolutegravir/tenofovir/emtricitabine. Human adipose stem cells (ASCs) were chronically treated with dolutegravir or raltegravir before or during adipogenesis. Adipogenic capacities, insulin response and extracellular matrix component expression were analysed.

Results: SCAT from the ObeVIH patients presented peri-lobular and peri-adipocyte fibrosis in most samples. Conversely, VAT of INSTI-treated patient presented a higher level of peri-adipocyte fibrosis than that of non-INSTI-treated patients. Dolutegravir-treated macaques presented a higher level of fibrosis and an increased adipocyte size in both SCAT and VAT, when compared with untreated macaques. Adipogenic marker expression was increased in SCAT and VAT, whereas adiponectin expression was decreased in SCAT, suggesting that, despite a pro-adipogenic effect, dolutegravir may favour insulin resistance.

Conclusions: We demonstrate here for the first time, by using in vivo and in vitro complementary models, that INSTI exert a direct impact on adipose tissue adipogenesis, fibrosis and insulin resistance. These results, which reveal the adipose tissue toxicity of dolutegravir and raltegravir, are important to explain fat modifications reported in INSTI-treated HIV-infected patients.
ABSTRACT O08

Antiviral Therapy 2019; 24 Suppl 1:A11

Dolutegravir-based regimens are associated with weight gain over 2 years following ART-initiation in ART-naive people living with HIV (PLWH)

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Objectives: Previous studies have suggested that PLWH who initiate integrase-inhibitor-based regimens may gain more weight than those who initiate other antiretroviral therapy (ART). These studies have often examined classes not individual agents, been small, combined ART-experienced and naive PLWH, and did not address key potential confounders such as regimen backbone. We evaluated weight change among PLWH initiating ART in the current treatment era.

Methods: Across eight CNICS sites we identified ART-naive PLWH initiating ART between 2012–2018, including efavirenz (EFV; n=404), rilpivirine (RPV; n=347), atazanavir (ATV; n=90), darunavir (DRV; n=245), raltegravir (RAL; n=89), elvitegravir (EVG; n=981) and dolutegravir (DTG; n=295) -based regimens with a tenofovir (TDF)/emtricitabine (or lamivudine) backbone. We also examined dolutegravir-based regimens with abacavir/lamivudine (ABC; n=338).

Weight change was estimated using linear mixed models adjusted for time on regimen, time on regimen x regimen interaction, age, sex, race, hepatitis C, hepatitis B, nadir CD4, smoking, diabetes, anti-psychotic medication use and site.

Results: Mean follow-up was 2.0 years. Compared with EFV, DTG/TDF was associated with a 2.6 kg (95% CI: 1.6, 3.6) per year greater weight gain while DTG/ABC was associated with a 2.1 kg (95% CI: 1.4, 2.8) per year greater gain. Other integrase-inhibitor-based regimens showed less weight gain per year. Weight gain on DTG was statistically significantly greater than EFV, RPV, ATV and EVG, but not DRV (1.8 kg per year, 95% CI: 0.9, 2.7). Generalized additive model plots suggested that weight gain on DTG occurred in the first 2 years following regimen initiation (Figure 1).

Conclusions: DTG users had the greatest 2-year weight gain, regardless of backbone, although weight gain was not significantly higher than in DRV users. For ART-naive PLWH, potential weight gain should be considered in conjunction with the benefits of viral suppression when comparing DTG with other ART regimens.
ABSTRACT 009

Antiviral Therapy 2019; 24 Suppl 1:A12

Switching to an integrase inhibitor containing antiretroviral regimen is not associated with above-average weight gain in middle-aged people living with HIV on long-term suppressive antiretroviral therapy, the AGEhIV cohort study

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Objectives/aim: Recently, several US-based cohorts reported significant weight gain in people with suppressed viraemia after switching to an integrase inhibitor (INSTI). We evaluated changes in standardized bodyweight measurements among individuals before and after switching to an INSTI-containing regimen and compared these changes to (1) non-switching HIV-positive and (2) lifestyle-comparable HIV-negative control groups, all participants in the AGEhIV Cohort Study.

Methods: In 598 HIV-positive and 550 HIV-negative AGEhIV participants bodyweight was measured biennially using calibrated scales. Virally suppressed HIV-positive participants switching to an INSTI-containing antiretroviral regimen during follow-up were matched 1:2:2 with participants from both control groups, using a time-dependent propensity score based on gender, ethnicity, age and body mass index (BMI). Controls were matched at the visit at which the control’s propensity score most resembled that of the corresponding index-participant’s visit prior to INSTI-switch, also rendering a hypothetical moment of switch for the control participants. Mean yearly bodyweight changes before and after (hypothetical) switch within and between groups were compared using linear mixed-effects models. In addition, frequencies of >5% and 10% weight gain were compared between index and control groups after (hypothetical) switch using logistic regression.

Results: 119 HIV-positive participants switched to an INSTI-containing regimen (53% dolutegravir; 35% elvitegravir; 13% raltegravir) and had a bodyweight measured ≥1 times before and after switch. At the visit prior to switch, median age was 55 years (IQR 50–61), BMI 24 kg/m² (IQR 22–26), 87% were male, and 89% were Caucasian. Median time between switch and end of follow-up was 2.0 (IQR 1.0–3.0) years. In 49%

Table 1. (Abstract 009)
the NRTI-backbone was simultaneously modified, the majority from tenofovir disoproxil/emtricitabine to tenofovir alafenamide/emtricitabine (18%) or abacavir/lamivudine (11%). Due to the propensity score matching, both the HIV-positive and -negative control groups were highly comparable to the index group regarding age (median 54 and 53), BMI (median 24 and 24 kg/m²), sex (91% and 84% male) and ethnicity (89% and 92% Caucasian). There were no significant differences in yearly mean change in bodyweight within or between groups before and after (hypothetical) switch (Table 1). A >5% increase in bodyweight occurred in 28 (23.5%) HIV-positive participants after INSTI initiation, and in 31 (13%; \( P=0.013 \)) non-switching HIV-positives, and in 28 (11.8%; \( P=0.005 \)) HIV-negative controls, after their hypothetical moment of switch. A >10% increase in bodyweight occurred in 6 (5.0%), 7 (2.9%; \( P=0.3 \)) and in 6 (2.5%; \( P=0.2 \)), respectively.

**Conclusion(s)/discussion:** We found no evidence for above-average weight gain in virologically suppressed patients switching to an INSTI-containing regimen. However, clinically relevant weight gain upon switching to INSTI may be a relatively rare phenomenon deserving further investigation.
ABSTRACT O10

Antiviral Therapy 2019; 24 Suppl 1:A14

Impact of the reproductive/hormonal status on weight, fat and insulin resistance in HIV-infected women switching from a PI regimen to dual raltegravir-etravirine therapy: results from the ANRS163-ETRAL trial at 48 and 96 weeks

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Objectives: The ANRS 163 ETRAL trial (NCT02212379) has previously shown the viral efficiency of a dual raltegravir/etravirine therapy in 165 PI-controlled ageing HIV-infected individuals followed-up for 96 weeks. While lipid and bone parameters improved, patients gained weight, trunk and limb fat and increased insulin resistance. In a sub-study, we evaluated whether these anthropometric/metabolic modifications were dependent upon sex, and upon the reproductive/menopausal status.

Methods: 48 women were included. Fat mass and bone mineral density were evaluated by DEXA at D0, W48 and W96. We recorded the menopausal status with a questionnaire. To assess the reproductive status, ovarian reserve was evaluated in 40 women by the level of the anti-Müllerian hormone (AMH, Gen II, ELISA) at D0 and W48. Insulin resistance was measured at D0, W48 and W96 by using the HOMA-IR index. We separated women into three groups according to their AMH level (detectable or not) and menopausal status. Baseline values and percent changes from baseline were compared between groups using Mann–Whitney and Kruskal–Wallis tests.

Results: ETRAL patients were 117 men and 48 women, median age 52 years. BMI, total, trunk and limb fat mass similarly increased in men and women at W48 and W96 (Table 1), indicating a global fat gain at the limb and trunk level. Baseline HOMA-IR was similar in men and women. It increased in men and women at W48 and in men at W96 (Table 1). Lipid parameters improved similarly (increased HDL, decreased triglycerides) in men and women at W48 and W96. As well, there was no gender differences in the evolution of bone mineral density at the hip and lumbar level from D0 to W96.

Regarding reproductive/menopausal status, 12 women (30%, age 46 years) had reproductive activity with ovarian reserve (group 1, AMH >0.06 ng/ml), 6 (15%, 47 years) were premenopausal with no ovarian reserve (group 2, AMH <0.02 ng/ml) and 22 (55%, 54 years) were post-menopausal (group 3). Baseline BMI and fat repartition did not differ between the three groups. At W48 and W96, BMI, total and trunk fat increased in groups 2 and 3 but not in group 1. Moreover, HOMA-IR worsened in groups 2/3 but tended to improve in group 1 (Table 1). The evolution of limb fat, bone and lipid parameters was not different according to the

Table 1. (Abstract O10)
group (except increased HDL in groups 1/2 but not 3 at W96).

Conclusions: Fat gain and insulin sensitivity seem to be related to the reproductive/menopausal status. Women with reproductive activity and a remaining ovarian reserve would be protected from raltegravir/etravirine-induced weight gain and associated insulin resistance while pre- and post-menopausal women increased weight, fat and insulin resistance, as did men. A role for the oestrogen/androgen status should be considered in the impact of antiretroviral drugs on weight gain. This sub-study was supported by a grant from ANRS/MSD.
ABSTRACT O11
Antiviral Therapy 2019; 24 Suppl 1:A16

Environmental exposures are associated with increased respiratory morbidity among persons living with HIV (PLWH)

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Objectives: Chronic lung disease has emerged as an important comorbidity for PLWH. HIV has been described to increase susceptibility to cigarette smoke, leading to lung injury. Indoor air pollutants related to particulate matter (PM), nitrogen dioxide (NO₂) and second-hand smoke (SHS) are common exposures as well which increase lung inflammation and lead to lung injury. While studies suggest that HIV alters susceptibility to smoking, the impact of indoor air pollutants among PLWH is unknown. We aimed to a) determine the association between sources of indoor air pollution and respiratory outcomes in a cohort of PLWH at risk for both pollutant exposure and lung disease, and b) describe how HIV modifies the impact of pollutants.

Methods: We analysed cross-sectional data from the Study of HIV Infection in the Etiology of Lung Disease (SHIELD) in Baltimore, MD, USA, consisting of both PLWH and HIV-uninfected participants. Participants complete lung function testing and questionnaires about environmental exposures; including SHS, NO₂ producing appliances (gas stoves/ovens), pest allergens (rodents, cockroach), mould and occupational exposures (vapours, dust, fumes). Respiratory symptoms captured through the American Thoracic Society-Division of Lung Diseases (ATS-DLD) questionnaire included: chronic cough, wheeze, phlegm and experiencing ≥2 wheezing attacks/year. We utilized logistic regression to determine associations between sources of indoor air pollution and respiratory outcomes, after adjusting for potential confounders (demographics, smoking status, injection drug use, lung function-FEV₁, household income and HIV status). We generated interaction terms to determine effect modification by HIV serostatus.

Results: Of 1997 participants, 1,109 (55.5%) were PLWH. Among PLWH 48.4% had undetectable viral load. Pollutant exposure was common, with 1,490 (74.6%) using NO₂ producing appliances, 646 (34.2%) with significant occupational exposures, and 1,373 (68.3%) noting household SHS. A number of exposures were associated with chronic respiratory symptoms after adjusting lung function and traditional risk factors. Occupational exposures (OR 1.37; P=0.007), mould (OR 1.79; P<0.001) and pest allergens (OR 1.37; P=0.016) were associated with higher odds of chronic phlegm and other symptoms. PLWH were notably more susceptible to the effects of SHS and NO₂ producing appliances (Figure 1). NO₂ exposure was linked to increased odds of chronic wheeze and wheezing attacks among PLWH (OR 1.41; P=0.023), but not in uninfected participants (OR 0.97; P=0.869; P-interaction =0.040). Regular household SHS exposure...
was associated with greater risk for chronic phlegm (OR 1.43; \( P \)-value =0.015), even after accounting for personal smoking status, but only among PLWH (\( P \)-interaction =0.045). Among PLWH, we did not detect effect modification by viraemia status.

**Discussion:** We describe in a cohort of PLWH that indoor environmental exposures are common and associated with greater respiratory morbidity. PLWH may also be more susceptible to the effects of NO\(_2\) and SHS, indoor environmental exposures which are modifiable. These results suggest that future studies of HIV-associated lung disease should involve more detailed environmental monitoring to increase our understanding of the full impact of indoor air pollution in PLWH.
ABSTRACT O12

Antiviral Therapy 2019; 24 Suppl 1:A18

HIV infection and smoking: functional PET imaging reveals early pulmonary perfusion abnormalities

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Rationale: COPD is the most common non-infectious pulmonary disease amongst people living with HIV. Studies suggest that the development of COPD is accelerated in this population. Although prior investigation has established an association between chronic HIV infection and the development of COPD independent of smoking, the cause for this enhanced susceptibility remains unclear. Because pulmonary perfusion alterations have been demonstrated with the development of COPD, multimodal functional imaging may detect early physiological abnormalities in the distribution of pulmonary perfusion in these susceptible individuals.

Methods: We used low dose computed tomography (LDCT) and positron emission tomography (PET) in 46 subjects, 23 with documented HIV infection. We collected anthropometrics, lung function and smoking history for all subjects. LDCT was used to assess the quantity and location of low-attenuation areas in the lung at mean lung volume. Global and regional perfusion in each subject were analysed using dynamic PET scans of intravenously infused nitrogen-13 (13NN). After removal of image noise, vertical and axial gradients in perfusion were calculated. We tested for a difference in the total spatial heterogeneity of perfusion (CV^2_Qtotal) and the heterogeneity caused by its components (CV^2_Qvgrad = CV^2_Qvgrad [vertical gradient] + CV^2_Qzgrad [axial gradient] + CV^2_Qr [residual heterogeneity]) between clinical groups, based on HIV infection and smoking.

Results: Of the 23 subjects with documented HIV infection, 21 had low to undetectable viral loads (<100 copies/ml), 19 were on antiretroviral therapy (ART) and 12 were current smokers. There were no significant differences in demographic parameters between subjects living with and without HIV. All subjects had minimal radiographic evidence of emphysema by visual assessment and % HU<-950 at mean lung volume (MLV). Compared with controls, nonsmokers living with HIV had a significantly greater CV^2_Qtotal/CV^2_Qr (0.36 versus 0.48; P=0.05) and reduced CV^2_Qvgrad/CV^2_Qtotal (0.46 versus 0.65; P=0.038). Current smokers, independent of HIV status, had a significantly reduced CV^2_Qvgrad/CV^2_Qtotal compared with nonsmokers (0.36 versus 0.6; P=0.002). Amongst smokers, there was no significant difference in CV^2_Qvgrad/CV^2_Qtotal between those living with and without HIV (0.39 versus 0.34; P=0.58), despite a trend towards an attenuated slope of vertical perfusion gradient in smokers living with HIV. See Figure 1.

Conclusions: In subjects living with well-controlled HIV and minimal radiographic emphysema, both HIV infection and smoking are associated with an increased perfusion heterogeneity and a reduction in the vertical
gradient of perfusion. These data indicate the onset of subclinical pulmonary perfusion abnormalities prior to the development of significant lung disease in these susceptible individuals.
ABSTRACT O13
Antiviral Therapy 2019; 24 Suppl 1:A20
Cigarette smoking disproportionately impairs nitric oxide signalling in pulmonary artery endothelial cells in HIV: role of viral and host factors
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Rationale: HIV-associated pulmonary arterial hypertension (HIV-PAH) is a well-recognized severe cardiovascular complication of HIV infection with an adverse prognosis irrespective of the stage of disease. The prevalence of PAH in individuals with HIV is several fold greater than individuals without HIV infection. This high rate of HIV-associated PAH has not declined in the current era of antiretroviral therapy. Moreover, the exact pathogenic mechanism that links HIV to PAH is not known.

Objective: Compared with general population, overwhelming percent of people with HIV are cigarette smokers. Therefore, the objective of this study is to determine whether cigarette smoking (CS) disproportionately impairs the pulmonary artery endothelial cell (PAEC) function and increases the risk of HIV-PAH.

Hypothesis: Studies have shown that the circulating HIV-1 viral accessory protein, Negative factor (Nef), binds to the host C-X-C motif chemokine receptor 4 (CXCR4) on endothelial and other cells. We hypothesized that CS increases CXCR4-Nef interaction, which results in the downstream impairment of endothelial nitric oxide synthase (NOS3) dependent vasodilation and the development of HIV-PAH.

Methods: Smokers and non-smokers with and without HIV-1 infection were recruited at the University of Alabama at Birmingham HIV 1917 clinic. All HIV-positive patients were on ART and had low blood viral loads (20–500 copies/ml). General demographic characteristics were not significantly different between groups (age range 47–55 years; race distribution 50–77% African American). Plasma was separated from blood obtained from these individuals and endothelial cell function markers, nitrite/nitrate ratio (stable metabolic products of nitric oxide), cGMP and prostacyclin were measured in plasma. To determine the role of CS in Nef-CXCR4 interaction, human PAECs (HPAECs) were treated with recombinant Nef protein in the presence or absence of cigarette smoke extract (CSE) ex vivo, and CXCR4 levels and CXCR4 binding to Nef were measured. It was also determined whether Nef impaired NOS3 expression, plasma membrane translocation, posttranslational modification, and function in HPAECs and whether the pharmacological inhibition of CXCR4 by AMD3100 attenuated Nef signalling.

Results: HIV-positive smokers had significantly lower plasma levels of nitrite/nitrate, cGMP and prostacyclin compared with HIV-positive non-smokers or HIV-negative smokers, suggesting that smoking adversely effects endothelial function in HIV-positive individuals compared with HIV-negative individuals. Further, exposure to 2% of CSE increased CXCR4 protein levels in HPAEC and increased CXCR4-Nef interaction when these cells were treated with recombinant Nef. Exposure of cells to CSE and Nef also reduced plasma membrane expression of NOS3, and cellular nitrite/nitrate and cGMP levels. Treatment of cells with AMD3100 abrogated effect of Nef on cells.

Conclusions: The data suggests that CS dependent Nef/CXCR4 signalling is an important driver of endothelial dysfunction in HIV and CXCR4 inhibition can be a potential therapeutic target for HIV-PAH.
ABSTRACT O14

*Antiviral Therapy* 2019; 24 Suppl 1:A21

Changes in bone mineral density over 2 years in men who have sex with men on tenofovir disoproxil fumarate-based HIV pre-exposure prophylaxis: longitudinal cohort data

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Objectives: Tenofovir disoproxil fumarate (TDF)-based HIV pre-exposure prophylaxis (PrEP) can reduce bone mineral density (BMD) by 1–2% or more over 12 months. Minimal longer-term data are available.

Methods: Men who have sex with men (MSM) initiating daily TDF-emtricitabine (FTC) PrEP through a PrEP demonstration project were offered BMD assessment by dual-energy X-ray absorptiometry (DXA) using a single scanner at baseline and after completing 1 and 2 years of PrEP. Hip data are the mean of left and right hip results. We excluded participants who ceased PrEP or who received antiresorptive therapy. Mean changes were assessed using paired t-tests.

Results: Of 185 men with baseline scans, 118 (64%) and 51 (43%) men were assessed at a median (IQR) of 420 (391–449) and 824 (776–885) days on PrEP. The mean (sd) ages and body mass index (BMI) of those men that had baseline BMD assessment compared with the 282 that did not was 35 (10) and 32 (9) years (*P* < 0.05) and 25 (4) and 25 (4) kg/m², respectively (*P* > 0.05). Changes in BMD are shown in Table 1. No participant experienced a low trauma fracture during the study.

Conclusions: Over 12 months, a substantial proportion of MSM on daily HIV TDF-FTC PrEP lose ≥3% BMD at all measured sites over 24 months. There may be a plateau in loss after 12 months. Long-term studies of TDF-based PrEP in MSM are warranted.

Table 1. (Abstract O14)

<table>
<thead>
<tr>
<th>BMD assessments</th>
<th>Baseline to Year 1 (n=118)</th>
<th>p value</th>
<th>Year 1 to Year 2 (n=51)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change (%) median (IQR) g/cm²</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L1 – L4</td>
<td>-0.86% (-2.6–1.5)</td>
<td>0.045</td>
<td>-0.78% (-2.7–2.5)</td>
<td>0.499</td>
</tr>
<tr>
<td>Femoral neck (total)</td>
<td>-1.1% (-3.3–0.54)</td>
<td>0.0001</td>
<td>-0.42% (-2.7–1.9)</td>
<td>0.502</td>
</tr>
<tr>
<td>Total hip</td>
<td>-0.87% (-2.3–0.87)</td>
<td>0.004</td>
<td>0.49% (-0.82–1.5)</td>
<td>0.147</td>
</tr>
<tr>
<td>&gt;3% BMD loss (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L1 – L4</td>
<td>23%</td>
<td></td>
<td>14%</td>
<td></td>
</tr>
<tr>
<td>Femoral neck (total)</td>
<td>27%</td>
<td></td>
<td>22%</td>
<td></td>
</tr>
<tr>
<td>Total hip</td>
<td>16%</td>
<td></td>
<td>6%</td>
<td></td>
</tr>
</tbody>
</table>
ABSTRACT O15

Antiviral Therapy 2019; 24 Suppl 1:A22

Limitations of FRAX equation for predicting low bone mineral density or bone loss progression among people living with HIV: the role of secondary causes of osteoporosis

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Objective: We assessed the usefulness of the Fracture Risk Assessment (FRAX) tool to identify HIV-infected patients with low bone mineral density (BMD) and bone loss progression. We further evaluated the effect of secondary causes of osteoporosis and HIV-related factors on FRAX results.

Methods: Longitudinal study of 217 consecutive patients (mean, 45.8 years, women 24%) included after whole-body dual X-ray absorptiometry (DXA) scan. Low BMD and osteoporosis were defined as a femoral neck T-score <2 and <2.5, respectively. The risk of major osteoporotic and hip fracture was calculated by FRAX equation, considering HIV as a secondary cause of osteoporosis, without/femoral neck BMD data. The threshold for high-risk of fracture was defined as >3% for hip and >10% for lumbar spine.

Results: A low femoral neck and spine BMD was observed in 56% and 64% of patients, respectively. FRAX without BMD data did not identify any patient aged <75 at high risk of fracture. The inclusion of BMD data increased the estimated fracture risk (up to +221% in individuals with osteoporosis), though only two patients reached the current high-risk threshold for fracture. Moreover, the estimated fracture risk decreased in the oldest patients (-33%) and in individuals with normal BMD (-93%) after including BMD data. Conversely, FRAX results increased significantly with the inclusion of BMD data among individuals with classical and HIV-related secondary causes of osteoporosis (Figure 1). Notably, patients with lower BMD and higher FRAX score at baseline had less bone decline in a consecutive DXA scan (rho=-0.21; P=0.008).

Conclusions: FRAX equation without BMD data does not identify HIV-infected patients with low BMD,
delaying DXA assessment. After including femoral neck BMD, most patients remain below the current high-risk threshold for fracture. Different secondary factors, classical and HIV-related, affect fracture risk estimation by FRAX in this population.
ABSTRACT O16

Antiviral Therapy 2019; 24 Suppl 1:A24

DXA scan versus FRAX score for the evaluation of fracture risk in a cohort of elderly people living with HIV

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1Research and Development Department, Chelsea and Westminster Hospital, London, UK; 2Medical and Surgical Sciences Department, ‘Magna Graecia’ University, Catanzaro, Italy; 3Department of Laboratory Medicine, Tokyo Medical University Hospital, Tokyo, Japan; 4Imperial College, London, UK

Background: Osteoporosis and fractures increase morbidity and mortality in people living with HIV (PLWH). EACS guidelines recommend routine assessment of fracture risk using FRAX, and dual-energy X-ray absorptiometry (DXA) scan only for those with FRAX over 10%, even though it can underestimate fracture risk in PLWH. Objective of our study was to evaluate level of concordance of DXA results (T score of the spine and of the femur) and FRAX in a population of PLWH over 50 years of age.

