Introduction Persistent systemic immune activation despite effective HIV treatment may be revealed by measuring plasma 'biomarker' levels. Here we investigate three established biomarkers within a well-characterised HIV cohort.
Methods Plasma sCD14, sCD163 and CXCL10 levels were measured by ELISA methods in 475 consecutive patients with documented CVD risk (age, ethnicity, gender, smoking, blood pressure, BMI, fasting metabolic profile), as well as HIV treatment history and immunological/virological outcomes, and analysed using multiple regression analysis.
Results All biomarkers were reduced with higher CD4 counts ($p < 0.05$), but showed distinct associations with virological response: CXCL10 strongly correlated with viral load ($p < 0.001$), sCD163 was significantly reduced among 'aviremic' patients only ($p = 0.02$), while sCD14 was unaffected by virological status under 10000 cpms ($p > 0.2$) however sCD14 was increased if HIV RNA viral load was >10000 cpm ($p = 0.003$). The choice of HIV treatment did not affect CXCL10, however, higher sCD163 was associated with PI's ($p = 0.05$) and lower sCD14 was associated with integrase inhibitors ($p = 0.02$). Several CVD risk factors were associated with sCD163 (age, ethnicity, HDL, BMI), with a favourable influence of Framingham score <10% ($p = 0.04$). Soluble CD14 levels were higher among smokers ($p = 0.002$), with no effect of other CVD risk factors, except age ($p = 0.045$), or overall Framingham score.
Conclusion These biomarkers reveal remarkably distinct associations, with levels of CXCL10 most readily explained by routinely monitored variables (viral load, CD4 counts), while sCD163 levels appear to reflect a deeper level of virological suppression as well as the influence of CVD risk factors. Levels of sCD14, which have been linked to overall mortality risk, are least associated with routinely monitored variables, with evidence of specific effects of smoking and integrase inhibitor therapy that warrant further investigation.
Disclosure of interest statement None to disclose.

O21.3 PRE-THERAPY INFLAMMATION/COAGULATION ACTIVATION AND LONG-TERM CD4 RESPONSE TO ANTIRETROVIRAL THERAPY

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Background Pre-antiretroviral therapy (ART) inflammation/coagulation activation biomarkers predict clinical outcomes, but whether they predict CD4 response to ART initiation is unknown.
Methods Study cohort was a subset of 2 international trials, SMART (evaluating continuous versus interrupted ART) and FIRST (evaluating 3 first-line ART regimens with ≥2 classes). At the start of follow-up (baseline), participants had to be ART-naïve/off ART, have C-reactive protein (CRP), interleukin-6 (IL-6) and D-dimer measured and be (re)initiating ART. Using random effects linear models, we assessed the association between quartiles of each of the baseline biomarker and change in CD4 to up to 24 months after ART-initiation. Analyses adjusted for baseline CD4, study arm, follow-up time and other known confounders. Sensitivity analyses included separate analyses by trials and excluding the interrupted ART arm in SMART.
Results Overall, 1084 individuals (659 from SMART (26% ART naïve) and 425 from FIRST) met the eligibility criteria, providing 8264 CD4 measurements. 75% were male with the mean age of 42 years, 37% and 47% were white and black respectively, and 10% and 33%, respectively, were hepatitis B and C positive. The median (inter-quartile range) baseline CD4 (cells/mm^3) were 360 (265–473) overall and 416 (350–530) and 100 (22–300) in SMART and FIRST, respectively. All of the biomarkers were inversely associated with baseline CD4 in FIRST but not in SMART. Curves of CD4 change over time by pre-ART biomarker quartiles significantly overlapped for all biomarkers. In adjusted models, there was no significant relationship between baseline biomarker levels and mean change in CD4 (P for trend: CRP: 0.97; IL-6: 0.25 and D-dimer: 0.29). Sensitivity analyses yielded similar results.
Conclusion Pre-ART inflammation/coagulation activation markers do not predict CD4 response to ART. These biomarkers appear to influence the risk of clinical outcomes through mechanisms other than by blunting long-term CD4 gain.
Disclosure The SMART