Methods: DXA scan results of PLWH who attended specialist over 50s clinic in Chelsea and Westminster Hospital between January 2009 and December 2018 were collected as well as demographic and clinical characteristics. FRAX was calculated using Sheffield algorithm. Mean and standard deviation were calculated. For univariate analysis Wilcoxon test was used.

Results: 744 patients were included, 92.9% were male, mean age of 56 ± 5 years. Prevalence of osteoporosis (in the spine and/or in the femur) was 12.2% and osteopenia 63.7%. A statistically significant association was found between age and time of exposure to boosted protease inhibitors and osteoporosis in the femur (P < 0.05). Two out of 744 cases FRAX major was > 10% indicating need to perform DXA scan according to EACS guidelines (Table 1), while 90/91 (98.9%) patients with osteoporosis had a normal FRAX score. Even when FRAX score was calculated considering HIV as a risk factor of secondary osteoporosis and using BMD results, only 1.5% (11/744) patients had FRAX score > 10%.

Discussion: Our results show that the FRAX score may not be a reliable screening tool for fracture risk in PLWH. Most patients with osteoporosis in our cohort had a normal FRAX score. These findings were maintained when BMD results and HIV infection were included in the FRAX calculation tool. Bone fracture screening in PLWH over 50 years of age requires optimization.

Table 1. (Abstract O16)

<table>
<thead>
<tr>
<th>Risk of Fracture with FRAX Major</th>
<th>DXA results (Spine)</th>
<th></th>
<th>DXA results (Femur)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal</td>
<td>Osteopenia</td>
<td>Osteoporosis</td>
<td>Normal</td>
</tr>
<tr>
<td>Normal (&lt;10%)</td>
<td>353 (47.4)</td>
<td>307 (41.4)</td>
<td>82 (11)</td>
<td>353 (47.4)</td>
</tr>
<tr>
<td>Perform DXA (10-20%)</td>
<td>1 (0.1)</td>
<td>0 (0)</td>
<td>1 (0.1)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Refer for treatment (&gt;20%)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Risk of Fracture with FRAX Major calculated with HIV and BMD</th>
<th>DXA results (Spine)</th>
<th></th>
<th>DXA results (Femur)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal</td>
<td>Osteopenia</td>
<td>Osteoporosis</td>
<td>Normal</td>
</tr>
<tr>
<td>Normal (&lt;10%)</td>
<td>351 (47.2)</td>
<td>304 (40.9)</td>
<td>74 (9.9)</td>
<td>353 (47.4)</td>
</tr>
<tr>
<td>Perform DXA (10-20%)</td>
<td>3 (0.4)</td>
<td>3 (0.4)</td>
<td>9 (12)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Refer for treatment (&gt;20%)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>
ABSTRACT O17

Antiviral Therapy 2019; 24 Suppl 1:A25

Development and validation of a comorbidity index for people living with HIV and its ability to predict frailty and mortality

D De Francesco1, SO Verboeket2, E Verheij3, J Underwood4, E Bagkeris1, FW Wit2, A Winston6, P Reiss1, CA Sabin1, the POPPY study and the AGEhIV cohort study

1Institute for Global Health, UCL, London, UK; 2Department of Global Health and Division of Infectious Diseases, Amsterdam University Medical Centers, University of Amsterdam, Amsterdam, the Netherlands; 3Division of Infectious Diseases, Imperial College London, London, UK

Objectives: Despite the increasing prevalence of multi-morbidity in people living with HIV (PLWH), there is no tool designed specifically for PLWH to assess overall comorbidity burden. We developed and externally validated a comorbidity burden index (CBI), specific to PLWH, assessing its cross-sectional association with health status and ability to predict mortality and frailty.

Methods: We developed the CBI deriving weights for each of 65 comorbidities and their pairwise interactions from age-adjusted regression coefficients reflecting the independent association with self-reported physical health in PLWH enrolled in the POPPY (development) cohort. Predictive performance of the CBI were compared against the comorbidity count and the VACS index in the AGEhIV (validation) cohort. Spearman’s correlation and the C-statistic assessed associations of indices with physical/mental health (SF-36), adapted Fried frailty phenotype prevalence and 4-year incidence, and 6-year all-cause mortality. These were compared across indices using the Steiger’s and DeLong tests, as appropriate.

Results: The development and validation cohorts included 1,073 (85% males, 16% Black Africans, median [IQR] age of 52 [47–59] years) and 598 (88% males, 14% Black Africans, median [IQR] age of 53 [48–59] years) PLWH, respectively. Of the three indices, the CBI demonstrated the strongest associations with physical and mental health (Table 1); these associations were significantly stronger than those of the VACS index (both P-values <0.001) but not of those of the comorbidity count (P=0.08; P=0.16). At baseline, 11.4% of PLWH were frail; frailty incidence and death rate were 19.5/1,000 and 12.0/1,000 person-years, respectively. Cross-sectionally, the CBI showed a stronger association with frailty than either the VACS index (P=0.02) or the comorbidity count (P=0.27). Whilst prospective associations with frailty development and mortality were strongest for the comorbidity count, the difference with associations of the CBI were not significant (P=0.55 and P=0.12, respectively).

Conclusions: The proposed CBI, specifically developed in PLWH showed strong associations with quality of life, frailty and mortality when externally validated. These findings justify support the construct validity of the CBI and its use when adjustment for comorbidity is needed and when evaluating the effectiveness of interventions.

Table 1. (Abstract O17)

<table>
<thead>
<tr>
<th>Index</th>
<th>Physical health</th>
<th>Mental health</th>
<th>Frailty</th>
<th>Frailty development</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>rho (95% CI) p vs. CBI</td>
<td>rho (95% CI) p vs. CBI</td>
<td>C-statistic (95% CI) p vs. CBI</td>
<td>C-statistic (95% CI) p vs. CBI</td>
<td>C-statistic (95% CI) p vs. CBI</td>
</tr>
<tr>
<td>CBI</td>
<td>-0.34 (-0.41, -0.26)</td>
<td>-0.18 (-0.26, -0.10)</td>
<td>0.73 (0.66, 0.79)</td>
<td>0.62 (0.52, 0.72)</td>
<td>0.66 (0.56, 0.75)</td>
</tr>
<tr>
<td>Comorbidity count</td>
<td>-0.30 (-0.38, -0.22)</td>
<td>0.08 -0.15 (0.23, -0.97)</td>
<td>0.15 (0.71, 0.36, 0.78)</td>
<td>0.27 (0.54, 0.74)</td>
<td>0.55 (0.71, 0.62, 0.79)</td>
</tr>
<tr>
<td>VACS index</td>
<td>-0.07 (-0.15, -0.02)</td>
<td>&lt;0.001</td>
<td>0.10 (0.02, 0.19)</td>
<td>&lt;0.001</td>
<td>0.63 (0.56, 0.70)</td>
</tr>
</tbody>
</table>

Note: for physical and mental health scores, higher scores indicate a more favourable health state
ABSTRACT O18

Antiviral Therapy 2019; 24 Suppl 1:A26

In vitro modelling of the therapeutic impact of statins and ApoA-I mimetics on atherogenesis in chronic treated HIV

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Objectives/aim: The mechanisms that drive HIV-related atherosclerosis (CVD) in chronic treated HIV remain unclear. Serum factors (such as bioactive lipids) from HIV+ individuals on potent antiretroviral therapy (ART) may drive atherosclerosis. Statins may have a favourable impact on CVD in chronic treated HIV but may be inadequate as single therapeutic strategy. ApoA-I peptides (such as 4F, 6F) mimic HDL, bind oxidized lipids and endotoxin and attenuate proatherogenic mechanisms such as monocyte/macrophage (M/M) chemotaxis. The 6F was expressed as a transgene in tomatoes (Tg6F) and reduced CVD in mice. Tg6F can be translated to human diet. Given that preclinical data are needed to assist efforts to bring Tg6F in the clinic, we used an established model of atherogenesis to assess ex vivo the therapeutic impact of statins and Apo-AI mimetics on early mechanisms of atherogenesis.

Methods: Our in vitro model of atherogenesis can dissect the impact of HIV-plasma on key mechanisms of early atherogenesis such as monocyte chemotaxis and monocyte-derived foam cell formation (MDFCF). Freshly isolated peripheral blood mononuclear cells (PBMCs) from healthy donors (n=6) were added to tumour necrosis factor-activated human umbilical vein endothelial cells monolayers (HUVECs) on type I fibrous collagen gels to transmigrate (% reverse migration) and form foam cells in the presence of pooled plasma, atorvastatin (50 and 500 µM) and/or 4F (10–100 µg/ml) as previously described (PMID: 28926407). Pooled plasma was isolated from healthy participants (18–40 years old) and HIV+ males (40–60 years old) with no known inflammatory comorbidities other than HIV or risk factors for CVD and on stable potent ART. Flow cytometry assessed MDFCF (ΔMFI BODIPY of CD33+ macrophages inside the gel: fluorescence intensity of BODIPY compared with negative staining control). Paired t-test was used for statistical comparison within the same donor.

Results: When media-containing HIV+ compared with HIV- plasma was added to HUVECs, a significantly increased proportion of monocytes underwent transendothelial migration (TEM; median migrated cells 16 versus 4.9%, respectively) and CD33+ macrophages inside the collagen gel had increased lipid content per cell (median ΔMFI BODIPY 673 versus 342, respectively; P<0.05; Figure 1). In the presence of HIV-plasma, both atorvastatin (at both 50 and 500 µM) and 4F (at both 10 and 100 µg/ml) attenuated TEM of M/M and MDFCF (P<0.05 for all comparisons). The combined treatment with 4F (100 µg/ml) and atorvastatin (50 µM) reduced TEM compared with 50 µM atorvastatin alone (P<0.05).

Conclusions/discussion: HIV plasma from patients on potent ART with no clinical CVD directly induces key mechanisms of early atherogenesis (TEM and MDFCF). The combination of statins and oral apoA-I mimetics can be a novel therapeutic strategy for atherosclerosis in chronic treated HIV and needs to be further validated in vivo.

Figure 1. (Abstract O18)
ABSTRACT 019

Antiviral Therapy 2019; 24 Suppl 1:A27

Could coronary artery features during acute coronary syndrome predict major cardiac events in people living with human immunodeficiency virus?

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1Cardiology Department, University Hospital, PEC 2, Univ. Bourgogne Franche-Comté, Dijon, France; 2INSERM, Sorbonne Université, Institut Pierre Louis d’Épidémiologie et de Santé Publique (IPLESP), Paris, France; 3AP-HP, Hôpitaux de l’Est Parisien, Hôpital Saint-Antoine, Department of Cardiology, Faculty of Medicine, Sorbonne Université, Paris, France; 4Infectious Disease Department, AP-HP, Hôpitaux de l’Est Parisien, Hôpital Saint-Antoine, Faculty of Medicine, Sorbonne Université, Paris, France; 5National Institute of Health and Medical Research, INSERM, UMR_S 938, UPMC, Paris, France

Introduction: Patients living with human immunodeficiency virus (PLHIV) who undergo percutaneous coronary intervention (PCI) have a substantial risk of recurrent ischaemic events after ACS.

Hypothesis: Our hypothesis was that angiographic features and SYNTAX scores could predict recurrent ischaemic events in PLHIV.

Methods: We conducted a nested case-control study from the PACS-HIV study (prospective, multicentre study on the prognosis of ACS in HIV+ in France) comparing coronary angiography features between PLHIV and matched HIV- patients (age, sex and type of ACS) with a first ACS undergoing PCI. Coronary angiograms at baseline were off-line analysed blinded to the HIV status.

Results: The cohort included 60 PLHIV and 107 HIV- (median age 47 years [41–56], male sex 95%). Cardiovascular risk factors were well balanced between the two groups (high tobacco consumption 63%). Illicit drug use was more frequent in PLHIV (20% versus 5%, P=0.006). STEMI was the predominant type of ACS (55%) follows by NSTEMI (23%) and unstable angina (22%). In terms of the number of vessel disease (VD) there was no significant difference between PLHIV and HIV- subjects with predominant 1 VD (48% versus 43%), 2VD (33% versus 33%), 3 VD (15% versus 12%), P trend =0.86. Of note, PLHIV had a higher rate of coronary artery aneurysms as compared with HIV- (15% versus 4%; P=0.009). PLHIV had higher number of significant coronary lesions (median 2 [1–3] versus 1 [1–2]; P=0.04). However, the initial SYNTAX score was not different between the two groups (12.4 ±9 versus 11.5 ±7.8 in PLHIV and HIV- respectively; P=0.42). By contrast, the residual SYNTAX score after PCI was significantly higher in PLHIV (4.7 ±7 versus 2.7 ±4.9; P=0.04). The rate of MACCE was not different between the two groups after 36 months of follow-up. However, a trend toward a higher rate of recurrent ACS was observed (HR: 3.80; 95% CI: 0.96, 15.00; P=0.06). Neither angiographic features nor the SYNTAX initial or residual score were associated with MACCE or recurrent ACS.

Conclusions: PLHIV had higher numbers of significant coronary lesions and aneurysms with higher residual SYNTAX score after PCI as compared to HIV-. However, the SYNTAX score was not associated with MACCE or recurrent ACS after a long-term follow-up.
ABSTRACT O20

Antiviral Therapy 2019; 24 Suppl 1:A28

Risk factors for incident hypertension within 1 year of initiating antiretroviral therapy (ART) among people with HIV

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Background: While hypertension (HTN) is a common comorbid condition among persons with HIV and a contributor to cardiovascular disease and CKD risk, the association of antiretroviral therapy (ART) with the risk for HTN remains unclear. We examined the prevalence and risk factors for hypertension in a cohort of ART-naive participants initiating ART on randomized clinical trials through the AIDS Clinical Trial Group between 1999 and 2011.

Methods: We determined the prevalence of HTN among 4,617 treatment-naive PWH randomized to different ART regimens and followed in the AIDS Clinical Trials Group Longitudinal Linked Randomized Trials (ALLRT) study, and the incidence of HTN at 48 weeks among 3,809 participants who were normotensive at study entry, defined as having a systolic blood pressure (SBP) <140 mmHg, diastolic blood pressure (DBP) <90 mmHg, no diagnosis of HTN, and not taking any antihypertensive medications. We assessed the role of baseline factors, including randomized ART agents, in the development of HTN at 48 weeks using Poisson regression models. Incident HTN was defined as blood pressure ≥140/90, clinical diagnosis of hypertension, or receipt of antihypertensive medications.

Results: At baseline, 808 participants (17.5%) were hypertensive and excluded from the analysis. After 48 weeks, 438 additional participants (11.5%) developed HTN. Receiving an NNRTI was associated with an increased risk of incident hypertension (adjusted relative risk [aRR] 1.29, 95% CI: 1.04, 1.61), while the risk was lower for PI use (aRR 0.74, 95% CI: 0.56, 0.91; see Table 1). Regarding specific ART agents, abacavir, stavudine and efavirenz were associated with an increased risk of developing hypertension (aRR: 1.27 [95% CI: 1.02, 1.59], 1.86 [95% CI: 1.17, 2.96] and 1.28 [95% CI: 1.03, 1.59], respectively), while tenofovir disoproxil fumarate (TDF), ritonavir and darunavir were associated with a decreased risk (aRR: 0.78 [95% CI: 0.62, 0.97], 0.69 [95% CI: 0.55, 0.87] and 0.65 [95% CI: 0.42, 0.98], respectively). Additionally, lower baseline CD4 count, older age, higher BMI, being male, Black race and current smoking were associated with an increased risk for developing hypertension.

Conclusions: Findings suggest traditional factors, advanced HIV disease and certain ART agents contribute to the development of HTN after ART initiation. Strategies to address modifiable risk factors, such as smoking and obesity, can be employed to decrease the consequences of HTN. Future research will explore the effects of newer ART agents and the specific mechanisms by which specific ARTs contribute to HTN.

Table 1. (Abstract O20)

<table>
<thead>
<tr>
<th>Antiretroviral therapy</th>
<th>Unadjusted</th>
<th>Adjusted*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Relative risk (95% CI)</td>
<td>p-value</td>
</tr>
<tr>
<td>NNRTI</td>
<td>1.00 (0.76-1.35)</td>
<td>0.958</td>
</tr>
<tr>
<td>PI</td>
<td>0.94 (0.71-1.25)</td>
<td>0.728</td>
</tr>
<tr>
<td>INST</td>
<td>0.98 (0.77-1.28)</td>
<td>0.771</td>
</tr>
<tr>
<td>Individual NNRTI</td>
<td>0.81 (0.61-1.09)</td>
<td>0.162</td>
</tr>
<tr>
<td>Abacavir</td>
<td>1.00 (0.78-1.28)</td>
<td>1.000</td>
</tr>
<tr>
<td>Stavudine</td>
<td>0.99 (0.79-1.24)</td>
<td>0.991</td>
</tr>
<tr>
<td>ADFP</td>
<td>1.00 (0.78-1.29)</td>
<td>0.991</td>
</tr>
<tr>
<td>Lopinavir/RTV</td>
<td>0.99 (0.79-1.28)</td>
<td>0.991</td>
</tr>
<tr>
<td>FTC</td>
<td>1.00 (0.78-1.28)</td>
<td>1.000</td>
</tr>
<tr>
<td>Individual PI</td>
<td>0.98 (0.76-1.27)</td>
<td>0.764</td>
</tr>
<tr>
<td>Atazanavir</td>
<td>1.00 (0.78-1.28)</td>
<td>1.000</td>
</tr>
<tr>
<td>Darunavir</td>
<td>0.99 (0.79-1.24)</td>
<td>0.991</td>
</tr>
<tr>
<td>Ritonavir</td>
<td>1.00 (0.77-1.27)</td>
<td>1.000</td>
</tr>
<tr>
<td>Individual INST</td>
<td>0.88 (0.67-1.16)</td>
<td>0.307</td>
</tr>
<tr>
<td>Abacavir</td>
<td>1.00 (0.78-1.28)</td>
<td>1.000</td>
</tr>
<tr>
<td>TDF</td>
<td>0.79 (0.60-1.02)</td>
<td>0.074</td>
</tr>
<tr>
<td>Ritonavir/RTV</td>
<td>0.99 (0.79-1.28)</td>
<td>0.991</td>
</tr>
<tr>
<td>Individual INST</td>
<td>0.98 (0.76-1.28)</td>
<td>0.728</td>
</tr>
</tbody>
</table>

Abbreviations: BMI, body mass index; kg/m²; hemagglutination units (HU); NNRTI, non-nucleoside reverse transcriptase inhibitor; INSTI, integrase strand transfer inhibitor; PI, protease inhibitor; ART, antiretroviral therapy; ART, antiretroviral therapy; ALLRT, AIDS Clinical Trials Group Longitudinal Linked Randomized Trials; HTN, hypertension; BMI, body mass index; HU, hemagglutination units.

*Relative risk estimates were obtained using a modified Poisson regression with robust error variance.
ABSTRACT O21

Antiviral Therapy 2019; 24 Suppl 1:A29

The relationship between diabetes and depressive symptoms in men with or at risk for HIV

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Objectives: To compare the prevalence of comorbid diabetes and depressive symptoms between men with (HIV+) and without (HIV-) HIV disease and to determine the associations between glycaemic control and depressive symptoms.

Methods: We conducted a cross-sectional analysis using data collected during a single semiannual visit (October 2017 to March 2018) from HIV+ and HIV- men participating in the Multicenter AIDS Cohort Study (MACS). The exposure of interest was glycaemic status, categorized as normal for fasting blood glucose (FBG) <100 mg/dl, prediabetes for FBG 100–125 mg/dl and type 2 diabetes (defined by self-report, report of diabetes medication use, or FBG ≥126 mg/dl for ≥2 consecutive visits prior to the current visit). Type 2 diabetes was further categorized as controlled (HbA1C <7.5%) or uncontrolled (HbA1C ≥7.5%). The primary outcome was elevated depressive symptoms, as defined by a Center for Epidemiologic Studies Depression Score (CES-D score) ≥16. A modified Poisson regression model with robust variance was used and adjusted for study site, age, race, education status, HIV-serostatus, body mass index, hypertension, dyslipidaemia, smoking, alcohol use, illicit drug use and depression treatment, which included current or prior antidepressant medication use or history of hospitalization for depression or consultation with a mental health professional. Interaction of glycaemic status and HIV-serostatus was tested. Stratification by depression treatment was conducted to determine whether glycaemic status was associated with suboptimal depression treatment. A model limited to HIV+ men was adjusted for HIV-specific variables, which included current CD4 lymphocyte count, detectable HIV viraemia and ART type.

Results: The study included 920 HIV+ men (mean age [sd] 55 [11] years) and 840 HIV- men (mean age [sd] 61 [12] years). HIV+ men had greater prevalence of both elevated depressive symptoms (28.5% versus 20.1% among HIV- men; P<0.001), and diabetes (12.83% versus 11.31%; P=0.330). The concomitant prevalence of diabetes and elevated depressive symptoms did not differ by HIV-serostatus (P=0.516). Compared with normal glycaemic status, the adjusted prevalence ratios of elevated depressive symptoms were 1.06 (95% CI 0.82, 1.37) in men with prediabetes, 1.21 (95% CI 0.89, 1.65) in men with controlled type 2 diabetes and 1.55 (95% CI 1.06, 2.28) in men with uncontrolled type 2 diabetes (Table 1). These associations did not differ by HIV-serostatus (P=0.59). Uncontrolled type 2 diabetes was associated with elevated depressive symptoms among participants with a history of depression.

Table 1. (Abstract O21)

<table>
<thead>
<tr>
<th>Table 1. Prevalence Values and Prevalence Ratios of Elevated Depressive Symptoms by Glycemic Status</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Glycemic Status</strong></td>
</tr>
<tr>
<td>--------------------</td>
</tr>
<tr>
<td>Normal</td>
</tr>
<tr>
<td>Prediabetes</td>
</tr>
<tr>
<td>Type 2 diabetes, controlled</td>
</tr>
<tr>
<td>Type 2 diabetes, uncontrolled</td>
</tr>
</tbody>
</table>

* Adjusted for age, study site, race, education, body mass index, HIV-serostatus, hypertension, dyslipidaemia, alcohol use, smoking, illicit drug use, and depression treatment.
treatment but not for those without a history of depression treatment. HIV-specific variables were not associated with elevated depressive symptoms.

**Conclusions:** Both controlled and uncontrolled diabetes were independently associated with depressive symptoms, regardless of HIV serostatus. Longitudinal studies are needed to examine whether the relationship between glycaemic status and incident elevated depressive symptoms differs by HIV serostatus.
ABSTRACT O22
Antiviral Therapy 2019; 24 Suppl 1:A31
Risk for incident diabetes is greater in pre-diabetic men with HIV than without HIV: the Multicenter AIDS Cohort Study
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the Multicenter AIDS Cohort Study (MACS)
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Background: Abnormalities in glucose metabolism contribute to the pathogenesis of ageing-related comorbidities in people with HIV (PWH). Hyperglycaemia below the diabetic range has been termed pre-diabetes mellitus (pre-DM) and may be more common in PWH compared with those without HIV. It is unclear whether the progression from pre-DM to DM differs by HIV serostatus.

Methods: Fasting glucose (FG) was measured at each semi-annual visit among men in the Multicenter AIDS Cohort Study (MACS) since April 1999. Men who had confirmed pre-DM, defined as an FG 100–125 mg/dl (baseline visit), were included. Men with prevalent DM at the baseline visit were excluded. Incident DM was defined as an FG ≥126 mg/dl, confirmed at a subsequent visit with anti-DM medication use or a second FG ≥126 mg/dl; self-reported DM, confirmed at a subsequent visit with anti-DM medication use or two FG ≥126 mg/dl; or report of anti-DM medication use at a visit. We used binomial transition models to determine whether the progression from pre-DM to DM differs by HIV serostatus.

Results: Between 1999 and 2018, 1,548 men (772 with HIV [MWH], 776 men without HIV) with pre-DM were included. At baseline, MWH were younger (median 48 versus 51 years; P<0.01), had lower BMI (median 25 versus 27 kg/m²; P<0.01), were more likely to be non-White (44% versus 28%; P<0.01), and were more likely to be HCV-infected (9% versus 5%; P<0.01) than men without HIV. Over a median of 12 years of follow-up (Q1, Q3 8, 14), 22% (166/772) of pre-DM MWH and 22% (169/776) of pre-DM men without HIV developed DM. In adjusted analyses, the probability of developing DM among men with pre-DM was 40% (95% CI: 10%, 80%) higher among MWH than men without HIV (P=0.02).

Conclusions: Among men with pre-diabetes, HIV serostatus was associated with increased risk of incident diabetes after adjustment for competing DM risk factors. Given the increased risk, diabetes prevention strategies in PWH may be particularly effective and should be investigated.
ABSTRACT O23

_Antiviral Therapy_ 2019; 24 Suppl 1:A32

Comparing a risk score against physiological markers for predicting diabetes incidence in HIV+ individuals

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**Purpose:** To compare the performance of a clinical diabetes risk score with physiological markers for predicting diabetes incidence in HIV+ and HIV- individuals.

**Methods:** We determined 10-year diabetes incidence (defined as self-reported diabetes medication use) in HIV+ and HIV- participants from the Women's Inter-agency HIV Study and the Multicenter AIDS Cohort Study. For each participant, we obtained baseline values for the Finnish Diabetes Risk Score (FINRISC), Homeostasis Model Assessment for Insulin Resistance (HOMA-IR), HOMA for β-cell function (HOMA-β), and triglycerides/HDL cholesterol ratio (TG/HDL). Discrimination of each model was assessed using the Harrell C-statistic. Calibration was assessed by comparing the observed versus the predicted cumulative probabilities of developing diabetes (determined from 1-Kaplan-Meier) in each tertile of the distribution.

**Results:** We included 2,499 men (1,285 HIV+ and 1,214 HIV-, median age =44 years, 60% non-Hispanic White, 25% non-Hispanic Black) and 2,408 women (1,812 HIV+ and 596 HIV-, median age =41, 12% non-Hispanic White, 62% non-Hispanic Black). Over 10 years of follow-up, 10% of HIV+ men, 9% of HIV- men, 11% of HIV+ women, and 12% of HIV- women developed diabetes. FINRISC had the best discrimination, though it performed better in HIV- participants (men c=0.74 [95% CI 0.69, 0.78], women c=0.75 [0.70, 0.80]) than in HIV+ participants (men c=0.68 [0.62, 0.73]), women c=0.70 [0.66, 0.74]). HOMA-IR discrimination was similar by HIV status but better in men (HIV+ c=0.70 [0.65, 0.75]), HIV- c=0.72 [0.67, 0.77]) than in women (HIV+ c=0.65 [0.61, 0.69], HIV- c=0.67 [0.60, 0.74]). TG/HDL and HOMA-β had poor discrimination (<0.7 and <0.6, respectively). Regarding calibration, FINRISC underestimated risk among HIV- men in the highest risk tertile, while HOMA-IR and TG/HDL underestimated risk among all participants in the highest risk tertiles. HOMA-β was well-calibrated.

**Conclusions:** In HIV+ men, FINRISC predicted incident diabetes similarly to physiological markers. In HIV+ women, FINRISC was superior.
Restless legs syndrome and health-related quality of life in HIV: results from the POPPY Sleep Substudy

KM Kunisaki1,2, D DeFrancesco3, C Sabin4, A Winston5, PWG Mallon6, J Vera7, F Post2, I Williams2,8, E Bagkeris2, N Doyle4, W Khalil1,2, S Redline9,10,11, the Pharmacokinetics and Clinical Observations in People Over Fifty (POPPY) Study

1Minneapolis VA Health Care System, Minneapolis, USA; 2University of Minnesota, Minneapolis, USA; 3 University College London, London, UK; 4Imperial College London, London, UK; 5University College Dublin, Dublin, Ireland; 6Brighton and Sussex University Hospital, Brighton, UK; 7Caldecot Centre, King’s College Hospital, London, UK; 8Mortimer Market Centre, Central and North West London NHS Foundation Trust, London, UK; 9Brigham and Women’s Hospital, Boston, USA; 10Beth Israel Deaconess Medical Center, Boston, USA; 11Harvard Medical School, Boston, USA

Purpose: Restless legs syndrome (RLS) is a sleep disorder characterized by leg dyasesthesias, typically relieved by movement, with sequelae that may include daytime sleepiness, mood problems, functional impairments and decreased work productivity. RLS often responds to dopaminergic drugs, suggesting a central nervous system (CNS) aetiology. Given the high burden of sleep symptoms and CNS disorders in persons with HIV (PWH), we evaluated RLS prevalence and associations with health-related quality of life (QoL) in PWH and lifestyle-similar HIV-negative controls.

Methods: A subset of POPPY participants (PWH ≥50 y/o, PWH <50 y/o and HIV-negative controls ≥50 y/o) completed standardized RLS and QoL questionnaires. RLS was defined using international consensus guideline criteria. Sleep-related QoL was assessed with PROMIS questionnaires. Physical and mental health QoL was evaluated with SF-36 scores. Logistic regression was used to compare RLS prevalence in PWH and controls. QoL in those with and without RLS were compared using Wilcoxon tests.

Results: Of 435 participants (220 older PWH [median age 60 years], 99 younger PWH [45 years] and 116 older HIV-negative [60 years]), RLS criteria were met by 77 (35%), 33 (33%) and 25 (22%) of the groups, respectively. In analyses adjusted for age, sex and race, PWH were more than twice as likely to meet RLS criteria than controls (aOR 2.4 [1.4 to 4.1]; P=0.002). Of the 110 PWH with RLS (55% of whom reported symptoms at least 2–3 times/week), only 7 (6%) reported a diagnosis of RLS and 3 (3%) reported a history of RLS medication treatment. PWH with RLS reported worse sleep-related QoL and poorer physical and mental health QoL compared with PWH without RLS (Table 1; all P-values <0.001).

Conclusions: Among PWH, RLS is common, associated with health-related QoL impairments, and rarely diagnosed or treated. Further research is needed to understand risk factors for RLS and the effects of RLS treatment.

Table 1. (Abstract O24)
POSTER PRESENTATIONS
ABSTRACT P01

*Antiviral Therapy* 2019; 24 Suppl 1:A37

Subcutaneous adipose tissue modifications induced by a switch to dual raltegravir-maraviroc therapy in controlled HIV-infected patients: a sub-study of the ANRS-ROCnRAL157 clinical trial

J-P Bastard¹, V Pelloux², R Alili², S Fellahi², J Aron-Wisnewsky³, L Assoumou¹, E Prifti², C Katlama³, K Clément², J Capeau¹

¹Faculty of Medicine, Sorbonne University, Inserm UMR_S938, CRS, ICAN, Paris, France; ²Faculty of Medicine, Sorbonne University, Inserm UMR_S1269, NutrOmics, ICAN, Paris, France; ³Faculty of Medicine, Sorbonne University, Inserm UMR_S1136, IPLESP, Department of Infectious Diseases, Pitié-Salpêtrière Hospital, APHP, Paris, France; ²IHU ICAN, Paris, France

**Objectives:** Integrase inhibitors including raltegravir have been associated with weight/fat gain. The mechanisms involved remain unknown. The ROCnRAL study enrolled suppressed HIV-infected patients with central fat accumulation switched to maraviroc/raltegravir. Herein, we analysed the effects of this switch on metabolic modifications and subcutaneous abdominal adipose tissue (scAT) transcriptome.

**Material and methods:** In eight patients, paired scAT samples, withdrawn by needle aspiration at inclusion and the end of the study, were available. We extracted total mRNA and examined the transcriptomic profile using Illumina microarrays, as well as scAT adipocyte size.

**Results:** All patients were male, aged 55 ± 3 y (mean ± sd), BMI=26.1 kg/m², waist circumference =94.6 cm, HOMA-IR=2.4. After a mean follow-up of 25 weeks, BMI increased to 26.4 kg/m² (P=0.01), HOMA-IR to 6.7 (P=0.05) and adipocyte size to 113 microns (P=0.09). In the 16 paired samples, we identified 16,094 variants: 458 genes were up-regulated with a fold-change of 10.6-1.1 while 244 genes were down-regulated with a fold-change of 0.66-0.9. We further examined the functional changes that characterized this transcriptomic profile using KEGG data base. The most enriched function (19.4%) was ubiquitin-mediated proteolysis. Functions related to apoptosis were also enriched. Moreover, the main impoverished functions (29.7%) were related to ribosomes, followed by functions related to cell adhesion, grouping genes involved into immune cell recognition (27%), and functions involved into immune-related diseases (10.8%) suggesting a major reduction of scAT immune function/activation. While IL25, IL7R, CD247, CD3D and CD58 gene expression was decreased, that of IL10 and IL18 was increased.

**Conclusions:** In eight controlled HIV-infected patients with central fat accumulation switching to raltegravir/maraviroc resulted in major modification of adipocyte size and transcriptomic pattern. Overall, function related to protein degradation and apoptosis were increased and to protein synthesis decreased. Immune-related genes were mainly decreased. Further investigation is required to examine the link between these modifications and raltegravir-associated weight/fat gain.
ABSTRACT P02

Validation of a measurement tool for estimating step counts under free-living conditions

C Wu1, K Thompson2, R Latif1, A Guerson Gil1, A Oke1, F Okoro1, DP Kotler1

1Jacobi Medical Center, Albert Einstein College of Medicine, Bronx, NY, USA; 2Coalition on Positive Health Empowerment, New York, NY, USA

Background: The recognition of frailty as a clinical entity has increased interest in the assessment of skeletal muscle function, which is predictive of clinical outcomes. Advances in low cost physiological monitoring devices have led to the possibility of making objective measures of physical activity available for clinical or research use. Developing a tool for assessing physical activity during free-living conditions may be important as an indicator of a change in behaviour. However, there are uncertainties about the precision and accuracy of various monitoring devices.

Aim: We estimated the accuracy and precision of a pedometer (P) and an activity monitor (AM) worn on the torso or on the wrist under laboratory conditions. We compared total daily and exercise step counts using the P and an AM and examined the effects of device type and location on the body on total daily step counts under free-living conditions. We also performed power calculations for a hypothetical clinical trial, using Cohen’s d and measurements of total daily and exercise step counts.

Methods: Studies were performed in nine healthy adults who wore a pedometer (P; Omron Alvita HJ-327T) and an activity monitor (AM; Letscom Fitness Tracker ID130Plus ColorHR), both with Bluetooth capability. Data and statistical analyses were by paired t-test, one-way ANOVA and Bland–Altman analyses.

Results: Immediate test-retest differences averaged 1% for steps and time during a 400-metre hall walk while delayed (>4 weeks) test-retest results averaged -2% and average times -5%. Total daily step counts averaged 1,215 steps higher on a wrist-worn AM than on a torso-worn P, while step counts during exercise, defined as 60 or more steps/min for 10 or more min, were similar using the two devices (6 measures per subject). Separate studies were performed varying the placement of both the P and AM. Daily step counts on wrist-worn devices were significantly higher than when worn on the torso. The AM had higher counts than the P when both were worn on the wrist but not on the torso. In a hypothetical intervention that would result in a 10% increase in total or a 20% increase in exercise steps, the number needed to demonstrate statistical significance was estimated using Cohen’s d and P data. Group sizes of 14 and 24 were needed for total daily and exercise steps, respectively, to provide statistical significance at the 0.05 level for a two-sided test at 80% power.

Conclusions: Both device sensitivity and location on the body affect step counts, with location having a stronger effect. Wearing the sensor on the torso may be the most accurate measurement. The power analysis demonstrates that the P measurement of changes in either total or exercise steps can demonstrate statistical significance with relatively small sample sizes.
ABSTRACT P03

*Antiviral Therapy* 2019; 24 Suppl 1:A40

Pilot study assessing the Rotterdam Healthy Aging Score in a cohort of HIV-positive adults

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1University Health Network; 2University of Toronto, Canada; 3 Biostatistical Research Unit; 4 Toronto General Hospital Research Institute

**Purpose:** A standard measure of healthy ageing would enable identification of factors predictive of health and facilitate evaluation of interventions. The Rotterdam Healthy Aging Score (HAS) is a validated multidimensional index constructed from five health domains (mental health, cognitive function, physical function, social support and quality of life). We describe the HAS distribution among a cohort of HIV-positive adults.

**Methods:** A prospective pilot study of 100 adults attending a tertiary HIV clinic, aged ≥40 on cART with suppressed HIV RNA. Participants completed questionnaires to calculate the HAS (range 0–14). Demographics, HAS and domain scores were compared by age and sex using the Kruskal–Wallis rank-sum or Fisher’s exact test.

**Results:** Median (IQR) age was 56 (50–62), 81 (81%) were male, and 50 (51.5%) born in Canada. Participants aged ≥61 were more often Caucasian (75%) compared with those 40–50 (47%) and 51–60 (59%; \(P=0.056\)). Women were more often Black (53%) compared with men (9%; \(P<0.001\)). Participants ≥61 had longer HIV duration (25y; \(P=0.001\)) and lower CD4 nadir (152 cells/mm\(^3\); \(P=0.05\)) compared with 40–50 (16y, 267 cells/mm\(^3\)) or 51–60 (22y, 190 cells/mm\(^3\)). Median (IQR) CD4 was 574 (417–790) cells/mm\(^3\). Median (IQR) HAS was 12 (10–13) and 38 (38.4%) achieved a score >12 (considered healthy ageing). HAS did not vary by age group (\(P=0.72\)) or sex (\(P=0.49\)). Younger participants were more likely to have low mental health scores (27% for age 40–50 and 27% for age 51–60) compared with those ≥61 (6%; \(P=0.04\)). Women were more likely to have low pain scores (that is, experience greater pain, 16%) compared with men (1%; \(P=0.02\)).

**Conclusions:** HAS scores ranged from 4–14 in this cohort of older treated HIV adults with 38% attaining the ‘healthy’ range. The HAS requires further study for its ability to discriminate health outcomes and determine health domains that dominate poor scores.
ABSTRACT P04

Antiviral Therapy 2019; 24 Suppl 1:A41

Multimorbidity in elderly subjects according to year of diagnosis of HIV-infection – a cross-sectional DATAIDS Cohort Study

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Background: The number of people ageing with HIV is growing. We assessed prevalence of multimorbid­ity (MM) according to year of HIV diagnosis in an HIV geriatric population.

Methods: We performed a cross-sectional study of MM involving patients from the Dat’AIDS French multicentric cohort, selecting patients over 70 years old. MM was defined as at least 3 concomitant comorbidities including either high blood pressure, diabetes mellitus, osteoporosis, non-AIDS cancer, chronic renal failure, cardio and cerebrovascular disease, obesity, cachexia or hypercholesterolaemia. We defined three groups of HIV-diagnosis period: between 1983 and 1996, 1997–2006 and 2007–2018. Logistic regression models evaluated the association between MM and predictors, including calendar period of HIV-diagnosis. A secondary analysis evaluated MM as a continuous outcome and a sensitivity analysis excluded subjects with less than 200 cells/mm³.

Results: Starting 1 January 2017 and ending on 29 September 2018, 2,476 patients were included. Median age was 73 years old, 75% were men. MM prevalence was 71% in our population (median number of comorbidities three). High blood pressure and hypercholesterolaemia were the most prevalent comorbidities. After adjustment for age, gender, smoking status, HCV, HBV coinfection, group of exposure, nadir CD4, and CD4/CD8 ratio, association between MM and calendar period of diagnosis was not statistically significant (P=0.169). MM was significantly associated with older age, CD4/CD8 ratio <0.8 and nadir CD4 cells <200 cells/ml. Similar results were found with secondary and sensitivity analysis.

Conclusions: In this study of elderly persons living with HIV, MM prevalence was high and increased with age, low CD4/CD8 ratio and nadir CD4 cells <200 mm³ but was not associated with calendar period of HIV-diagnosis. Duration of HIV-diagnosis should not be a criteria for selecting a population at risk of MM.
ABSTRACT P05

Antiviral Therapy 2019; 24 Suppl 1:A42

Immune activation and chronic inflammation: is there an additional effect of HIV in a geriatric population?

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Introduction: HIV infection has become a chronic disease, with a lower mortality, but a consequent increase in age-related non-infectious comorbidities. Metabolic disorders have been linked to the effect of combined antiretroviral therapy as well to the effects of immune activation and chronic inflammation. Whereas it is known that ageing is intrinsically associated with hyper-inflammation and immune system deterioration, the relative impact of chronic HIV infection on such inflammatory and immune activation has not yet been studied on an ageing HIV-infected population.

Objectives and methods: The objectives were to assess blood markers of immune activation and inflammation, using ultrasensitive techniques (Luminex & Simoa), in HIV-infected patients aged 75 years and older with no or one comorbidity (hypertension, renal disease, neoplasia, diabetes mellitus, cardiovascular disease, stroke, dyslipidaemia and osteoporosis), in comparison with age-adjusted HIV-uninfected individuals aged 75 years and older (control group), to identify whether biomarkers were associated with comorbidities. 28 inflammatory and immune biomarkers were performed in a centralized laboratory (INSERM U1135, Paris). Wilcoxon non-parametric tests were used to compare the levels of each biomarkers between control and HIV+ groups; logistic regression to identify biomarkers associated with comorbidity in the HIV+ group and principal component analysis (PCA) to determine clusters associated with a group or a specific comorbidity.

Results: 111 HIV+ subjects of whom 39 without comorbidity with a median age of 81 years (IQR 78–84) and a median duration of HIV infection and antiretroviral therapy of 18.2 (12–23) and 15.9 (9–19) years, respectively, were included from the Dat’AIDS cohort and compared with a control group of 63 HIV-negative subjects (median age of 83.4 years [IQR 78–89]). In the HIV+ group, four biomarkers were associated with the risk of comorbidity: MCP-1 OR (CI 95%) 0.78 (0.68, 0.91), NFL 1.42 (1.08, 1.87), neopterin 1.99 (1.33, 2.97) and sCD14 1.01 (1.00, 1.02). Six biomarkers (IL-1B, IL-7, IL-18, neopterin, sCD14 and FABP) were significantly higher in the HIV+ group compared with the control group, 11 biomarkers (MPO, IL-1RA, TNFR1, IFN gamma, MCP-1, TNF-R2, IL-22, usCRP, fibrinogen IL-6 and NFL) were lower. Despite those differences, PCA analysis did not reveal clustering between healthy control and HIV-infected patients. Similarly, PCA did not discriminate between the absence or the presence of comorbidity within HIV+ group.

Conclusions: No specific inflammatory or immune profile has been identified in HIV+ group according to comorbidity status. In this highly selected geriatric HIV population, HIV infection does not seem to have an additional impact on age-related inflammation and immune disorder. In the ageing HIV population, prevention and treatment of comorbidities could have limited both immune activation and inflammation. In order to validate this preliminary hypothesis, other studies need to be performed on a larger number of geriatric HIV-infected subjects.
Objective: Frailty is a geriatric syndrome characterized as a state of diminished reserve and increased vulnerability to stressors due to dysregulation in multiple physiological systems. More HIV-infected persons are experiencing ageing-related diseases, including frailty, with the introduction of highly active antiretroviral therapy (HAART). Vitamin D deficiency, which has been linked to increased comorbidities such as osteoporosis and metabolic syndromes, may interfere with immune restoration following HAART and accelerate the onset of frailty in HIV-infected populations. We examined the association between vitamin D and frailty among HIV-infected men from the Multicenter AIDS Cohort Study.

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

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

Conclusions: Vitamin D deficiency was not associated with transitions to frailty, while the active vitamin D metabolite, 1,25(OH)2D, captured an increased risk of becoming frail among non-frail men. Risk factors contributed in varying degrees to increase or decrease the risk of transitions into frailty, consistent with prior work.
ABSTRACT P07

*Antiviral Therapy* 2019; 24 Suppl 1:A44

CD4/CD8 ratio is a better indicator of acute phase inflammation than absolute CD4 count during virally suppressed HIV infection

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**Purpose:** Life expectancy of treated HIV infection approaches that of the general population. Persistent increased mortality and non-AIDS comorbidity is driven by residual immune activation/inflammation. Absolute CD4 count (CD4 count) and CD4/CD8 ratio (CD4/CD8) both correlate with poorer clinical outcomes in prospective cohorts. We sought to identify which parameter best correlates with biomarkers of acute phase immune activation.

**Methods:** We enrolled 83 consenting ART-treated HIV-positive participants with viral load suppression and diverse CD4 count and CD4/CD8 responses from a tertiary care HIV site in Toronto, Canada. In a cross-sectional study, blood plasma and peripheral blood mononuclear cells were isolated and stored for batched measurement of soluble immune activation markers by ELISA (CRP, TNF, IFNγ, sCD14, D-Dimer, I-FABP, MCP-1, VCAM, ICAM), and co-expression of HLA-DR and CD38 on CD8 T-cells (CD8 activation). Multiple log-linear regression models adjusted for age, sex, duration of ART and recent infection/vaccination were used to estimate the association of each outcome with: (1) CD4 count and (2) CD4/CD8.

**Results:** CD4 count and CD4/CD8 were strongly correlated (0.76; P<0.0001). A 0.1 increase in CD4/CD8 was associated with a 3% decrease in plasma TNF (P<0.01) and a 5% decrease in plasma CRP (P=0.05). Higher CD4 count (per 100 cells/mm³) was associated with a 2% decrease in sCD14 (P=0.02) while no association was observed with plasma TNF or CRP levels. Neither CD4 count nor CD4/CD8 were associated with CD8 activation.

**Conclusions:** CD4/CD8 and CD4 count are strongly linked, but CD4/CD8 correlates more strongly with two soluble markers of acute phase immune activation (TNF, CRP). CD4 count was more strongly associated with a marker of a distinct immune activation pathway (sCD14; TLR4 activation by LPS). Novel therapies to reduce non-AIDS comorbidity by targeting residual immune activation pathways warrant exploration in the context of persistently low CD4/CD8.
Introduction: Despite significant gains in lifespan due to antiretroviral therapy (ART) use, people living with HIV (PLWH) experience higher risk for age-related comorbidities compared with HIV-uninfected adults. In particular, frailty presents at a higher prevalence and earlier age in PLWH compared with the general population. PLWH age 50–65 in the CNICS cohort had a physical function status equivalent to 80+ year old adults without HIV. Nutrition interventions, specifically additional dietary protein for muscle maintenance, may reduce frailty risk in this vulnerable population, but PLWH have unique nutrition requirements that could impact the role of nutrition in disease prevention. Our objective was to determine how dietary factors may influence the frailty status of PLWH.

Methods: As part of the multisite, observational PROSPER-HIV study, adults (≥18 years) living with HIV, who are on HIV antiretroviral therapy, are virally suppressed, and part of the CNICS cohort completed three (two weekdays and one weekend) 24-h diet recalls. Dietary data were analysed using NDSR Nutrition Analysis Software to determine average consumption of dietary protein (g/day) and omega-3 fatty acids (g/day). Frailty risk was assessed using the following measures of physical function: hand-grip strength of the dominant hand (measured using the Jamar Hand grip Dynamometer); 5-time repeated sit/stand chair test; and the Short Physical Performance Battery (SPPB) consisting of timed gait speed, repeated chair stands, and balance tests, each assigned with a score 0–4. SPPB summary scores ranged 0 (frail) to 12 (not frail). Models were adjusted for age and present gender of participants.

Results: To date, 170 PLWH have been enrolled in the PROSPER-HIV study. Participants’ mean age was 53.5 years; 65% self-reported Black race; 26% were female; 1% transgender. Mean waist and hip circumferences were 101.9 cm and 106.3 cm, respectively. Participants consumed an average 78 g/day dietary protein, well below the recommended daily consumption of 1.2 g/kg/body weight. Mean hand grip strength was 33.1 ±11.4 kPa; and participants completed the chair sit/stand test in 11.9 ±3.8 s. The majority scored as non-frail (score 10–12) on the SPPB test. After controlling for age and present gender, higher dietary protein intake was correlated with hand grip strength (r=0.28; P<0.01). No association was observed with chair sit/stand testing or overall SPPB performance.

Conclusions/discussion: In this cross-sectional analysis, dietary protein intake was associated with hand grip strength, a marker of frailty risk, among PLWH. Future investigations, including the 5-year PROSPER-HIV study, should include longitudinal assessments of dietary protein intake and physical function status to determine whether protein intake influences frailty risk over time, and what dose of dietary protein is needed to maintain adequate physical function status among PLWH.

Acknowledgements: This study was supported by research grants from the National Institute of Nursing Research (5R01NR018391) and from the National Institute of Allergy and Infectious Diseases (R24AI067039).
ABSTRACT P09
Antiviral Therapy 2019; 24 Suppl 1:A46
Failure to restore CD4 cell count with combination antiretroviral therapy is associated with increased systemic inflammation

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Purpose: Systemic immune activation is thought to drive non-AIDS comorbidity despite suppressive antiretroviral therapy (ART). Immunological non-responders (INR) do not restore blood CD4 T-cells to >350/mm³. We sought to characterize the inflammatory profile of INRs, including the level of T-cell activation and inflammation-associated soluble markers linked to non-AIDS comorbidity. We hypothesized that co-expression of HLA-DR and CD38 on CD8 T-cells (CD8 activation) would be elevated in INRs.

Methods: 101 consenting adults were enrolled in a cross-sectional study at HIV care sites in Toronto, Canada. Virally suppressed HIV-positive participants were categorized as INR (n=36), or CD4 restorers (CR); >350/mm³; n=47). An HIV-negative group was included (n=18). Peripheral blood mononuclear cells and blood plasma were cryopreserved before measurement of T-cell activation by flow cytometry (co-expression of HLA-DR and CD38) and soluble immune activation-related markers by ELISA (CRP, TNF, IFNg, sCD14, D-Dimer, I-FABP, MCP-1, VCAM, ICAM). Multiple log-linear regression models were used to estimate the association between INR phenotype and markers after adjusting for age, sex, duration of ART and recent infection/vaccination.

Results: HIV-positive individuals had median (IQR) infection 16 (9–26) years, and ART duration 12 (6–21) years, with no difference between groups. In adjusted log-linear regression models, INRs had 35% higher CD8 activation (P=0.02), 54% higher CD4 presentation of HLA-DR (P<0.001), and 20% higher plasma VCAM (P<0.01) compared with CRs. HIV-positive individuals had higher median (IQR) CD8 (2.96 [1.88–4.46]) compared with HIV-negatives (1.82 [1.17–2.81]; P<0.01).

Conclusion: INRs, compared with CRs (and controls), had higher disease-associated CD8 activation that could be assessed as a target of intervention to improve outcomes. VCAM (marking endothelial activation) and CD4 activation were elevated amongst INRs and require exploration as prognostic indicators.
ABSTRACT P10
Antiviral Therapy 2019; 24 Suppl 1:A47

Fitness tracking wearable devices and a dedicated smart phone app (MySAwH App) to predict quality of life in PLWH: a multi-centre prospective study

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

Methods: We included 261 PLWH who were recruited from Italy (128), Australia (100) and Hong Kong (33). Two scheduled visits were performed, at baseline and follow-up (9 months). Frailty index was measured with a 36-item FI which objectively detect the presence of health deficits, while 27-item IC index was self-assessed with fitness tracking wearable devices and a MySAwH app. Outcome variables were QOL and health score (HS), using EQ5D5L questionnaire.

Results: Mean age was 56.9 years; 88% patients were men. Median CD4 was 657 c/µl (480–817 IQR) and 98% of patients had undetectable HIV viral load. Mean FI at baseline and follow-up were 0.22 (±0.1 sd) and 0.20 (±0.09 sd), respectively, P<0.001. Mean IC at baseline and follow-up were 0.69 (±0.12 sd) and 0.71 (±0.12 sd), P=0.27. Median QOL at baseline and follow-up were 0.88 (0.8–1 IQR) and 0.90 (0.83–1 IQR), P<0.03. Mean HS at baseline and follow-up were 7.6 (±1.68 sd) and 7.63 (±1.56 sd), P<0.001. In a multivariate logistic model, positive predictors for a good health status at follow-up were IC at baseline (OR=6.74, 3.86–11.77) and recruitment site (Hong Kong [OR=1.25, 1.01–1.54]). Positive predictors for QOL at follow-up were IC at baseline (OR=7.62, 4–14.51) and recruitment site (Hong Kong [OR=1.33, 1.05–1.69]).

Conclusions: Utilizing MySAwH with smart phone technology, FI and IC are performative tools that can be used in research and clinical setting to describe, respectively, disease and health status in PLWH. IC score in comparison to FI displayed higher sensitivity to predict both QOL and self-perceived health in PLWH.
Fighting fat in HIV: the role of physical activity in the modern HIV era

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Background: Throughout the world, people living with HIV (PWH) are living longer and developing chronic comorbidities at higher rates than those without HIV infection. Ageing is associated with increased abdominal adiposity, which is also a risk factor for chronic comorbidities including cardiovascular disease, diabetes mellitus, chronic kidney disease and frailty. Additionally, PWH are at high risk for increased adiposity. In the general population, few interventions can improve adiposity in an ageing population as well as physical activity. The relationship between physical activity and adiposity in people living with well-controlled HIV is unclear. The purpose of this study is to describe the association between objectively-measured physical activity and abdominal adiposity (that is, waist circumference and waist-hip ratio) in PWH.

Methods: As part of the multisite, observational PROSPER-HIV study, adults (≥18 years) living with HIV, who are on HIV antiretroviral therapy, are virally suppressed, and part of the CNICS cohort wore an Actigraph accelerometer for 7–10 days and completed duplicate, standardized measures of waist and hip circumference at one time point. Valid accelerometer data included those who wore the device for ≥10 h a day for a minimum of 4 days (that is, 1 weekend day and 3 weekdays). Physical activity intensities were classified using 2011 cut points. Demographic and medical characteristics were abstracted from the CFAR Network of Integrated Clinical Systems (CNICS) dataset. Descriptive statistics and multiple linear regressions were used to analyse the data.

Results: To date, 175 PWH have been enrolled in the PROSPER-HIV study. On average, they are 52.9 years of age (±10.5), male (68%), and Black or African American (68%). Over a week, on average, participants engaged in 37.35 (±67.78) min of moderate-to-vigorous physical activity and had an average of 13,764 (±5,482) steps per day. Participants also had 415 (±183) min of sedentary time per day. Mean waist circumference was 102.4 cm (±16.1) and the mean waist-to-hip ratio was 0.96. Controlling for age and sex, the number of steps taken per day was associated with reduced abdominal adiposity (β=-75.4; P=0.030). Relationships between moderate-vigorous physical activity, sedentary time per day and measures of abdominal adiposity were not observed (P>0.05).

Conclusions: These data suggest that physical activity reduces abdominal adiposity in ageing PWH. In particular, increasing the number of steps per day is likely an acceptable early physical activity intervention in a mostly sedentary population. Future work should investigate how to precisely tailor the amount, type and intensity of physical activity needed to reduce adiposity and, in turn, related comorbidities in PWH.

Acknowledgements: This study was supported by research grants from the National Institute of Nursing Research (5R01NR018391) and from the National Institute of Allergy and Infectious Diseases (R24AI067039).
ABSTRACT P12

*Antiviral Therapy* 2019; 24 Suppl 1:A50

Weight gain in people living with HIV switched to dual therapy with dolutegravir plus rilpivirine: changes in body fat mass

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Objectives: We investigated changes in weight and body composition, and associated factors, in virologically suppressed HIV-infected adults switching to a dolutegravir-based dual therapy.

Methods: Weight, fat mass and lean mass were measured in a prospective cohort of HIV-infected individuals switching to dolutegravir-based dual therapy using whole-body dual-energy X-ray absorptiometry (DXA; NCT02491242). Data were compared with a control group of HIV-infected adults switched to boosted darunavir-based dual therapy. Individuals with lipodystrophy, or prior exposure to integrase inhibitors were excluded.

Results: Overall, 54 individuals met the inclusion criteria (mean age 53 years, male 61%), 37 (69%) switched to dolutegravir plus rilpivirine and 17 (31%) switched to darunavir plus lamivudine. At baseline, median weight was 73 kg (standard deviation, sd 14.7) and 70 kg (sd 13.1) in the dolutegravir and darunavir group, respectively (P=0.14). After 48 weeks, weight increased by 1.80 kg (sd 3.8, +2.5%; P=0.03) in the dolutegravir group and 0.70 kg (sd 3.9; +1%; P=0.28) in the darunavir group, without significant differences between groups (P=0.45).

After a median of 16 months (IQR 11.1–22.6) of switching, DXA scan exhibited similar increases in median fat mass in trunk, arms and legs in both groups (Table 1). Fat mass ratio was unaltered, and there were no significant changes in lean mass or muscle-related index in any group. In adjusted multivariable linear regression analysis, total fat mass increase was associated with baseline fat mass (Beta, -0.19, 95% confidence interval, CI: -0.08, -0.30) and nadir CD4+ count (Beta, -0.006, 95% CI: -0.0001, -0.012).

Conclusions: Weight gain observed with dolutegravir plus rilpivirine dual therapy was significant and was related with fat mass gain in the different body compartments, with no modifications of lean mass. Nevertheless, comparable changes were observed in individuals switching to darunavir plus lamivudine. Fat mass increase was associated with baseline fat mass and immunological status.

Table 1. Changes in body fat mass (Abstract P12)

<table>
<thead>
<tr>
<th></th>
<th>Dolutegravir plus rilpivirine</th>
<th>Boosted darunavir plus lamivudine</th>
<th>P-value</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>(n=37)</td>
<td>(n=17)</td>
<td></td>
</tr>
<tr>
<td>Total fat mass [%], median (SD)</td>
<td>31.7 (8.2)</td>
<td>25.6 (8.4)</td>
<td>0.13</td>
</tr>
<tr>
<td>− Median change in percentage (IQR)</td>
<td>+1.1 (0.2-7.5)</td>
<td>+1.7* (-0.5, 3.8)</td>
<td>0.69</td>
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<tr>
<td>Trunk fat mass [%], median (SD)</td>
<td>32.8 (9.1)</td>
<td>25.6 (8.4)</td>
<td>0.07</td>
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<tr>
<td>− Median change in percentage (IQR)</td>
<td>+1.4* (-0.3, 3.8)</td>
<td>+1.85* (-0.1, 4.1)</td>
<td>0.57</td>
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<tr>
<td>Arms fat mass [%], median (SD)</td>
<td>35.3 (12.2)</td>
<td>26.1 (12.2)</td>
<td>0.05</td>
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<tr>
<td>− Median change in percentage (IQR)</td>
<td>+1.45* (-0.9, 3.87)</td>
<td>+2.45* (0.2-5.1)</td>
<td>0.22</td>
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<tr>
<td>Legs fat mass [%], median (SD)</td>
<td>28.2 (9.2)</td>
<td>26.5 (10)</td>
<td>0.67</td>
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<td>− Median change in percentage (IQR)</td>
<td>+1.2* (-0.55, 2.6)</td>
<td>+0.7 (-0.4, 4.9)</td>
<td>0.72</td>
</tr>
</tbody>
</table>

*P<0.05, Wilcoxon rank test
ABSTRACT P13

Antiviral Therapy 2019; 24 Suppl 1:A51

Body composition changes in HIV: do INSTI matter?

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Objectives: The aim was to assess weight gain (WG) and body composition changes in people living with HIV (PLWH) switching to INSTI-based regimens in comparison to INSTI-naive patients. We assessed WG impact on incidence of comorbidities.

Methods: In a prospective observational study, we included ART-experienced INSTI-naive PLWH from 2007 to 2019. Patients were divided in two groups: patients who remained INSTI-naive and patients who switched to an INSTI regimen either in 3 drugs regimens (3DR) or in 2 drug regimens (2DR). The groups were matched for sex, age, baseline BMI and switch duration. WG was defined as an annualized increase of 7% in BMI. Predictors of WG were analysed in a multivariable regression model comparing INSTI-naive 3DR to INSTI-naive 2DR, and patients who switched to INSTI either in 3DR or 2DR.

Results: A total of 1,158 PLWH (68.7% males) were analysed at baseline and at 4 years (±2.23) follow-up. Patients who switched to INSTI showed significant changes in age, BMI, waist circumference (WC), fat-free mass index (FFMI), appendicular skeletal muscle index (ASMI) and leg fat % (P<0.001). Mixed lipodystrophy, visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT) did not change over time. INSTI-naive showed significant changes in age, BMI, WC, FFMI, ASMI, leg fat %, sarcopenia, VAT and SAT.

Figure 1. (Abstract P13)

Multivariate logistic regression — weight gain defined as increase of BMI>7%

Lipodystrophy

ASMi

never INSTI 2DR

INSTI 3DR

INSTI 2DR

Lum BMD

BMI

Waist

Gender Male

Age

OR

0.21 (0.02-2.2) 0.2

1.02 (0.86-1.2) 0.81

0.98 (0.93-1.04) 0.5

0.75 (0.35-1.61) 0.46

0.95 (0.91-0.99) 0.01

1.12 (0.56-2.41) 0.76

0.82 (0.6-1.12) 0.21

2.08 (0.57-6.14) 0.22

2.61 (1.28-5.43) 0.01

3.14 (1.46-6.82) <0.01

A51
Higher prevalence of WG was observed in patients who switched to INSTI (68.9% versus 31.2%; $P<0.001$). Figure 1 describes independent predictors of WG. PLWH who experienced WG had higher incidence of T2DM (1.97 versus 1.22), CVD (1.67 versus 0.53), HTN (13.2 versus 7.07), CKD (6.82 versus 3.49), COPD (3.4 versus 1.06) cases per 100 patient-years, with the latter being the only statically significant. 

Conclusions: We observed WG both in 3DR and 2DR in INSTI-based switch. Clinical relevance of this phenomenon needs to be explored in larger cohorts.
ABSTRACT P14

Antiviral Therapy 2019; 24 Suppl 1:A53

NRTI backbone modification impact on weight, lipids and cardiovascular risk

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Purpose: Switch from tenofovir disoproxil fumarate (TDF) to tenofovir alafenamide (TAF) may be associated with weight gain and worsening of lipid profile. It is unclear if this is related to loss of protective effect of TDF or an effect of TAF. The impact of these findings on cardiovascular risk (CVR) has not been specifically investigated.

Method: This is a retrospective data collection from clinical notes of people living with HIV, switched to TAF-based antiretroviral treatment at Chelsea and Westminster Hospital, London, without changing other regimen components. Body weight, lipid profile, blood pressure were measured and CVR scores (QRisk2-2017 and Framingham) calculated before and every 12–24 weeks after the switch.

Results: 274 patients were included in the analysis: 216 switched from TDF (group 1) and 58 switched from non-TDF-containing regimens to TAF (group 2). Mean (sd) age was 59 ± 9.9 years, 88.7% were male, 75.2% Caucasian, with a BMI of 23.95 ± 4.6 kg/m² and CD4 count of 682 ± 300 cells/μl at switch. Overall, weight increase 1 year post-switch to TAF was 1.7 ± 6.8 kg. Statistically significant weight and cholesterol increases from baseline were observed in group 1 (1.4 ± 5.6 kg, P=0.02 and 0.3 mmol/l ± 1.0, P<0.05). 1 year after the switch to TAF the proportion of subjects with BMI > 25 kg/m² had risen by 10%. In a logistic regression analysis the odds of having a BMI increase >10% was associated with older age (odds ratio: 0.9; 95% CI [0.9, 1.0]; P=0.02); CD4 < 200 cells/μl (P=0.04) and smoking (P=0.04). QRisk2-2017 and Framingham scores remained stable (P=0.0997 and P=0.17) with no changes observed from baseline to 1-year post-switch.

Conclusions: Our real-world analysis suggests that weight and lipid increases may relate to switching away from TDF rather than the independent effect of TAF, however, long-term data in larger populations are warranted.
ABSTRACT P15

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Predictors of sarcopenia and its impact on components of the frailty phenotype in an Asian population living with HIV

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Objectives: We aimed to study the prevalence and predictors of sarcopenia in people living with HIV (PLWH) in Asia. The impact of sarcopenia on the components of frailty phenotype is explored in this population.

Methods: We performed a prospective observational cohort study. Adult HIV-infected patients aged ≥18 years, followed in an HIV metabolic clinic in Hong Kong were enrolled. Clinical data was collected. Dual-energy X-ray absorptiometry (DXA) scan was performed to measure body composition. Sarcopenia was defined by appendicular skeletal muscle index/ASMI (lean mass of extremities/height2) <7.0 kg/m2 in men and <5.4 kg/m2 in women according to recommendations by the Asian Working Group for Sarcopenia. The Fried frailty phenotype (unintentional weight loss, exhaustion, low physical activity, and diminished gait speed and grip strength) was assessed in a subgroup of this cohort. Multivariable binary logistic regression model was performed to determine predictors of sarcopenia. The association of sarcopenia with each component of frailty phenotype, and the association between number of deficits in frailty phenotype and ASMI were determined by Chi square and one-way ANOVA, respectively.

Results: 251 PLWH were enrolled. Mean ±sd age was 52 ±13 years, 209 (83.3%) were male and 233 (92.8%) were Chinese. The duration of HIV diagnosis was 7 (IQR 1–13) years, 83 (33.1%) had history of AIDS, median (IQR) CD4 was 490 (215–705) cells/mm3. Diabetes was present in 77 (30.7%), hypertension in 88 (35.1%), hepatitis B in 27 (10.8%) and hepatitis C in 13 (5.2%). In this cohort, 105 (41.8%) had sarcopenia. Sarcopenia was more prevalent in Chinese, and those with hepatitis B, hepatitis C, history of AIDS, lower CD4 count, lower CD4:CD8 ratio, higher HIV RNA, lower body weight and exposure to stavudine (Table 1). Sarcopenia was not associated with age or sex. Multivariable logistic regression model showed sarcopenia was independently associated with Chinese ethnicity (adjusted odds ratio [aOR] 6.2 [95% CI 1.0, 39.1]), hepatitis B (aOR 4.9 [95% CI 1.6, 15.7]), body weight (aOR 0.87 [95% CI 0.84, 0.91]) and exposure to stavudine (aOR 2.4 [95% CI 1.1, 5.4]).

In a subgroup of 142 PLWH, 74 (52.1%) were pre-frail and 8 (5.6%) were frail. Among the five components of frailty phenotype, sarcopenia was associated with weak hand grip (39.4% versus 13.7%; P=0.001), low physical activity (24.2% versus 10.7%; P=0.032) and weight loss (21.9% versus 8.2%; P=0.024). A significant reduction of ASMI was observed with increasing number of deficits in the frailty phenotype (for example, 7.5 ±1.1 versus 5.7 ±1.3 kg/m2 in those with none and four deficits; P=0.001).

Table 1. (Abstract P15)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Sarcopenia</th>
<th>No sarcopenia</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chinese</td>
<td>103 (98.1%)</td>
<td>130 (89.0%)</td>
<td>0.006</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>17 (16.2%)</td>
<td>10 (6.8%)</td>
<td>0.018</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>10 (9.5%)</td>
<td>3 (2.1%)</td>
<td>0.008</td>
</tr>
<tr>
<td>History of AIDS</td>
<td>42 (40.0%)</td>
<td>41 (28.1%)</td>
<td>0.048</td>
</tr>
<tr>
<td>CD4 count, cells/mm³</td>
<td>423 [250-670]</td>
<td>533 [359-731]</td>
<td>0.007</td>
</tr>
<tr>
<td>CD4:CD8 ratio</td>
<td>0.54 [0.31-0.81]</td>
<td>0.70 [0.43-0.95]</td>
<td>0.016</td>
</tr>
<tr>
<td>HIV RNA, copies/mL</td>
<td>40 [40-68]</td>
<td>40 [20-40]</td>
<td>0.002</td>
</tr>
<tr>
<td>Body weight, kg</td>
<td>58.1±8.0</td>
<td>71.4±13.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Exposure to stavudine</td>
<td>26 (24.8%)</td>
<td>20 (13.7%)</td>
<td>0.025</td>
</tr>
</tbody>
</table>
Conclusions: In an Asian cohort of PLWH, sarcopenia was present in 42% and was associated with Chinese ethnicity, hepatitis B, low body weight and exposure to stavudine. Sarcopenia was associated with components of the frailty phenotype.
ABSTRACT P16

*Antiviral Therapy* 2019; 24 Suppl 1:A56

Body size modifies the relationship between internalized HIV stigma and pain in people with HIV in the southeastern USA

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**Background:** Both pain and obesity have emerged as common comorbidities in the context of HIV. Meanwhile, HIV-related stigma poses a significant barrier to improving health outcomes for people with HIV, with research supporting an association between internalized HIV stigma and pain. Extant research suggests obesity is also associated with pain but may interact with other variables in its association. In the present analysis, we investigated the role of body size as a moderator of the association between internalized HIV stigma and experiences of pain.

**Methods:** Participants included 180 men and women with HIV who were not currently using substances and completed measures during a study visit at an HIV primary clinic located in Birmingham, Alabama. Internalized HIV stigma was measured using the self-stigma subscale of the revised HIV Stigma Scale. Height and weight measures were collected for computation of BMI. BMIs were categorized as ‘healthy weight’ (BMI=18.5–24.9), ‘overweight’ (BMI=25–29.9) and ‘obese weight’ (BMI=30+). Only two participants had underweight (BMI<18.5) and were omitted from the analysis.

![Figure 1. Interaction between BMI category and internalized HIV stigma on acute bodily pain among people with HIV, with age, sex, race, socioeconomic status, and time on antiretroviral medications as covariates.](image-url)
analysis. Current pain was reported 1 week following initial study measures using a numerical rating scale from 0: ‘no pain’ to 10: ‘worst imaginable pain’. Model covariates included participant age, sex, race, sexual orientation, socioeconomic status and time on antiretroviral medications in months.

**Results:** Of the participants, 31% were in the healthy weight range, 39% were in the overweight range and 30% were in the obese weight range. In the multivariable model, both internalized HIV stigma and BMI category were positively associated with pain. The interaction of stigma with weight category was significant (B=-1.02, SE=0.45, 95% CI [-1.90, -0.13]). Upon examination of simple slopes, individuals with lower BMI had a positive association between internalized HIV stigma and pain (B=1.48, SE=0.55, 95% CI [0.40, 2.56]). Internalized HIV stigma was not associated with pain for people in the overweight range (B=0.46, SE=0.36, 95% CI [-0.24, 1.17]) or the obese weight range (B=-0.55, SE=0.60, 95% CI [-1.73, 0.62]). Significant covariates associated with pain included female sex and lower socioeconomic status. See Figure 1.

**Conclusions:** Our findings provide further evidence that internalization of negative societal attitudes regarding HIV relate to greater perceptions of bodily pain. However, that association may depend on body size and composition. Further research is needed to understand individuals’ perceptions of body size in relation to HIV stigma, which can inform health communication for patients with HIV managing their weight or pain.
ABSTRACT P17

Antiviral Therapy 2019; 24 Suppl 1:A59

Discordance in diagnosis of osteoporosis in HIV-infected patients: prevalence, characteristics and impact on FRAX equation

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Objective: We examined the prevalence and characteristics of people living with HIV (PLHIV) with spine-hip bone mineral density (BMD) measurement discordance.

Methods: Cross-sectional study of consecutive PLHIV included after whole-body dual X-ray absorptiometry (DXA) scan. BMD categories of osteoporosis, osteopenia and normal bone mass were defined as T-scores ≤-2.5, -2.5 to 1.0 and >-1.0, respectively. Discordance was defined as different BMD categories at lumbar spine (LS) and femoral neck (FN): major discordance in the case of osteoporosis versus normal BMD, and minor discordance in the case of osteoporosis versus osteopenia, or osteopenia versus normal BMD.

Results: Of a total of 208 PLHIV (mean 46 years, women 23%), 91 (44%) presented BMD discordance (major discordance, 2%; minor discordance, 42%); similar values were observed in individuals aged under and over 50. Discordance due to lower LS-BMD was more frequent, and 81% (30/37) of individuals with LS osteoporosis had discordance. Conversely, of 10 cases of FN osteoporosis, 43% were missed from measurements at the LS. Individuals with BMD discordance had distinctive characteristics: PLHIV with lower FN-BMD had a significantly higher prevalence of smoking (P=0.01), lipodystrophy (P=0.03) and HCV co-infection (P=0.04), and longer duration of HIV infection (P=0.04) and antiretroviral therapy (P=0.01) than

Figure 1. Fracture risk in patients with discordance according to the site of lower bone mineral density (Abstract P17)
individuals with lower LS-BMD. Moreover, the risk of major osteoporotic and hip fracture was significantly higher in PLHIV with lower FN-BMD versus lower LS-BMD (+36%, \( P=0.04 \), and +135%, \( P<0.01 \), respectively; Figure 1).

**Conclusions:** BMD measurement discordance was observed in 44% of PLHIV, largely due to lower LS-BMD. BMD measurement at a single site underestimates the prevalence of osteoporosis, as over 80% of cases of LS osteoporosis were not reflected by FN-BMD. HIV-related factors contribute to lower FN-BMD and in part, to discordance. Fracture risk estimation by FRAX was higher for PLHIV with discordant results.
**ABSTRACT P18**

*Antiviral Therapy* 2019; 24 Suppl 1:A61

Menopause in ageing women living with HIV: changes in bone mineral density and trabecular bone score

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**Objective:** HIV infection and tenofovir disoproxil fumarate (TDF)-containing antiretroviral regimens alone or in association with boosted protease inhibitors are associated with impaired bone quality and quantity and high fracture risk. Bone loss has never been studied across the menopausal transition in women living with HIV (WLWH). The aim of the study was to describe pattern of bone quantity (lumbar bone mineral density [BMD]) and bone quality (trabecular bone score [TBS]) changes across menopause in WLWH undergoing ART with or without TDF.

**Methods:** We conducted a longitudinal retrospective study including WLWH attending Modena HIV Metabolic Clinic from 2012 to 2019. The observation period was divided into reproductive, transitional, early and late menopause according to STRAW criteria. Lumbar BMD and TBS derived from DEXA evaluation. GEE models were built to predict changes in BMD and TBS across menopause and TDF or TDF+PI/c/r containing ART regimens.

**Results:** We included 185 (mean age =49.3 years) ART-experienced women observed for a median of 6.08 years. 134 observations were assessed in the ‘Reproductive Period’, 180 in the ‘Menopause Transition Period’, 185 in the ‘Early Menopause Period’ and 20 in the ‘Late Menopause Period’, for a total of 519 DEXA observations. At baseline, median duration of HIV infection was 244 months, median CD4 cell count was 635 cells/μl. Across menopause, LDL, HDL, CRP, vitamin D and PTH significantly increased, while ASMI, FFMI, lumbar BMD, TBS score and FRAX® score worsened (P<0.001). In GEE models, independent predictors of BMD and TBS changes were time from menopause and calcium concentration; waist circumference was positively correlated with BMD and negatively correlated with TBS. TDF and PI/c/r were not predictors of BMD and TBS lowering in menopause.

**Conclusions:** BMD and TBS remained stable in the pre-menopause period. Bone loss was more rapid in the early than late menopausal period, captured both with BMD and TBS. Current TDF or PI/c/r exposure was not independently associated with either BMD or TBS lowering in menopause.
ABSTRACT P19

Antiviral Therapy 2019; 24 Suppl 1:A63

Atherosclerotic cardiovascular events in people living with human immunodeficiency virus

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Background: People living with human immunodeficiency virus (PLWHIV) under antiretrovirals (ARV) have an increased risk of atherosclerotic cardiovascular disease (ASCVD) events. The factors associated with ASCVD events in this high-risk population are various, mixing traditional vascular risk factors and specific HIV-related factors and remain controversial.

Purpose: Our aim was to determine the incidence of ASCVD events in a large cohort of PLWHIV and to identify the risk factors associated.

Methods: We conducted a longitudinal observational cohort study of asymptomatic PLWHIV under non-invasive cardiovascular evaluation. The first ASCVD event was censored and included CV death, acute coronary syndromes, coronary and peripheral revascularizations (PCI or CABG or endarterectomy or limb procedures) and ischaemic strokes.

Results: From January 2003 to December 2014, 763 consecutive asymptomatic PLWHIV were enrolled (mean age of 51.3 ±8.3 years, 87% men, 90% were free of known coronary artery disease, mean left ventricular ejection fraction 60%). At baseline, traditional CV risk factors were as follows: 54% had dyslipidaemia, 43% hypertension, 35% were active smokers, 22% had family history of CAD and 11% were diabetics. Statins were prescribed in 38% of the cohort, aspirin in 14%, clopidogrel in 14%, beta blockers in 14%, RAS blockers in 32%, calcium channel blockers in 8%. At baseline, median duration of HIV seropositivity was 19.8 years (14.0–23.6), 94% were under ARV predominantly protease inhibitors (68%). Median CD4 cell count was 545/mm3 (404–745) and 92% had undetectable HIV viral load. During a median follow-up of 5.8 years (3.7–8.7), 58 (7.3%) subjects had a first ASCVD event (incidence of 12.70 [9.78–16.51] per 1,000 persons-years) including 5 cardiovascular deaths, 14 ACS, 20 coronary revascularizations, 13 peripheral vascular procedures and 6 strokes) with a median time of occurrence of 3.1 years (1.5–5.1). CV death was the second cause of death (after malignancies: 12 patients, 33% causes of death) and occurred in 8 patients (25% of causes of death) followed by unexplained causes (21%), infectious disease (13%), liver disease (8%) and 2 suicides. Coronary events including coronary death, MI and stroke occurred in 39 patients (5.2%; incidence of 8.28 [6.00–11.43] per 1,000 persons-years). Conventional multivariate Cox model shows that age and tobacco were the independent risk factors associated with ASCVD events (hazard ratio [HR] 1.04, 95% CI 0.99, 1.09, P=0.05 and HR 2.17, 95% CI 1.07, 4.38, P=0.03).

Conclusions: Traditional vascular risk factors (age and active smoking) are associated with the occurrence of ASCVD events predominantly coronary artery disease in our observational cohort of PLWHIV. Cardiovascular prevention including tobacco cease action is mandatory in the ageing HIV population.
ABSTRACT P20

Antiviral Therapy 2019; 24 Suppl 1:A64

Prognostic value of non-invasive ischaemic testing in people living with human immunodeficiency virus

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Introduction: People living with human immunodeficiency virus (PLWHIV) under antiretrovirals have an increased risk of atherosclerotic cardiovascular (ASCVD) events. The prognostic value of silent myocardial ischaemia in this high-risk population has been poorly studied.

Hypothesis: To assess the relevance of targeted screening for myocardial ischaemia in asymptomatic PLWHIV with multiple risk factors at high risk for ASCVD and the prognostic value of myocardial ischaemia testing in this specific population.

Methods: Longitudinal observational cohort of asymptomatic PLWHIV addressed to our preventive cardiovascular unit for cardiovascular risk stratification. The first ASCVD event was censored and included CV death, acute coronary syndromes, coronary and peripheral revascularizations (PCI or CABG or endarterectomy or limb procedures) and ischaemic strokes. Major coronary events included coronary death, ACS and coronary revascularization.

Results: From January 2003 to December 2014, 763 consecutive asymptomatic PLWHIV were enrolled (mean age of 51.3 ± 8.3 years, 87% men, mean left ventricular ejection fraction 60%). At baseline, 90% were free of known coronary artery disease, 54% had dyslipidaemia, 43% hypertension, 35% were active smokers, 22% had family history of CAD and 11% were diabetics. 750 had a non-invasive diagnostic ischaemic testing including 243 exercise treadmill tests, 292 exercise

Figure 1. Kaplan–Meier survival estimates (Abstract P20)
echocardiography exams, 165 dobutamine stress echocardiography exams and 21 nuclear imaging tests. 41 (5%) subjects had a positive test (electrocardiographic and/or echocardiographic or scintigraphic imaging). During a median follow up of 5.8 years (3.7–8.7), 58 subjects (7.7%) had an ASCVD event (incidence of 12.70 [9.78–16.51] per 1,000 persons-years) including 5 cardiovascular deaths, 14 ACS, 20 coronary revascularizations, 13 peripheral vascular procedures and 6 strokes. Major coronary events occurred in 39 patients (5.2%) corresponding to an incidence of 8.28 [6.00–11.43] per 1,000 persons-years. Kaplan–Meier survival curve for ASCVD events stratified according to the result of non-invasive ischaemic test is depicted in Figure 1. Negative predictive value of ischaemic tests for the occurrence of ASCVD events was 96% (95% confidence interval, 94.2, 97.3%), and similar for the occurrence of major coronary events 95.9% (95% confidence interval, 94.2, 97.3%).

Conclusions: Rate of silent myocardial ischaemia was low in this high-risk HIV population. Non-invasive ischaemic testing can effectively and safely risk stratifies PLWHIV at high risk of CVD. PLWHIV with a negative ischaemic test have an excellent long-term prognosis.
ABSTRACT P21

Antiviral Therapy 2019; 24 Suppl 1:A66

Hypertension prevalence, awareness and barriers to control among persons living with HIV in northern Tanzania: a mixed methods study

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Objectives: People living with HIV (PLWH) have elevated risk for cardiovascular disease, necessitating focus on hypertension as a modifiable risk factor. We determined hypertension prevalence in a sample of adults engaged in HIV care in Tanzania and identified barriers to improved care.

Methods: From October to December 2018, 555 HIV-infected adults were screened consecutively at one clinic in Moshi, Tanzania. Hypertension was defined as: a single blood pressure measurement ≥160 mmHg systolic or ≥100 mmHg diastolic, two measurements at separate visits ≥140 mmHg systolic or ≥90 mmHg diastolic, self-reported hypertension diagnosis or current antihypertensive use. Participants who met criteria for hypertension completed a hypertension knowledge, attitudes and practices (KAP) survey. Separately, in-depth interviews (IDIs) were conducted with 13 participants purposively selected from two HIV clinics in Moshi, Tanzania who reported a history of high blood pressure. Interviews were coded and analyzed using NVivo.

Results: Hypertension prevalence was 18.9% (19.7% among women and 16.0% among men). The mean age of hypertensive patients was 50.4 (sd=10.9) years, compared with 42.2 (sd=10.5) years for normotensive patients. Among the 105 patients with hypertension, 72 (69%) were unaware of their diagnosis, 53 (50%) reported no prior blood pressure measurements and 22 (21%) reported current or prior use of antihypertensives. Of the seven patients reporting current antihypertensive use, none had a controlled blood pressure. Ninety-one hypertensive participants completed the KAP survey; 58 (64%) reported never receiving information about high blood pressure from a health-care provider, while almost all (96%) agreed to a statement that they needed more information about high blood pressure. When asked to define hypertension, only three participants provided a correct response. The majority of participants (n=86, 95%) reported stress and worries were the most common cause of high blood pressure. IDI participants also demonstrated limited hypertension knowledge. IDI participants included 11 women and 2 men with a mean age of 52.5 (sd=14.7) years, and the majority (92%) with a primary school level of education or less. Participants perceived hypertension as being caused by thinking too much, as temporary but curable, but as often fatal. All participants reported non-compliance or disengagement from hypertension care and reported receiving minimal hypertension education and counselling. For patients who received hypertension care, the HIV clinic often served as the gateway into care.

Conclusions: This study confirms a high prevalence of hypertension among PLWH in Tanzania. Absence of routine screening may result in missed diagnoses, and a lack of hypertension education and counselling may impede blood pressure control. Interventions to improve screening, treatment and control and that are integrated into existing HIV care are urgently needed.
ABSTRACT P22

*Antiviral Therapy* 2019; 24 Suppl 1:A67

Hypertension control in HIV-infected individuals at Princess Marina Hospital Infectious Disease Care Clinic

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**Background:** People living with HIV infection (PLWHI) are 1.5 to 2 times more likely to experience cardiovascular diseases (CVD). The extent to which treated PLWHI with a co-existent diagnosis of hypertension are adequately treated for their elevated blood pressure is not well known. The current study aimed at assessing the association between hypertension control and viral load suppression among PLWHI in Gaborone, Botswana.

**Methods:** This cross-sectional study was undertaken at a large Infectious Disease Care Clinic with a patient population of about 6,500 in Gaborone, Botswana. PLWHI with a known diagnosis of hypertension who were prescribed antihypertensive medications were recruited into the study. Sociodemographic, hypertension and HIV treatment data were collected. Participants had to have a viral load and blood pressure measurement in their medical record within 6 months at the time of recruitment. Viral load suppression was defined as a viral load <400 copies/ml, while hypertension control was defined as blood pressure <140/90 mmHg. Among all virally suppressed participants (main exposure), we assessed the association of viral suppression with the outcome of controlled blood pressure in univariate and multivariate logistic regression models.

**Results:** Among 329 participants enrolled, the mean age was $51.9 \pm 8.8$ years and $n=67.9\%$ were female. The proportion of participants with controlled hypertension was 47.3\%, and those with virological suppression was 95.4\%. Hypertension control was not associated with virological suppression ($P=0.8$). In the final multivariate analysis, both female gender and increasing age were associated with hypertension control OR 2.3 (95% CI: 1.4, 3.9) and OR 1.0 (95% CI: 1.0, 1.1), respectively. However, being prescribed calcium channel blockers OR 0.4 (95% CI: 0.3, 0.7), beta-blocker OR 0.5 (95% CI: 0.2, 0.9), angiotensin receptor blocker OR 0.2 (95% CI: 0.0, 0.9) and living with chronic kidney disease OR 0.2 (95% CI: 0.0, 0.9) were inversely associated with hypertension control.

**Conclusions:** Almost half of PLWHI in this one clinic-based study in Botswana had suboptimal hypertension control despite having achieved viral suppression. Future studies should explore factors associated with the inability to attain blood pressure targets despite attempts to treat hypertension among PLWHI in this setting.
ABSTRACT P23

Antiviral Therapy 2019; 24 Suppl 1:A68

Immune cell activation as a risk factor for hypertension in people living with HIV in sub-Saharan Africa using the recent American Heart Association and American College of Cardiology guidelines

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Objectives: This study was aimed at determining factors associated with hypertension and the role of immune activation in people living with HIV (PLWH) using the new hypertension guidelines by the American Heart Association (AHA) and the American College of Cardiology (ACC) in sub-Saharan Africa.

Methods: We conducted three cross-sectional, one systematic and one prospective study. The World Health Organization Stepwise approach to Surveillance (WHO STEPs) and the international physical activity questionnaire (IPAQ) were used to collect data for cross-sectional studies while preferred reporting items for systematic reviews and meta-analyses was employed for the systematic study. FlowJo for flow-cytometry analysis and statistical evaluations were employed to elucidate relationships between hypertension and response variables.

Results: Factors significantly associated with increased odds for developing hypertension among 226 PLWH after adjustments in multivariate logistic regression were waist circumference, sedentary lifestyle, age, body
mass index, employment status, fasting blood sugar, table salt consumption and moderate physical activity, respectively \((P<0.05)\). 94% had uncontrolled blood pressure. The new AHA/ACC criteria for hypertension shifted 26% of the originally normotensives into hypertension category. Hypertension was associated with higher neutrophil, white blood cell counts and neutrophil lymphocyte ratio \((P<0.05)\). IL-6 and IL-10 were associated with hypertension in a carefully selected age-sex matched group \((n=38)\) of PLWH \((P<0.05)\). Interleukin (IL)-17A, interferon (IFN)-\(\gamma\), and higher CD4\(^+\) T-cell counts were associated with hypertension in antiretroviral-treated participants in 45 carefully selected studies from 13 unique African countries. High salt intake was associated with increased innate immune cell activation markers \((CD86+, CD80+)\) and hypertension. See Figure 1. **Conclusions:** Targeting modifiable risk factors and adaptive immune activation could provide improved care for hypertensive PLWH, however, further research is needed to characterize the inflammatory milieu contributing to hypertension in PLWH especially in African populations where the burden of HIV is the highest.
ABSTRACT P24

Antiviral Therapy 2019; 24 Suppl 1:A70

Virological failure as a predictor of (or risk factor for) metabolic syndrome among patients receiving antiretroviral therapy in Zambia: a cross-sectional study

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Background: HIV-infected individuals receiving antiretroviral therapy (ART) are at increased risk of metabolic related conditions/diseases. However, in sub-Saharan African countries, including Zambia, screening for metabolic syndrome (MS) is typically not embedded in the management of HIV. Amidst this is the burden of virological failure (VF) among ART patients. This study aims at determining whether MS is associated with VF among HIV patients on ART at Livingstone Central Hospital (LCH), Zambia.

Methods: We conducted a cross-sectional study of HIV-infected individuals aged ≥18 years on ART for ≥6 months, excluding pregnant women and those with known active opportunistic infection or neoplasm at LCH. We collected the following data: demographic information, physical measurements (blood pressure [BP], waist circumference [WC], height, weight), biochemical and immunological measurements, lipid profiles, fasting blood sugar (FBS), ART adherence and behavioural measurements. MS was defined as having three or more of the following: raised BP (diastolic ≥85 mmHg or systolic ≥130 mmHg or self-reported use of antihypertensives), triglycerides (TG; ≥1.7 mmol/l), WC (men ≥95 cm and women ≥80 cm), FBS (≥5.6 mmol/l) and reduced high-density lipoprotein cholesterol (HDL-c [<1.0 males; <1.3 females]). VF defined as viral load (VL) ≥1,000 copies/µl. Descriptive statistics and logistic regression were used to analyse the data.

Results: From April to June 2019, 435 participants (64% women) enrolled, with mean age 45 years (range 18–79), median CD4 absolute count (IQR 412–962) and median VL 21 copies/µl (IQR 0–507). Median time on ART was 108 months (IQR 60–144). MS was prevalent in 65/313 (21%) of participants and VF in 76/420 (18%). Of those with VF, 47% were on a fixed combination of efavirenz, emtricitabine and tenofovir. The predominant components of MS were raised BP (43%), WC (41%) and reduced HDL-c (38%). The prevalence of VF was 24% among the participants with MS. After controlling for sex, age, duration of ART and body mass index, VF was significantly associated with MS (OR 2.17; 95% CI 1.01, 4.67).

Conclusions: Metabolic syndrome and VF are prevalent among HIV patients receiving ART in Livingstone, Zambia, and an observed association between MS and VF warrants further understanding by robust study designs.
ABSTRACT P25

Antiviral Therapy 2019; 24 Suppl 1:A71

Modelling 2018 AHA Cholesterol Guidelines in HIV

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Objective: The objective was to assess statin use in people living with HIV (PLWH) in relation to the 2018 AHA Cholesterol Clinical Practice Guideline (CCPG) recommendations and related LDL targets. Data were analysed vis-a-vis the recent AHA scientific statement on prevention and management of CVD in people living with HIV.

Methods: Cross-sectional study of PLWH followed at the Modena HIV Metabolic Clinic (MHMC) in 2017–2018. Mutually exclusive groups were built according to CCPG treatment algorithms recommending high and moderate intensity hypolipaemic therapy (HIH or MIH).

Results: We included 2,123 patients (74% men, mean age 53.5 years). Mean LDL-c and 10-year risk of CV events were 114 ± 33 mg/dl and 8.1 ± 0.9%. Figure 1 shows the distribution of risk among 2,039 primary prevention PLWH.

CCPG recommends HIH in groups A, C, I. HIH was prescribed in 13.8%, 40.6% and 29.5% of patients in those categories. Among the treated patients, 0%, 67.3% and 47.1% reached an LDL <100 mg/dl.

CCPG recommends MIH in groups B, G, H. MIH was prescribed in 34.2%, 18% and 22.6% of patients in those categories. Among the treated patients, 69.8%, 50% and 40% reached an LDL <100 mg/dl.

In 114 secondary prevention PLWH aged <75 years (6% of our cohort), HIH was prescribed in 34 patients (29%) and MIH in 25 patients (21.9%). Among these patients, only 26.5% reached the LDL-C target <70 mg/dl.

Discussion: In real life statins are largely under-prescribed. The recommended LDL target was reached most often in

Figure 1. (Abstract P25)
patients with diabetes mellitus type 2. AHA-PLWH statement failed in identifying recommendations that may clarify statin prescription needing in PLWH. The recent AHA statement on CV disease in PLWH is ambiguous with regards to treatment indications and LDL goals leaving a therapeutic gap that needs to be filled to improve patients’ outcome.
ABSTRACT P26

*Antiviral Therapy* 2019; 24 Suppl 1:A73

Prevalence, risk factors and outcomes of cardiovascular, metabolic and chronic kidney diseases in HIV-infected versus uninfected adults in sub-Saharan Africa: a systematic review and meta-analysis

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**Background:** Sub-Saharan Africa (SSA) has the highest burden of HIV in the world; more than 25.5 million Africans are living with HIV in the region, including nearly 15 million on antiretroviral therapy (ART). Expanding use of ART has led to a notable decline in HIV-associated morbidity and death in SSA. Nonetheless, people living with HIV (PWH) in SSA are at substantially increased risk for both cardiovascular and metabolic disease (CVMD) and chronic kidney diseases (CKD). Quantifying prevalence, risk factors and outcomes of CVMD and CKD in PWH in sub-Saharan African represents a pressing research priority.

**Methods:** We searched electronic databases (Ovid MEDLINE and EMBASE) from 1985 to July 2018. We included studies that reported prevalence estimates for any CVMD and CKD in SSA and information on HIV status and treatment status. We used random-effects meta-analyses to pool prevalence estimates.

**Results:** A total of 89 studies involving 263,262 participants were included in the meta-analysis. Prevalence estimates were reported in 41 studies on hypertension (HTN), 29 on type 2 diabetes mellitus (T2DM), 14 on metabolic syndrome (MS), 9 on cardiovascular disease (CVD) and 22 on CKD. The reported prevalence estimates varied greatly within countries, between countries and within regions: HTN (5.2% to 45.0%), T2DM (0.9% to 28.1%), MS (2.1% to 20.4%) and CKD (0.6% to 53.3%). There was no significant difference in the prevalence of HTN and T2DM between HIV-infected and -uninfected participants. The prevalence of MS (OR=1.66, 95% CI 1.01, 2.72, 2 studies) and CKD (OR=2.30, 95% CI 1.12, 4.72, 6 studies) were higher in HIV-infected participants than HIV-uninfected participants. PWH who were treatment-experienced were significantly more likely to be hypertensive than those who were treatment-naive (OR=2.66, 95% CI 1.58, 4.77). There was no significant difference in the prevalence of T2DM, MS and CKD among people living with HIV that were treatment-experienced compared with those who were treatment-naive.

**Conclusions:** The burden of CVMD and CKD among PWH in SSA is high, although there are wide variations within and across countries and regions. A better understanding of the complex interplay of genetic, environmental and HIV-factors in the pathogenesis of these comorbidities is essential. Furthermore, rigorous implementation science to determine optimal screening, prevention and treatment strategies in PWH in SSA is also critical.
ABSTRACT P27

Antiviral Therapy 2019; 24 Suppl 1:A74

People living with HIV are more likely to be screened for cardiovascular disease risk factors than other members of the general population in Botswana – a community-based study

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Objectives: People living with HIV (PLWH) are more likely to experience cardiovascular diseases compared with members of the general population. Therefore, we aimed to assess whether PLWH were more likely to have previously been screened for cardiovascular disease risk factors (CVDRF) compared with those without HIV.

Methods: A population-based, cross-sectional study was conducted among individuals aged 16 to 64 years across 22 communities in Botswana between February and August 2017 as part of a larger community-based HIV prevention trial. Participants were asked if they were screened for and counselled about CVDRF (history of hypertension or blood pressure check, blood glucose and cholesterol measurements, weight check and weight control, tobacco smoking and cessation, alcohol use and physical activity) in the last 3 years. HIV testing was offered to those with unknown HIV status. Multivariate logistic regression analysis controlling for age and sex, was used to assess the relationship between CVDRF screening and HIV status.

Results: Among 3,981 participants enrolled, 2,547 (64%) were female, and 1,196 (30%) were PLWH (93% already on ART). PLWH were more likely to report previous screening for diabetes (25% versus 19%; P<0.001), elevated cholesterol (17% versus 12%; P<0.001) and to have had their weight checked (76% versus 55%; P<0.001) than participants without HIV. PLWH were also more likely to have received counselling on salt intake (42% versus 32%; P<0.001), smoking cessation (66% versus 46%; P<0.001), weight control (38% versus 29%; P<0.001), physical activity (46% versus 34%; P<0.001) and alcohol consumption (35% versus 23%; P<0.001) than those without HIV. Overall, HIV-positive status was significantly associated with screening and counselling for CVDRF (AOR 1.84, 95% CI: 1.46, 2.32).

Conclusions: PLWH were almost two times more likely to have been previously screened for CVDRF indicating a need for scale-up of integrated management and prevention of CVD in those without HIV.
ABSTRACT P28

*Antiviral Therapy* 2019; 24 Suppl 1:A75

Adiponectin levels linked to subclinical myocardial fibrosis in PLWH

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**Aim:** Impaired myocardial function and heart failure with preserved ejection fraction (HFpEF) are increased in persons living with HIV (PLWH) and remains an area of active research. Previously, we demonstrated that global intramyocardial fibrosis by cardiac MR imaging (CMR) was increased in PLWH without known cardiovascular disease (CVD) and may serve as a marker of subclinical myocardial injury. Adiponectin is an adipocyte-specific cytokine with metabolic effects including insulin sensitivity, and potential protective effects in CVD. However, research has demonstrated that adiponectin levels are elevated in patients with chronic heart failure. This study aims to characterize the relationship between myocardial fibrosis, adiponectin and related metabolic parameters to better understand the pathophysiologic mechanisms of myocardial injury in PLWH.

**Methods:** We completed a cross-sectional study of 87 PLWH and 28 healthy matched controls without known CVD (median age 48 years, 28% women). Myocardial fibrosis (quantified as extracellular volume index) was measured by CMR (partial results previously reported). Laboratory determinations included metabolic parameter, adiponectin, brain natriuretic peptide (BNP) as well as HIV viral load, CD4 count.

**Results:** While there was no difference between PLWH and controls in age, sex, BMI, prevalence of metabolic syndrome, adiponectin or BNP levels, myocardial fibrosis index was increased in PLWH ($P=0.02$). There was a significant positive correlation between adiponectin and myocardial fibrosis ($r=0.26; P=0.004$) and BNP ($r=0.25; P=0.009$). In a multivariate regression analysis that included BMI and BNP, adiponectin ($P=0.04$), sex ($P<0.0001$) and HIV status ($P=0.02$) were significant factors associated with myocardial fibrosis.

**Conclusions:** While adiponectin classically has been described as metabolically protective, the present study, as well as research in non-HIV populations, suggest that the relationship between adiponectin levels and cardiovascular health is more complex. We identify a significant correlation between higher adiponectin levels and myocardial fibrosis in both PLWH and healthy controls, but it remains unclear if this is causal or compensatory.

Adiponectin may be a useful serological biomarker for subclinical myocardial fibrosis in future research.
ABSTRACT P29

Antiviral Therapy 2019; 24 Suppl 1:A76

In vitro modelling of the impact of TLR4-LOX-1 cellular signalling in atherogenesis in chronic treated HIV

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Objectives/aim: The mechanisms that drive HIV-related atherosclerosis (CVD) in chronic treated HIV remain unclear. Serum factors (such as bioactive lipids) from HIV+ individuals on potent antiretroviral therapy (ART) may drive atherosclerosis. Oxidized lipids are danger-associated molecular patterns than can interact with pattern recognition receptors such as Toll-like receptor 4 (TLR-4) and lectin-type oxidized LDL receptor 1 (LOX-1). We hypothesized that increased TLR4-LOX-1 cellular signalling is a key mechanism of atherogenesis in chronic treated HIV. Given that observational human studies cannot dissect differential impact of HIV versus antivirals on key mechanisms of atherogenesis, we used an established model of atherogenesis to assess ex vivo the role of the TLR4-LOX-1 axis in early mechanisms of atherogenesis in the presence of plasma from HIV+ individuals on potent ART.

Methods: Our in vitro model of atherogenesis can dissect the impact of HIV plasma on key mechanisms of early atherogenesis such as monocyte chemotaxis and monocyte-derived foam cell formation (MDFCF). Freshly isolated peripheral blood mononuclear cells (PBMCs) from healthy donors (n=6) were added to tumor necrosis factor-activated human umbilical vein endothelial cells monolayers (HUVECs) on type I fibrous collagen gels to transmigrate (transendothelial migration [TEM] or % reverse migration) and form foam cells in the presence of pooled plasma, as previously described. Pooled plasma was isolated from healthy participants (18–40 years old) and HIV+ males (40–60 years old) with no known inflammatory comorbidities other than HIV or risk factors for CVD and on stable potent ART. Flow cytometry assessed MDFCF (∆MFI BODIPY of CD33+ macrophages inside the gel: fluorescence intensity of BODIPY compared with negative staining control) and cellular levels of TLR4 and LOX-1 in CD33+ myeloid cells. Paired t-test was used for statistical comparison within the same donor (HIV+ plasma versus HIV- plasma).

Results: When media-containing HIV+ compared with HIV- plasma was added to HUVECs, a significantly increased proportion of monocytes underwent transendothelial migration (TEM; median migrated cells 16 versus 4.9%, respectively) and CD33+ macrophages inside the collagen gel had increased lipid content per

Figure 1. (Abstract P29)
cell (median ΔMFI BODIPY 673 versus 342, respectively; \( P<0.05 \)). Compared with HIV plasma, HIV+ plasma induced a mean 3.6-fold increase in TEM, a mean 2.4-fold in MDFCF, a mean 1.75-fold increase in TLR4 and a mean 8.3-fold increase in LOX-1 in CD33+ macrophages inside the collagen gel (\( P<0.05 \) for all paired comparisons; Figure 1).

Conclusions/discussion: HIV plasma from patients on potent ART with no clinical CVD directly induces key mechanisms of early atherogenesis (TEM and MDFCF) in parallel to increases in membrane protein levels of TLR4 and LOX-1 in macrophages within the collagen gel (\textit{ex vivo} model of arterial wall). The role of the TLR4-LOX-1 axis in atherosclerosis in chronic treated HIV needs to be further studied \textit{in vivo}. 

ABSTRACT P30

Antiviral Therapy 2019; 24 Suppl 1:A79

Discrepancies in grading of drug–drug interactions in an elderly HIV population using three different expert databases

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Objectives: Comorbidities and polypharmacy have been associated with adverse drug reactions, misuse and drug–drug interactions (DDI) with an increasing risk in the elderly population living with HIV. Different expert databases can be used to evaluate DDIs with sometimes divergent interpretations that complicate therapeutic management. The objective was to describe DDIs between antiretrovirals (ARVs) and co-medications in an elderly HIV-population and to compare analyses and interpretations between three accessed databases.

Methods: All prescribed treatments (ARVs and co-medications) of HIV-infected subjects aged 65 years and older followed in five French HIV centers were collected during an HIV routine visit. Three expert databases, the Summary of Product Characteristic (SPC), the National DDI Thesaurus (THES), and the Liverpool HIV DDI (LIV) were used to define each DDI and specific grade. Relevant DDIs were defined as DDI mentioned in SPC and/or THES whatever the grade and/or moderate/high quality of evidence of interaction in the Liverpool website. DDIs were classified in potential weak interaction (undefined grade 1* in SPC and THES or potential weak interaction 1* in LIV), potential interaction (grade 1 or 2 in SPC and THES and grade 1 in LIV) and contraindication (grade 3 or 4 in SPC and THES and grade 2 in LIV).

Results: From January to March 2017, 239 HIV-infected subjects aged 65 years and older receiving both ARVs and comediations were included: median age 69 years (IQR 67–73), male 78%, median duration of HIV infection 18 years (12–24), 73% with at least one comorbidity, receiving a median of 5 comediations (2–7). Of these, 60 subjects (25.1%) presented at least one DDI for a total of 128 DDIs: 23/128 DDIs were contraindicated in 10 subjects. Contraindications are detailed in Table 1.

All DDIs have been identified in LIV but only 12/21 (57%) at the highest grade, among which THES missed 5 high grade DDIs. Only seven contraindications have been identified in the three databases concomitantly at the highest grade: darunavir/alfuzosin, darunavir/apixaban, darunavir/ticagrelor, ritonavir/alfuzosin, ritonavir/apixaban, ritonavir/ticagrelor and nevirapine/ketoconazole.

Conclusions/discussion: Protease inhibitors and boosters are frequently involved in serious DDIs as well as comediations mostly prescribed in the ageing population such as anti-platelet agent and alpha blocker (prescribed in benign prostatic hypertrophy). Different methodologies can explain the discrepancies between the three accessed databases. SPC and THES based

Table 1. (Abstract P30)

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<th>THES</th>
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<td>alfuzosine/amiodarone/apixaban/atorvastatine/ciclosporine/tamsulosine/ticagrelor</td>
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<td>2/2/2/1*/1/1/2</td>
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<td>4/0/3/3/0/3/4</td>
<td>2/2/2/1*/2/1*</td>
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<td>kétoconazole/mianserin/sertraline</td>
<td>3/0/3</td>
<td>4/3/3</td>
<td>2/1*/1*</td>
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</table>

21st International Workshop on Co-morbidities and Adverse Drug Reactions in HIV
their recommendations on clinical and pharmacological data, while LIV, the most used and convenient database, with evidence-based DDI resource is mainly based on pharmacological data. A consensus within the databases would be helpful for clinicians.
ABSTRACT P31
Antiviral Therapy 2019; 24 Suppl 1:A81

BESIDE – clinical relevance and implications for management of antiretroviral therapy due to recreational drug use in PLWH in Germany

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Background: Recreational drug use among people living with HIV (PLWH) in Germany is common. This puts patients at risk for drug–drug interactions potentially leading to adverse events and/or loss of efficacy of antiretroviral therapy (ART). Here, we assessed the clinical relevance of illicit drug consumption and potential implications for management of ART.

Methods: BESIDE was a cross-sectional study, evaluating the prevalence of concomitant diseases, prescription and over the counter co-medication as well as illicit drugs in PLWH on ART. Regional distribution of study sites (n=20), consecutive recruitment and age-stratified sampling ensured a representative sample of the PLWH population in Germany. Data on recreational drug use were gathered via anonymized patient questionnaires.

Results: Between 09/2016 and 12/2018, centres collected data of 453 PLWH on ART. A high proportion of patients with data available (76%; 223/293) consumed recreational drugs, 21% (47/223) to stimulate sexual activities. 71% (207/293) of patients had been asked about drugs by their doctors and 66% (194/293) had been educated on potential risks and interactions. However, no more than 29% (65/223) of patients sought consultation with their doctor about their drug use and only 7% (15/223) saw a problem in the use of drugs in combination with ART. Strikingly, 39% (86/223) of patients had undergone medical treatment and 36% (81/223) had been hospitalized due to their drug consumption, with even more concerning numbers in patients aged <30 years (medical treatment: 60%, 12/20; hospitalization: 65%, 13/20). This was consistent with a high number of patients who had problems with their ART (31%, 70/223; <30 y: 60%, 12/20) or needed to switch it (28%, 62/223; <30 y, 60%, 12/20) due to recreational drug use.

Conclusions: These data demonstrate the high clinical relevance of recreational drug use in PLWH and the need for pro-active education on potential risks and drug–drug interactions with ART by treating physicians, especially of younger patients.
ABSTRACT P32

Antiviral Therapy 2019; 24 Suppl 1:A83

Switching from tenofovir disoproxil fumarate (TDF) to tenofovir alafenamide (TAF) lowers alanine transaminase (ALT) and aspartate transaminase (AST) in patients with HIV infection with or without viral hepatitis coinfection

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Objectives: Our aim was to investigate the effect of switching TDF to TAF on liver enzymes and renal and lipid profile.

Methods: Consecutive HIV patients enrolled in Surveillance Cohort Long-term Toxicity Antiretrovirals/Antivirals (SCOLTA) project switching from TDF to TAF for any reasons were included. Changes from baseline (T0) to 6-month follow-up (T1) were evaluated using paired t-test if differences were normally distributed and using signed rank test if not.

Results: 291 patients switched from TDF to TAF, 163 had at least one follow-up visit. They were mostly males (131, 80.4%) and Caucasian (151, 92.6%). Twenty-seven (16.6%) had been intravenous drug users, 43 (26.4%) were in CDC stage C, 48 (29.4%) on second-line antiretroviral therapy (ART), and 154 (94.5%) had HIV RNA <50 copies/ml at switch. 35 (21.5%) were HCV-Ab-positive (8 with detectable HCV RNA), and 14 (8.6%) HBsAg-positive. Median time on TDF was 669 days (IQR 417–911). At baseline, mean age was 46.3 (standard deviation [sd] 10.7), body mass index 24.9 kg/m² (sd 3.7), total cholesterol 196 mg/dl (sd 40), HDL cholesterol (HDL) 49 mg/dl (sd 16), glucose 91.7 mg/dl (sd 21.5), creatinine 1.0 mg/dl (sd 0.2), estimated glomerular filtration rate 85.7 ml/min (sd 18.6). Median CD4+ was 637 cells/ml (interquartile range [IQR] 440–898), triglycerides (TG) 109 mg/dl (IQR 81–154), aspartate aminotransferase (AST) 23 IU/l (IQR 18–30), alanine aminotransferase (ALT) 24 IU/l (IQR 17–34), 12 (7.4%) patients had AST >40 IU/l and 24 (14.7%) ALT >40 IU/l at T0.

At T1, both ALT (median -2, IQR -7–3 IU/l; P =0.0008) and AST (median -1, IQR -5–2 IU/l; P=0.003) were significantly reduced. AST and ALT reduction remained significant in patients negative for HCV-Ab and HBsAg (P<0.05 for both). Among 24 patients with ALT >40 IU/l, a significant proportion reduced this parameter (median change -20, -34 to -4; P=0.0001). Total cholesterol (TC) and HDL cholesterol increased significantly (mean change 14.8 ±4.3 mg/dl; P<<0.0001) and 3.0 ±1.3 mg/dl [P=0.05], respectively) and eGFR decreased significantly (3.3 ±1.0 ml/min; P=0.002) with no impact on TC/HDL ratio and on triglycerides.

Conclusions: Switching from TDF to TAF demonstrated a significant reduction of ALT and AST and was associated with an improvement in eGFR and increased TC and HDL. A possible mild hepatotoxicity of TDF were described. We can argue that TAF could have a better liver toxicity profile that TDF. Further studies are needed to confirm this hypothesis.
ABSTRACT P33

*Antiviral Therapy* 2019; 24 Suppl 1:A84

Non-Hispanic White individuals with HIV–HBV are at increased risk for developing cirrhosis

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**Introduction:** Given the widespread use of hepatitis B virus (HBV)-specific ART which leads to HBV viral suppression, it remains unknown if progression to cirrhosis occurs while on ART in HIV–HBV patients.

**Methods:** We conducted a retrospective longitudinal analysis of HIV–HBV with chronic HBV (CHB) from three sites in Texas and obtained incidence of cirrhosis. Those with cirrhosis prior to or within 182 days of HBV diagnosis or study entry were excluded. We examined risk for developing cirrhosis by race, gender, age, HBV viral suppression by months, having AIDS at baseline, hepatitis C coinfection, alcohol use and diabetes (DM) by Cox proportional hazards analysis.

**Results:** Among the 765 patients, 501 had CHB (87% male, 23% non-Hispanic White [NHW], 62% Black, 15% Hispanic) and 3,767 person-years of follow-up data. Incident cirrhosis developed in 70 patients at a median of 7.89 years with an incidence rate of 18.2 (overall) and 28.6, 19.2 and 14.6 per 1,000 person-years in NHW, Hispanic and Black individuals, respectively. Hepatitis C (HCV) coinfection (hazard ratio [HR] 2.40, 95% CI: 1.38, 4.16), age at baseline (HR 1.04, 95% CI: 1.01, 1.07) and Black versus NHW (HR 0.49, 95% CI 0.28, 0.85) were associated with incident cirrhosis. Diabetes had a trend towards increased risk (HR 1.77, 95% CI: 0.97, 3.23). No differences were seen by gender, HBV viral suppression, AIDS and alcohol use. After adjusting for HCV, age, HBV viral suppression and AIDS, Black versus NHW individuals (adjusted HR 0.42, 95% CI: 0.22, 0.84) was associated with incident cirrhosis. See Figure 1.

**Conclusions:** The incidence of developing cirrhosis in HIV–HBV patients on HBV-specific ART is 18.2 per 1,000 person-years. Non-Hispanic White individuals are at increased risk for developing cirrhosis after

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**Figure 1. (Abstract P33)**

![Graph showing risk for cirrhosis by race adjusted by age, AIDS, HBV viral suppression & HCV](Liver_disease_&_hepatotoxicity.indd 84)
adjusting for HCV, age, AIDS and months of HBV suppression. Careful monitoring for development of cirrhosis is needed in HIV–HBV on HIV treatment.
ABSTRACT P34
Antiviral Therapy 2019; 24 Suppl 1:A86
Targeting liver fibrosis in chronic treated HIV with oral ApoA-I mimetics
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Objectives/aim: Novel therapies are needed to attenuate liver fibrosis in chronic treated HIV infection. ApoA-I peptides (such as 6F) mimic HDL and attenuate pro-inflammatory mechanisms. The 6F was expressed as a transgene in tomatoes (Tg6F) and can be translated to human diet. Given that gut dysfunction and inflammation may contribute to liver fibrosis in chronic treated HIV, we used a humanized mouse model of chronic treated HIV to study whether Tg6F attenuates in vivo HIV- and/or ART-driven impact on liver fibrosis.

Methods: The C57BL/6 Rag2−/−γc−/−CD47−/− bone marrow/liver/thymus mice do not develop early graft versus host disease. After 4 weeks of infection with the 89.6 HIV-1 virus, mice were treated with daily emtricitabine, tenofovir, raltegravir for up to 12 weeks. Oral ApoA-I mimetics were given as Tg6F (at 0.06% by weight of diet) to HIV+/ART-treated mice (n=20) after suppression of viraemia with ART. The groups were: A (n=10): uninfected (HIV-); B (n=10): HIV+; C (n=20): HIV+, ART; D (n=20): HIV+/ART/Tg6F. Human and murine plasma levels of matrix metalloproteinases (MMPs) MMP-1, MMP-2, MMP-9, MMP-12 and tissue inhibitors of metalloproteinase (TIMP)-1.

Table 1. (Abstract P34)
were determined by Luminex Assays. Liver murine mRNA levels of collagen I, III and TIMP-1, MMP-2, MMP-9 were determined by real-time PCR. Results are described as mean + sem and t-test was used for statistical analysis.

**Results:** Potent ART induced a mean >20% increase in human plasma biomarkers of fibrosis (Table 1) compared with HIV viraemic and uninfected mice. ART induced a mean >15% increase in mRNA levels of collagen I, III, TIMP-1, MMP-2, MMP-9 in HIV+/ART+ compared with HIV+ and uninfected mice (P<0.05). Tg6F attenuated all ART-induced increases in plasma biomarkers of fibrosis and in mRNA levels of mediators of liver fibrosis (P<0.05).

**Conclusions/discussion:** Tg6F attenuated ART-induced increase in mediators of liver fibrosis. Given that Tg6F is not absorbed systemically, gut dysfunction may contribute to liver fibrosis in chronic treated HIV. Further studies are needed to determine whether oral ApoA-I mimetics can be a novel strategy to attenuate liver fibrosis in chronic treated HIV.
ABSTRACT P35

Antiviral Therapy 2019; 24 Suppl 1:A88

Targeting liver fibrosis in chronic treated HIV with MitoQ

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Objectives/aim: Elucidating mechanisms of HIV-related liver fibrosis will set the basis for therapies that can lessen its impact including cirrhosis, morbidity and mortality. As mitochondria are the main source of intracellular reactive oxygen species (ROS; mito-ROS), therapies that target oxidative stress and mitochondrial dysfunction such as the mitochondria-targeted antioxidant MitoQ, may target HIV-related liver fibrosis. MitoQ has been used in clinical trials in humans for diseases like Parkinson and liver disease. We used a physiologically relevant humanized mouse model of chronic treated HIV to study whether MitoQ attenuates in vivo HIV- and/or ART-driven liver fibrosis.

Methods: The C57BL/6 Rag2−/−γc−/−CD47−/− bone marrow/liver/thymus mice do not develop early graft versus host disease and thus HIV- and/or ART-driven changes on liver fibrosis can be dissected in vivo. After 4 weeks of infection with the dual-tropic 89.6 HIV-1 virus, mice (n=20) were treated with daily emtricitabine (200 mg/kg), tenofovir (208 mg/kg), raltegravir (80 mg/kg) for up to 12 weeks. MitoQ was given in water at 250 μM daily. The groups were: A (n=5): uninfected (HIV-); B (n=10): HIV+, ART; C (n=10): HIV+/ART/MitoQ. Liver fibrosis was assessed histopathologically by Picrosirius red staining of fibrotic mouse liver and a digital imaging expert system. Quantified Digital Fibrosis % (QDF%) was calculated as the percentage of the total section or biopsy that is masked as fibrosis relative to the entire tissue area. Real-time PCR was also used to determine mRNA levels of key mediators of liver fibrosis (TIMP-1, TGF-beta, MMP-9). Results are described as mean ±SEM and t-test was used for statistical analysis.

Results: Liver fibrosis was not detected in uninfected mice (Figure 1). Potent ART for 12 weeks suppressed viraemia within 4 weeks. Humanized HIV mice exposed to HIV/ART for 12 weeks demonstrated a moderate lobular and sinusoidal fibrotic pattern and had an approximately 12-fold increase in fibrosis. In the liver of HIV+/ART+ mice there was a mean 22%, 16%, 18% and 12.3% increase in Picrosirius Red signal, TGF-b, TIMP-1 and MMP-9 compared with uninfected mice (P<0.05). MitoQ attenuated HIV/ART-induced increase in Picrosirius Red signal, TGF-b, TIMP-1 and MMP-9 (P<0.05).

Conclusions/discussion: Our in vivo model provided preclinical data that support the use of MitoQ as therapeutic strategy for liver fibrosis in chronic treated HIV. MitoQ attenuated HIV/ART-driven increase in collagen content and molecular mediators of fibrosis in the liver. Further studies are needed to determine whether MitoQ can be a novel therapeutic strategy for liver fibrosis in chronic treated HIV.

Figure 1. (Abstract P35)
Evolutive NAFLD predicts frailty in people living with HIV

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Objective: The objective of the study was to investigate the contribution of liver steatosis and significant fibrosis alone and in association (evolutive NAFLD) with frailty in PLWH in order to optimize the estimation of biological age.

Methods: This was a cross-sectional study of consecutive patients attending Modena HIV Metabolic Clinic in 2018–2019. Patients with hazardous alcohol intake and HBV or HCV coinfection were excluded. Controlled attenuation parameter (CAP) and liver stiffness measurement (LSM) were evaluated by transient elastography. Liver steatosis was diagnosed by CAP as follows: S0 (no steatosis; CAP < 248 dB/m), S1 (mild steatosis; 248 ≤ CAP < 268), S2 (moderate steatosis; 269 ≤ CAP < 280), S3 (severe steatosis; CAP ≥ 280) dB/m. Liver fibrosis was diagnosed by LSM as follows: stage F0–F1 (mild fibrosis, LSM < 7.1 kPa), F2–F3 (significant fibrosis, 7.1 < LSM < 13), F4 (cirrhosis, LSM > 13 kPa). Evolutive NAFLD was defined as the contemporary presence of liver steatosis (CAP ≥ 248) and significant liver fibrosis or cirrhosis (stage ≥ F2). Frailty was assessed using 36-item frailty index (FI). FI was categorized as fit (<0.25), frail (0.25–0.4), most frail (>0.4). Logistic regression was used to explore frailty predictors using steatosis and evolutive NAFLD as covariates.

Results: We analysed 707 PLWH. Mean age was 53.5 (±8.2) years, 76.2% males, current median was CD4 = 700 μl (IQR = 539–889), HIV viral load undetectable in 98.7%. Evolutive NAFLD was present in 10.2%; frail and most-frail in 18.9% and 3.9%, respectively. Evolutive NAFLD group had a higher prevalence of obesity, elevated waist circumference and BMI, lower HDL cholesterol levels, higher total and LDL cholesterol levels, longer HIV duration and lower CD4 nadir, current use of NNRTI (P < 0.001). Univariate analysis demonstrated that neurocognitive impairment (OR = 5.1, 1.6–15), vitamin D insufficiency (OR = 1.94, 1.2–3.2), obesity (OR = 8.1, 4.4–14.6), diabetes (OR = 3.2, 1.9–5.6) and osteoporosis (OR = 0.4, 0.2–0.8) were statistically significantly related to evolutive NAFLD. Predictors for FI were: age (OR = 0.6, 0.4–0.9), steatosis (OR = 2.1, 1.3–3.5) and fibrosis (OR = 2, 1–3.7), evolutive NAFLD (OR = 9.2, 5.2–16.8), diabetes (OR = 1.7, 1–2.7), multimorbidity (OR = 2.5, 1.5–4).

Conclusions: Evolutive NAFLD increases the risk of frailty in PLWH by 9.2-fold and we may suggest it as an indicator of metabolic age. Liver steatosis alone was associated with frailty, implying that health-care interventions such as lifestyle changes, should be promoted in PLWH.
ABSTRACT P37

Antiviral Therapy 2019; 24 Suppl 1:A90

Combined kidney–liver transplant in HIV-positive patients: Modena experience

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Objective: To describe indication, survival and clinical outcomes of a case series of five combined liver–kidney transplants in HIV-infected patients.

Results: Since 2001 in the Liver and Multivisceral Transplant Centre of the Policlinico Modena Hospital, Italy, five combined liver–kidney transplants were performed in people living with HIV (PLWH). Table 1 describes patients characteristics at transplantation and clinical outcomes at follow-up.

All patients were male, Caucasian and had an HIV-VL undetectable at LT. Four patients had HCV-related cirrhosis and one of them had hepatocarcinoma. The other one had HBV and HDV-related cirrhosis. Every patient had undetectable HIV viral load at transplant. HCV median viral load at transplant was 464,327 copies/mmc and all three alive patients with HCV obtained a sustained virological response (SVR) to HCV therapy after transplant.

Kidney transplant indication was HIV-associated nephropathy in three out of five patients, whereas the other two had focal glomerulosclerosis and mesangial proliferative glomerulonephritis, respectively. All the patients were on haemodialysis at the time of transplantation.

Four out of five patients are still alive with a median follow-up of 3,407 days. Patient number 2 died on post-transplant day 41 for a disseminated candidiasis with cerebral involvement.

Discussion: Contrary to previously published data, this case series describes a favourable clinical outcome in PLWH who received combined liver and kidney transplant. Dedicated immunosuppression strategies, infection screening and prophylaxis were used in our case series. Infectious disease specialists, nephrologists, liver transplant surgeons, clinical pharmacologists and intensive care physicians need to work together in an interdisciplinary team to find shared strategies to manage the unique aspects of the combined kidney–liver transplant needs including fluids management in the immediate post-transplant period, induction immunosuppression and HCV therapy after transplant.

Our results could lead other transplant programmes to consider combined kidney–liver transplants as a reliable clinical option in PLWH with liver and kidney insufficiency.

Table 1. (Abstract P37)
ABSTRACT P38

Antiviral Therapy 2019; 24 Suppl 1:A91

Incidence and prevalence of hepatitis C in two prospective studies of HIV pre-exposure prophylaxis adherence interventions in men who have sex with men in southern California

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Objectives: There is concern that increased risk behaviour during HIV pre-exposure prophylaxis (PrEP) will be associated with increased incidence of hepatitis C virus (HCV) infection in men who have sex with men (MSM). We sought to establish the prevalence of HCV prior to PrEP in a high-risk cohort of MSM and transgender women (TGW) to determine the incidence of HCV seroconversion during PrEP.

Methods: Participants were 603 MSM and 2 TGW at high risk of acquiring HIV infection who all received daily PrEP with tenofovir disoproxil fumarate-emtricitabine (TDF-FTC) and had available paired specimens from two parallel, prospective, 48-week studies conducted in southern California. These were a randomized trial of text messaging for PrEP adherence (CCTG 595) with 395 participants enrolled from February 2013 to February 2015, and a longitudinal strategy study of real-time plasma tenofovir levels to support PrEP adherence (PATH-PrEP) with 301 participants enrolled from April 2014 to July 2016. Routine screening for rectal, urethral, and pharyngeal gonorrhea and chlamydia as well as syphilis was done at regular intervals in both studies. Paired specimens were obtained at entry and week 48. HCV antibodies were assayed at week 48 in all participants. For those with positive week 48 antibodies, the entry specimen was also assayed.

Results: Four participants (prevalence 0.66%) had HCV antibodies detected at week 48. All four were also seropositive at entry. Thus, zero incident HCV cases were detected during the study period. Risk factors for HCV seropositivity at entry included greater age (median 53 years HCV+ versus 37 years HCV−; P=0.001, two sample t-test), lower education level (P<0.001, Fisher’s exact test), and lower PrEP adherence estimated by dried blood spot tenofovir levels (P=0.029, Fisher’s exact test). Incident sexually transmitted infections (STI) were common among participants in both studies: 47.5% were diagnosed with a new bacterial STI in CCTG 595 and 46.4% in PATH-PrEP.

Conclusions: Among early PrEP adopters engaged in clinical trials, the prevalence of HCV antibodies was modest. Incident HCV did not occur during the study period, despite ongoing risk behaviour and a high incidence of STI. These results suggest that daily TDF-FTC PrEP in MSM/TGW is not associated with increased risk of acquiring HCV in this setting.
ABSTRACT P39

Depression and comorbidities in people with HIV

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Objectives/aim: Depression is the most common neuropsychiatric comorbidity among people with HIV (PWH), with prevalence rates 3–4 times that of non-infected individuals. We aimed to describe the relationship between depression and comorbidity diagnoses in a sample of PWH.

Methods: Cross-sectional secondary analysis of medical record and symptom data collected in an international, multisite study of physical activity patterns in PWH. We abstracted data from participant medical records to determine current diagnoses with mental health, cardiovascular, pulmonary, endocrine, neurocognitive, hepatic and cancer comorbidities. To determine the effect of depression, we used forward selection to build a regression model from a set of statistically significant (P ≤ 0.05) candidate predictor variables. We used Poisson regression to analyse the relationship between a current diagnosis of major depressive disorder and the total number of current comorbidity diagnoses. We then used correlation matrices to identify specific comorbidity diagnoses that were significantly associated with a current diagnosis of major depressive disorder.

Results: We included data from 503 PWH for whom we had accurate chart abstraction data. Approximately 60% (n=304) were men, 55% (n=276) were Black, with a mean age of 52 (±10.41) years. Nearly half (46.32%) of the participants were diagnosed with at least one comorbid condition at the time of the study (range: 0–8 diagnoses). Major depressive disorder (P<0.001), recent higher fatigue symptom rating (P<0.01) and White race (P=0.045) had significant positive associations with being diagnosed with a greater number of comorbid conditions at the time of the study. PWH with major depressive disorder were diagnosed with significantly greater numbers of comorbidities when controlling for fatigue levels and race, and no interaction effects between major depressive disorder, fatigue, or race were found in our analysis. Major depressive disorder diagnosis was most strongly associated with cardiovascular (HTN, ischemic heart disease, valvular heart disease; P<0.001) and pulmonary (COPD, asthma; P<0.001) comorbidities. See Table 1.

Discussion: We found that a current depression diagnosis was associated with a greater number of comorbidities, in particular cardiovascular and pulmonary diagnoses. Despite its high prevalence, depression remains under-diagnosed and under-treated in PWH.

Table 1. (Abstract P39)
Depression is both a major risk factor and a consequence of comorbidities. Failure to address depression increases mortality and decreases adherence to treatment regimen(s). Future research should examine specific pathways between depression and comorbidities in PWH and develop interventions to promote and maintain long-term treatment in PWH who suffer from comorbid depression.
Prevalence of HIV-associated neurocognitive disorder (HAND) in Turkey and assessment of Addenbrooke’s Cognitive Examination Revised (ACE-R) test as a screening tool

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Objectives: We aimed to determine the prevalence and associated factors for HAND among HIV-infected patients in Turkey. In addition, Addenbrooke’s Cognitive Examination Revised (ACE-R) and three Simioni questions (3Qs; EACS Guidelines) were also assessed as potential screening tools for HAND.

Methods: HIV-infected patients were enrolled consecutively from two different teaching hospitals in Istanbul, Turkey, between March 2018 and September 2018. Persons with a history of confounding neurological or psychiatric disorders or active substance abuse and non-native speakers were excluded from participation. Patients underwent the two screening tools, a neuropsychological (NP) test battery covering seven cognitive domains and an assessment of activities of daily living. HAND was diagnosed according to the Frascati’s criteria and applying Global Deficit Score (GDS) approach. A receiver operating characteristic (ROC) curve analysis was performed to compare the predictive accuracy of ACE-R to the NP test battery. Several demographic and disease factors were evaluated for association with HAND using a multivariate logistic regression analysis.

Results: The study population included 162 participants (median age: 43.5 years, 94% male, median education: 13 years, median nadir CD4: 295 cells/ml and median current CD4: 630 cells/ml). Plasma HIV RNA was <200 copies/ml in 158 (97.5%) subjects. The median time on ART was 3 years (IQR 1.5–6.6). HAND prevalence was 45.7% (asymptomatic neurocognitive impairment [ANI]=37.7%; mild neurocognitive disorder [MND]=7.4%; HIV-associated dementia [HAD]=0.6%) according to the Frascati criteria, and 31.5% (ANI=25.9%; MND=4.9%; HAD=0.6%) using the GDS. Memory (learning, recall; 27.2%), attention/working memory (24.7%) and planning/executive (20.4%) were the most frequently impaired domains.

In ROC analysis, the ACE-R showed an area under the curve of 0.74 at a cutoff score of 89 (Figure 1). Sensitivity, specificity and correct classification rate (CCR) of screening tests for HAND diagnosis were as follows: ACE-R (62.2%, 67%, 64.8%) and 3Qs (10.8%, 88.6%, 53%). Considering only symptomatic neurocognitive disorders, ACE-R presented a CCR of 61%. In multivariate analysis, only education level (aOR: 0.84; 95% CI: 0.76, 0.92; P<0.001) was an independent risk factor for HAND.

Conclusions: This is the first study evaluating neurocognitive impairment in Turkish HIV population using normative data. Despite a very well controlled population, HAND is a prevalent comorbidity in HIV-infected persons in Turkey. The sensitivity of ACE-R and 3Qs as screening tools are lower than desired.
Figure 1. Receiver Operator Curves for Addenbrooke’s Cognitive Examination Revised (ACE-R) test
ABSTRACT P41

Antiviral Therapy 2019; 24 Suppl 1:A97

Reproductive and sexual health knowledge, experiences and milestones in young adults with life-long HIV

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Objective: Reproductive and sexual health outcomes of adults with perinatal human immunodeficiency virus (PHIV) have not been well-characterized to date. Little is known about the impact HIV has on this population’s reproductive and sexual outcomes and satisfaction, their transmission knowledge, or their experiences with the health-care system as it pertains to family planning. Using a secure web-based platform, we assessed these questions in a cohort of reproductive aged persons living with HIV (PLWH) since early childhood compared with matched HIV-negative controls.

Methods: This is a prospective cross-sectional study of 35 adult PLWH who acquired HIV in early life and 20 matched HIV-negative controls. Quality of life, depressive symptoms, HIV transmission knowledge, sexual/reproductive outcomes and behaviours were evaluated through self-report questionnaires.

Results: PLWH had a mean age of 29 years, 65% virally suppressed, with a mean CD4 T-cell count 527 cells/ul. PLWH scored significantly worse than controls on depressive symptoms (P=0.04) and two quality of life domains (physical domain P=0.03, level of independence P=0.0002). By contrast, PLWH scored significantly higher on questions assessing family planning transmission knowledge (P=0.002), with no differences between groups in general HIV transmission knowledge. PLWH were more likely to learn about sexual matters from health-care providers (P=0.002) and were more confident in the adequacy of their sexual/reproductive health knowledge (P<0.05). Both groups reported inconsistent condom use (59% PLWH and 75% controls; P=0.23), but PLWH were more likely to have planned pregnancies (P=0.005) and to have discussed becoming pregnant with their partner (P<0.05) compared with controls.

Conclusions: Despite the challenges of living with a chronic and stigmatized condition, adult PLWH since childhood were knowledgeable about HIV transmission and family planning and demonstrated sexual practices and reproductive outcomes similar to age-matched controls. However, sub-optimal rates of viral suppression, inconsistent condom use and the psychosocial impact of living with HIV continue to require the attention of health-care providers for young adults with PHIV.
Correlation between cerebrospinal fluid (CSF) and plasma concentrations of neurofilament light protein (NFL) in treated HIV infection in the COMorBidity in Relation to AIDS (COBRA) Study

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Purpose: CSF NFL is an established biomarker of central nervous system neuro-axonal injury. A novel ultra-sensitive assay can determine plasma NFL. In untreated people with HIV (PWH), plasma and CSF NFL are strongly correlated. We assessed this correlation in antiretroviral therapy (ART)-treated PWH and lifestyle-similar HIV-negative controls, and determined factors associated with plasma and CSF NFL in PWH.

Methods: Differences in paired plasma (Simoa digital immunoassay, QuanterixTM) and CSF (sandwich ELISA, UmanDiagnostics AB) NFL between PWH and HIV-negative controls were tested for significance using Wilcoxon’s test; associations between the values (after log-transformation) were assessed using Pearson’s correlation. Log-transformed plasma and CSF NFL, standardized to Z-scores, were included as dependent variables in linear regression models to identify factors independently associated with values in PWH; factors significant (P<0.05) in univariable analyses for either outcome were included in the multivariable models.

Results: We included 132 PWH (median age 56 years, 94% male, 88% White, 100% HIV-1 RNA <50 copies/ml) and 79 HIV-negative controls (57 years, 92% male, 97% White). Neither CSF (570 versus 568 pg/ml; P=0.37) nor plasma (10.7 versus 9.9 pg/ml; P=0.15) NFL differed significantly between the two groups. Plasma and CSF NFL correlated moderately, with no significant difference by HIV status (PWH: r=0.52 [95% CI 0.38, 0.63]; HIV-negative: r=0.47 [0.27, 0.62]; P [interaction]=0.63). In multivariable regression, older age and lower weight were each associated with higher plasma and CSF NFL Z-scores in PWH. Whereas lower plasma albumin and higher serum creatinine were associated with higher plasma NFL Z-scores, higher CSF protein was associated with higher CSF NFL Z-scores. See Table 1.

Conclusions: In PWH on suppressive ART, the correlation between CSF and plasma NFL is weaker than previously described in untreated PWH but similar to that observed in lifestyle-similar controls. Consideration of renal function and body composition may be required when utilizing plasma NFL.
Table 1. (Abstract P42)

<table>
<thead>
<tr>
<th>Dependent variable</th>
<th>Independent variables</th>
<th>Parameter estimate (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Log₁₀ (plasma NFL)</td>
<td>Age (/10 years older)</td>
<td>0.60 (0.42, 0.79)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Weight (/5kg higher)</td>
<td>-0.13 (-0.18, -0.08)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Serum creatinine (/10μmol/L higher)</td>
<td>0.12 (0.04, 0.19)</td>
<td>0.002</td>
</tr>
<tr>
<td></td>
<td>Plasma albumin (/10g/L higher)</td>
<td>-0.39 (-0.69, -0.09)</td>
<td>0.012</td>
</tr>
<tr>
<td>Log₁₀ (CSF NFL)</td>
<td>Age (/10 years older)</td>
<td>0.69 (0.50, 0.89)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Weight (/5kg higher)</td>
<td>-0.07 (-0.12, -0.01)</td>
<td>0.021</td>
</tr>
<tr>
<td></td>
<td>CSF protein (/1g/L higher)</td>
<td>1.33 (0.50, 2.16)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

*Parameter estimates reflect the associated impact (measured in standard deviations) of each independent variable in the model on the dependent variable.

*Variables included in the multivariable linear regression models were age, weight, serum creatinine, plasma albumin, CSF protein, male gender, being on antihypertensive medication, duration diagnosed with HIV infection, duration on ART.
**ABSTRACT P43**  
*Antiviral Therapy* 2019; 24 Suppl 1:A100

**In vitro** modelling of the impact of TAF on cellular bioenergetics in immune cells and hepatocytes

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**Objectives/aim:** The mechanisms that drive differential effects of antivirals on HIV-related immune dysfunction and alterations in metabolism remain unclear. Markedly lower plasma levels of tenofovir (TFV) are thought to lead to the more favourable bone and renal safety profile of tenofovir alafenamide (TAF) compared with tenofovir disoproxil fumarate (TDF). However, it is unknown whether an increase in intracellular levels of the active metabolite, tenofovir-diphosphate (TFV-DP) with TAF (compared with TDF) may affect mitochondrial function and contribute to alterations in cellular metabolism. This study was designed to address whether TAF affects *in vitro* cellular bioenergetics in human peripheral blood mononuclear cells (PBMCs) and the HepG2 cell line.

**Methods:** Zalcitabine (ddC) has known mitochondrial toxicity and was used as positive control. PBMCs were isolated from healthy 18–40 years old participants. Standardized number of cells was used for all experiments (14,000 HepG2 cells/well and 100,000 PBMCs/well). 2-h incubation conditions with TDF and/or TAF at concentrations that have been shown to model cellular levels of TFV-DP similar to those observed in PBMCs in clinical studies with TDF and/or TAF were selected to model clinically relevant plasma exposure. The XF96 Extracellular Flux Analyzer was used to monitor cellular bioenergetics in PBMCs and HepG2 cells. A decrease in the ATP-linked respiration (ATP-OCR) and/or the maximum respiration rate (max-OCR) caused by addition of the FCCP uncoupler may suggest mitochondrial dysfunction. Results are described as median and interquartile range (IQR) and the Wilcoxon and Mann–Whitney tests were used for statistical comparison between groups.

**Results:** After 2 h of *in vitro* exposure of HepG2 cells to 0.12–3.3 µM TAF, TDF and ddC, 3.3 µM ddC induced a mean >30% decrease in both ATP-OCR and max-OCR compared with DMSO vehicle control (*P*<0.001). 1.1 µM TAF induced a mean ~18% increase in ATP-OCR (*P*<0.001) and a mean ~15% increase in max-OCR (*P*<0.05) compared with vehicle control. 1.1 µM TAF also induced a mean ~9% increase in ATP-OCR (*P*<0.001) compared with 0.12 and 1.1 µM TDF. 2 h of *in vitro* exposure of primary PBMCs to 0.12–3.3 µM TAF, TDF and ddC did not impact OCR (data not shown).

**Conclusions/discussion:** In the setting of delivering higher intracellular levels of TFV-DP than TDF, TAF may alter cellular bioenergetics at *in vitro* incubation conditions that model clinically relevant plasma exposure in hepatocytes as early as 2 h. We did not find any evidence of *in vitro* mitochondrial toxicity (reduction in OCR) with TAF. TAF could cause a differential metabolic reprogramming on substrate dependency in hepatocytes compared with immune cells. The clinical relevance of these *in vitro* findings is unknown. The effect of TAF on cellular bioenergetics in chronic treated HIV should be further explored in patients switching from TDF to TAF regimens.
Targeting inflammation in chronic treated HIV with oral ApoA-I mimetics


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Objectives/aim: Novel therapeutic approaches are needed to attenuate inflammation that may contribute to morbidity in chronic treated HIV infection. ApoA-I peptides (such as 6F) mimic HDL, bind oxidized lipids and endotoxin and attenuate proinflammatory mechanisms. The 6F was expressed as a transgene in tomatoes (Tg6F) and reduced cardiovascular disease in mice. Tg6F can be translated to human diet. Given that preclinical data are needed to assist efforts to bring Tg6F in the clinic, we used a physiologically relevant humanized mouse model of chronic treated HIV to study whether oral apoA-I mimetics attenuate *in vivo* HIV- and/or ART-driven impact on inflammation.

Methods: The C57BL/6 Rag2−/−γc−/−CD47−/− bone marrow/liver/thymus mice do not develop early graft versus host disease and thus HIV- and/or ART-driven changes on inflammation can be dissected *in vivo*. After 4 weeks of infection with the dual-tropic 89.6 HIV-1 virus, mice (n=40) were treated with daily emtricitabine (200 mg/kg), tenofovir (208 mg/kg), raltegravir (80 mg/kg) for up to 12 weeks. Oral ApoA-I mimetics were given as Tg6F (at 0.06% by weight of diet) to HIV+/ART-treated mice (n=20) after suppression of viraemia with ART. The groups were: A (n=10): uninfected (HIV-); B (n=10): HIV+; C (n=20): HIV+, ART; D (n=20): HIV+/ART/Tg6F. Human cytokines and chemokines were determined by Luminex Assays. Results are described as median and interquartile range (Tukey’s) and Mann–Whitney test was used for statistical analysis.

Results: HIV-1 induced a mean >30% reduction in plasma h-IL-1b, h-IL-6, h-IL-8, h-IL-10, h-IL-18 and h-TNF-a and a mean >25% increase in plasma h-CCL3,
h-CCL5, h-CX3CL1, h-CXCL10 and VEGF in infected compared with uninfected mice ($P<0.05$; Figure 1). Potent ART for 12 weeks suppressed viraemia within 4 weeks and induced a mean $>15\%$ increase in human cytokines compared with HIV viraemic mice. ART induced a mean $>30\%$ increase in h-CCL2, hCXCL1, murine IL-1b and TNF-a in HIV+/ART+ compared with HIV+ and uninfected mice ($P<0.05$). All other murine cytokines and chemokines did not change with HIV and/or ART (data not shown). Tg6F attenuated all ART-induced increases in m-TNF-a, m-IL-1b and human cytokines and chemokines except for h-IL-6 and h-CXCL10.

**Conclusions/discussion:** Our data provide unique insight about differential effects of HIV-1 versus potent ART on human cytokines and chemokines. HIV-1 reduced human cytokines (possibly through cytotoxic effects), whereas potent ART did not change or even increased cytokines and chemokines. Tg6F attenuated ART-induced increase in inflammation. Given that Tg6F binds endotoxin and bioactive lipids in the gut and is not absorbed systemically, our model confirms that gut dysfunction is a major instigator of inflammation in chronic treated HIV. Further studies are needed to determine whether oral ApoA-I mimetics can be a novel strategy to attenuate inflammation in chronic treated HIV.
Differential impact of HIV, antivirals and oral ApoA-I mimetics on mitochondrial function in chronic treated HIV

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Objectives/aim: The mechanisms that drive comorbidities in chronic treated HIV remain unclear. Mitochondria are responsible for creating the energy needed for function of organs. Mitochondrial dysfunction likely plays a role in ageing in chronic treated HIV. HDL-associated apolipoprotein A-I (ApoA-I) may attenuate mitochondrial dysfunction. Given that observational human studies cannot dissect the differential effects of HIV versus antivirals (ART) on mitochondria, we used a physiologically relevant humanized mouse model of chronic treated HIV to study whether oral apoA-I mimetics attenuate in vivo HIV-1 and/or ART-driven mitochondrial dysfunction.

Methods: The C57BL/6 Rag2−/−γc−/−CD47−/− bone marrow/liver/thymus mice do not develop early graft versus host disease and thus HIV- and/or ART-driven changes on tissues can be dissected in vivo. After 4 weeks of infection with the dual-tropic 89.6 HIV-1 virus, mice (n=20) were treated with daily emtricitabine (200 mg/kg), tenofovir (208 mg/kg), raltegravir (80 mg/kg) for up to 12 weeks. Oral ApoA-I mimetics were given to HIV+/ART-treated mice (n=10) as a concentrate of transgenic tomatoes expressing the 6F peptide (Tg6F) at 0.06% by weight of diet. The groups were: A (n=5): uninfected (HIV−); B (n=5): HIV+; C (n=10): HIV+, ART; D (n=10): HIV+/ART/Tg6F. Reduction in mitochondrial DNA (mtDNA) levels compromises cellular function and was used as a biomarker of mitochondrial dysfunction. mtDNA copy number and the mtDNA/ntDNA ratio were determined by real-time PCR (Figure 1). Results are described as median and interquartile range and non-parametric (un)paired tests were used for statistical analysis.

Results: HIV-1 induced a mean 28% reduction in human mtDNA/ntDNA ratio in the liver of infected compared with uninfected mice (P<0.05) but did not affect the human and murine mtDNA/ntDNA ratio in the brain (data not shown). Potent ART for 12 weeks suppressed viraemia within 4 weeks and induced a mean >20% reduction in human and mouse (not shown) mtDNA/ntDNA ratio in the liver and human mtDNA/ntDNA ratio in the brain of infected compared with uninfected mice (P<0.05). Tg6F attenuated ART-induced reduction in human mtDNA/ntDNA ratio in the brain (P<0.05) but not in the liver.

Conclusions/discussion: HIV-1 and/or potent ART had a differential direct impact on mitochondria at the tissue level (brain, liver) in vivo. Potent ART consistently induced mitochondrial dysfunction in both the liver and the brain and may be a more important (than HIV-1) instigator of mitochondrial dysfunction in chronic treated HIV. Tg6F attenuated ART-induced mitochondrial dysfunction in the brain but not in the liver. Given that Tg6F binds endotoxin and bioactive lipids in the gut and is not absorbed systemically, our model suggests that gut dysfunction may drive human neuroinflammation and mitochondrial dysfunction in chronic...
treated HIV. Further studies are needed to determine whether oral ApoA-I mimetics can be a novel strategy to attenuate mitochondrial dysfunction and comorbidities in chronic treated HIV.
ABSTRACT P46

*Antiviral Therapy* 2019; 24 Suppl 1:A105

Subtherapeutic efavirenz concentrations positively correlate with cytomegalovirus coinfection in HIV-1-infected pregnant women

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**Aim:** Effective combination antiretroviral therapy (cART) has tremendously reduced HIV-associated morbidity, mortality and mother to child transmission (MTCT). However, the benefits of cART are threatened by comorbidities, adverse drug reactions (ADRs) and virus resistance to existing regimens. One of the most occurring comorbidities is cytomegalovirus (CMV). This project aimed to investigate the role of HIV treatment (measured by plasma efavirenz concentration and viral load) in the occurrence of CMV infection among pregnant women.

**Methods:** A cross-sectional study collected demographic and clinical data from 175 HIV-1-infected pregnant women. CMV DNA was measured using real-time PCR. Plasma efavirenz concentrations were determined using HPLC. In addition, CYP2B6 c.516G>T and CYP2B6 c.983T>C single nucleotide polymorphisms, which are genomic markers for plasma efavirenz levels, were characterized using PCR/RFLP and TaqMan assays, respectively.

**Results:** Participants positive for CMV DNA (median: 847 ng/ml, 25th–75th percentile: 250–3,307) were significantly (*P*<0.001) more likely to experience sub-therapeutic plasma efavirenz concentrations than participants negative for CMV DNA (median: 2,024 ng/ml, 25th–75th percentile: 250–14,039). The median plasma efavirenz concentrations for CYP2B6 c.516T/T genotype were significantly higher than for 516G/G (*P*<0.001) and 516G/T (*P*<0.01) genotypes carriers. Median plasma efavirenz concentrations were also significantly higher (*P*<0.001) in CYP2B6 c.983T/C than CYP2B6 c.983T/T genotype carriers.

**Discussion and conclusions:** HIV and its treatment disrupt the balance between host and co-infecting microbes. Sub-therapeutic levels of antiretroviral drugs, which could be exacerbated by genetic polymorphisms in drug metabolism genes predisposes infected individuals to increased risk of CMV infection in pregnancy.
ABSTRACT P47

Antiviral Therapy 2019; 24 Suppl 1:A106

Prevalence and risk factors of proximal tubular dysfunction and its correlation with glomerular function among children with HIV seen in Lagos University Teaching Hospital, Nigeria

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Objectives: Renal tubular abnormalities occur in children with HIV but little is known about its prevalence and risk factors in children in Africa. The few studies in children that reported proximal tubular dysfunction (PRTD) used hypophosphataemia and hypercalciuria, which are not specific to proximal tubular dysfunction. In addition, studies in adults with PRTD were done in persons, the majority of whom were receiving tenofovir, an established cause of PRTD. However, involvement of the renal tubules in HIV may be directly related to the virus and the host immunological response to the virus. Therefore, we determined the prevalence and factors associated with PRTD in children with HIV.

Methods: We included 155 children living with HIV and no recent febrile illness or known history of sickle cell disease, diabetes or cardiac disease. We determined the presence of PRTD by measuring β2-microglobulin:creatinine ratio (β2M:Cr) in freshly voided urine sample. We classified the severity of HIV infection using the WHO clinical and immunological staging criteria. For comparison, we included one age and sex-matched control for every child with HIV. Proximal renal tubular dysfunction was defined as urinary β2M:Cr>300 µg/g.

Results: The mean age of the children with HIV was 11.1 ±3.6 years and 52.7% were females. The prevalence of PRTD was 23.9% among the children with HIV and 11.6% among the controls (P=0.005). Children with HIV and PRTD were younger than those without PRTD (8.9 ±3.8 versus 11.8 ±3.3 years; P<0.001). Children with stage IV HIV disease had 64.3% prevalence of PRTD which was about three times higher than the rates in children with milder forms of HIV disease (P=0.003). Also, children with severe immunosuppression had prevalence of PRTD that was at least two times higher than in children with no or mild immunosuppression (P=0.038). In addition, children with detectable HIV viral load on polymerase chain reaction had two times the prevalence of PRTD of those without PRTD (29.6% versus 14.0%; P=0.025). Children receiving tenofovir-based HAART regimen had similar prevalence of PRTD to those on other regimens (25% versus 23.8%; P=0.606). In multiple regression analysis, the risk of developing PRTD was five times for children in stage IV (4.83 [1.01–23.08]) compared with those in stage I and 10 times (10.00 [1.58–63.45]) for those with severe immunosuppression compared with those with no immunosuppression.

Conclusions: PRT dysfunction occurs in one out of every four children with HIV irrespective of exposure to tenofovir. Children with WHO stage IV clinical and severe immunological stages of HIV were 5 and 10 times more likely to develop PRTD, respectively, than those with milder stages of HIV.
ABSTRACT P48

Antiviral Therapy 2019; 24 Suppl 1:A107

Targeting immune activation in chronic treated HIV with oral ApoA-I mimetics

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Objectives/aim: Monocyte/macrophage (M/M)-related (rather than T-cell) inflammation and immune activation may contribute to morbidity and mortality in chronic treated HIV-1 infection. Novel therapeutic approaches are needed to attenuate M/M activation in chronic treated HIV infection. Novel therapeutic approaches are needed to attenuate M/M activation in chronic treated HIV infection. ApoA-I peptides (such as 6F) mimic HDL, bind oxidized lipids and endotoxin and attenuate proinflammatory mechanisms. The 6F was expressed as a transgene in tomatoes (Tg6F) and reduced cardiovascular disease in mice. Tg6F can be translated to human diet. Given that preclinical data are needed to assist efforts to bring Tg6F in the clinic, we used a physiologically relevant humanized mouse model of chronic treated HIV to study whether oral apoA-I mimetics attenuate in vivo HIV- and/or ART-driven alterations in human biomarkers of M/M activation (sCD163, sCD14) that predict morbidity and mortality in chronic treated HIV.

Methods: The C57BL/6 Rag2−/−γc−/−CD47−/− bone marrow/liver/thymus mice do not develop early graft versus host disease and thus HIV- and/or ART-driven changes on M/M activation can be dissected in vivo. After 4 weeks of infection with the dual-tropic 89.6 HIV-1 virus, mice were treated with daily emtricitabine (200 mg/kg), tenofovir (208 mg/kg), raltegravir (80 mg/kg) for up to 12 weeks. Oral ApoA-I mimetics were given as Tg6F (at 0.06% by weight of diet) to HIV+/ART-treated mice (n=20) after suppression of viraemia with ART. The groups were: A (n=10): uninfected (HIV-); B (n=10): HIV+; C (n=20): HIV+, ART; D (n=20): HIV+/ART/Tg6F. Plasma levels of human sCD14 and sCD163 were determined by Luminex Assays. Results are described as median and interquartile range (Tukey’s) and Mann-Whitney test was used for statistical analysis.

Results: HIV-1 induced a mean 59% and 56% reduction in plasma h-sCD14 and h-sCD163, respectively, in infected compared to uninfected mice (P<0.05). Potent ART for 12 weeks suppressed viraemia within 4 weeks and induced a mean 49% and 38% increase in h-sCD14 and h-sCD163 (P<0.05) in HIV+/ART+ compared with HIV+ mice (P<0.05). Tg6F attenuated ART-induced increases in h-sCD14 and h-sCD163 (P<0.001). See Figure 1.

Conclusions/discussion: Our data provide unique insight about differential effects of HIV-1 versus potent ART on human M/M activation. HIV-1 reduced h-sCD14 and h-sCD163 (possibly through cytotoxic effects), whereas potent ART increased h-sCD14 and h-sCD163. Our mechanistic data complement prior observational human studies that M/M activation persists in chronic treated HIV despite potent ART. ART rather than HIV-1 per se may contribute to elevated M/M activation in chronic treated HIV. Tg6F attenuated ART-induced increase in M/M activation. Given that Tg6F binds endotoxin and bioactive lipids in the gut and is not absorbed systemically, our model confirms that gut dysfunction is a major instigator of M/M activation in chronic treated HIV. Further studies are needed to determine whether oral ApoA-I mimetics can be a novel strategy to attenuate M/M activation in chronic treated HIV.

Figure 1. (Abstract P48)
ABSTRACT P49
Antiviral Therapy 2019; 24 Suppl 1:A108
Age- and sex-related differences in concomitant diseases and use of co-medication in patients with treated HIV infection in Germany
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Background: Demographic ageing of HIV-infected populations poses new challenges to physicians. Advancing age is associated with (multiple) chronic diseases and need for co-medication.

Methods: BESIDE was a cross-sectional study evaluating the prevalence of concomitant diseases and prescription and over the counter co-medication in people living with HIV (PLWH) on antiretroviral therapy from 2016–2017. Regional distribution of study sites (n=20), consecutive recruitment and age-stratified sampling ensured a representative sample of the PLWH population in Germany.

Results: n=453 PLWH were enrolled: female 22%, median age 46 years (y), median time living with HIV 9 y; CDC C 15%, median CD4 count 650 cells/µl. Among the top three comorbidities per age group, vitamin D deficiency (29% overall) and depressive episodes (28% overall) were consistently reported across age groups. The third most common comorbidity differed: in younger PLWH, acute respiratory infections (<30 y, 11%) and gastro-oesophageal reflux disease (30–39 y, 8%) were most prevalent, while for older PLWH, hypertension was increasingly reported (40–49 y, 12%; >60 y, 41%).

Women more often (f/m, difference ∆>5%) suffered from nutritional anaemias (11%/4%), other nutritional deficiencies (39%/28%), bone density/structure disorders (9%/1%) and thyroid gland disorders (10%/4%). Conversely, metabolic disorders (10%/21%), sexually transmissible infections (2%/9%), polyneuropathies/peripheral nervous system disorders (1%/7%) and dorsopathies (2%/8%) were more common in men.

Most common drugs used across all ages were vitamin supplements (32% overall). Anti-inflammatory/anti-rheumatic agents (16%) also belonged to the top three drugs in all age groups, except >60 y where antithrombotic agents were more frequent (30%). In addition, younger patients received vaccines (<30 y, 9%) and used psychoactive drugs (30–39 y, 10%; 40–49 y, 12%), whereas in older patients renin-angiotensin system agents (50–59 y, 21%; >60 y, 30%) ranked higher. Women more commonly used (f/m, ∆>5%) antinaemia preparations (14%/6%), vitamins (38%/30%) and mineral supplements (10%/5%); men more commonly used antithrombotic agents (4%/11%), renin-angiotensin system agents (7%/14%) and lipid modifiers (6%/12%).

Conclusions: Although prevalence of concomitant diseases and use of co-medication among PLWH in Germany are high across gender and all ages, the disease and drug patterns change in an age- and sex-related manner.
ABSTRACT P50

Antiviral Therapy 2019; 24 Suppl 1:A109

Comparative effectiveness of raltegravir-based dual therapy versus other regimens in patients switched for maintenance

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Background: In clinical practice raltegravir is used in nuke-free dual therapy. Here, we compared profiles and 48-week treatment outcomes of patients on RAL-based dual versus other RAL-based ART in a historical German real-life cohort.

Methods: The WIP study was a real-life, prospective, observational cohort study with data collection from 2010–2014. Safety and efficacy outcomes of RAL-based ART in a population enriched for ageing patients (274, 61% ≥50 years) were documented. Detailed methods are described elsewhere.

Results: The cohort included 77 (17%) patients on dual and 372 patients on other ART. 85% were male, no differences by treatment group. Compared with patients on other ART, patients initiated on RAL-based dual therapy were on average 3.9 years older and suffered more likely from hypertension (26% versus 18%), coronary artery disease (12% versus 4%) and renal insufficiencies (10% versus 4%) at baseline. They were less frequently therapy-naive (17% versus 22%) or pretreated with suppressed viral load (VL; 45% versus 51%) but more often failing (35% versus 22%). Dual therapies mainly included a PI (94%, 72/77); most other regimen combinations included NRTI (77%, 287/374). Treatment outcomes of dual versus other ART differed slightly: 48-week virological response (VL<50 c/ml; early DC [discontinuation]=failure) was numerically lower in therapy-naive patients (69% versus 76%). However, in virologically suppressed patients switched for maintenance efficacy of RAL-based dual therapy was high and comparable to other RAL-based regimens (83% versus 81%; Table 1).

Conclusions: Patients on RAL-based dual versus other ART showed differing comorbidity profiles and RAL utilization patterns. While outcomes in therapy-naive and pretreated failing patients were less favorable, response rates in virologically suppressed patients were high and comparable supporting the concept of maintenance switch to RAL-based dual therapy to avoid drug toxicities or intolerances.

Table 1. (Abstract P50)

<table>
<thead>
<tr>
<th></th>
<th>Dual therapy</th>
<th>Other regimens</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>VL&lt;50 c/mL N (%)</td>
<td>VL≥50 c/mL N (%)</td>
</tr>
<tr>
<td>Therapy-naive</td>
<td>9 (69%)</td>
<td>1 (8%)</td>
</tr>
<tr>
<td>Pretreated suppressed</td>
<td>29 (83%)</td>
<td>2 (6%)</td>
</tr>
<tr>
<td>Pretreated failing</td>
<td>18 (67%)</td>
<td>7 (26%)</td>
</tr>
<tr>
<td>Pretreated - ART interruption</td>
<td>1 (50%)</td>
<td>1 (50%)</td>
</tr>
<tr>
<td>Total</td>
<td>57 (74%)</td>
<td>11 (14%)</td>
</tr>
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</table>

Table 1: Therapeutic outcomes at week 48
ABSTRACT P51

Antiviral Therapy 2019; 24 Suppl 1:A110

Gender-specific analysis of a German cohort of HIV-infected patients on raltegravir-based therapy shows distinctive baseline comorbidity profiles of women versus men but no impact on treatment outcomes

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Background: HIV-infected women are facing specific needs in the context of antiretroviral therapy. For a better understanding, we performed a gender-specific post hoc analysis for patients on raltegravir (RAL)-based therapies in the German real-life cohort WIP.

Methods: The WIP study was a prospective, observational, multicentre cohort study in routine clinical care with data collection between 2010 and 2014. Safety and efficacy outcomes of RAL-based antiretroviral therapy in a population enriched for ageing patients (274, 61% ≥50 years) were documented. Detailed methods are described elsewhere.

Results: The cohort included 69 (15%) female and 382 (85%) male HIV-infected patients. Mean age was 51 years in both groups. At RAL initiation women and men were 13% versus 23% therapy-naive, 49% versus 51% pretreated with virological suppression and 33% versus 23% without virological suppression. At baseline, female patients suffered more frequently from depression (23% versus 16%) as well as chronic HCV infection (20% versus 9%) and male patients more often from cardiovascular diseases including hypertension (15% versus 20%) as well as lipid abnormalities such as hypercholesterolaemia (6% versus 11%) and hypertriglyceridaemia (1% versus 6%). Concomitant medications at baseline were consistent with these comorbidity profiles. No gender-specific differences in RAL-based therapy were observed in women versus men: RAL was combined with PI in 17% versus 16%, with NRTI in 64% versus 64% and with others in 19% versus 20%. Regarding treatment outcomes, virological response rates were comparable between women and men (Table 1).

Conclusions: In this German real-life cohort, characterization of female versus male patients demonstrated divergent comorbidity profiles and minor differences in utilization patterns of RAL-based therapy. Nevertheless, in both women and men similar and high response rates comparable to clinical trial results could be observed.

Table 1. (Abstract P51)

<table>
<thead>
<tr>
<th>Therapy Status</th>
<th>Women N (%)</th>
<th>Men N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy-naive</td>
<td>VL&lt;50 c/mL</td>
<td>7 (78%)</td>
</tr>
<tr>
<td></td>
<td>VL≥50 c/mL</td>
<td>0 (0%)</td>
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<tr>
<td></td>
<td>early DC</td>
<td>2 (22%)</td>
</tr>
<tr>
<td>Pretreated - suppressed</td>
<td>29 (85%)</td>
<td>2 (6%)</td>
</tr>
<tr>
<td>Pretreated - failing</td>
<td>15 (65%)</td>
<td>4 (17%)</td>
</tr>
<tr>
<td>Pretreated - ART interruption</td>
<td>1 (33%)</td>
<td>2 (67%)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>52 (75%)</td>
</tr>
</tbody>
</table>

Table 1: Therapeutic outcomes at week 48
ABSTRACT P52

*Mycobacteria*-induced immune responses by mucosal-associated invariant T (MAIT) cells are impaired in patients with tuberculosis (TB) and HIV-associated TB

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Background and objectives: MAIT cells are non-classical T lymphocytes that recognize and rapidly respond to microbial vitamin B metabolites and have the capacity to kill bacteria-infected cells. Circulating MAIT cell numbers decrease in patients with active TB and HIV, but previous findings regarding functional changes have been conflicting. We conducted a cross sectional study to assess the effect of HIV, TB and HIV-associated TB (HIV–TB) on MAIT cell numbers, activation, inhibitory and functional profile in a TB endemic setting in South Africa.

Methods: Blood was collected from healthy controls (HC; n=26), individuals with HIV infection only (HIV; n=30), with active TB only (aTB; n=30) and with HIV–TB (n=26). All TB participants were newly

Figure 1. (Abstract P52)
diagnosed with TB and sampled prior to treatment. Peripheral blood mononuclear cells (PBMC) were isolated and stimulated with BCG expressing GFP (BCG-GFP) or heat-killed (HK) *Mycobacterium tuberculosis* (Mtbc) and analysed using flow cytometry.

**Results:** There were lower frequencies of MAIT cells in HIV (median: 0.3%; \( P=0.04 \)) and aTB (0.4%; \( P=0.02 \)) compared with HC (0.7%). BCG-specific MAIT cell activation (measured by HLA-DR expression [median fluorescent intensity]) was higher in aTB (230; \( P=0.006 \)) and HIV–TB (280; \( P=0.0008 \)) compared with HC (114). BCG-induced MAIT cell degranulation (measured by CD107a expression) was lower in aTB (4.5%; \( P=0.003 \)) and HIV–TB (4.6%; \( P=0.04 \)) compared with HC (9.8%). Similarly, IFN-\( \gamma \) expression was lower in aTB and HIV–TB (3.2% and 1.0%; \( P=0.0005 \) and \( P=0.0006 \), respectively) compared with HC (17.6%). Similar results to BCG were obtained with HK-Mtb stimulation. Compared with HC, MAIT cells from individuals with aTB had higher basal PD-1 expression (2.1% versus 5.2%; \( P<0.0001 \)). See Figure 1.

**Conclusions:** Our data show that compared with HC, HIV and aTB result in a decrease in circulating MAIT cells, while aTB and HIV–TB resulted in a significant increase in activation and inhibitory status, and an impaired mycobacteria-induced functional profile.

**Funding:** This study was funded by the National Research Foundation (NRF) of South Africa and the Wellcome Trust.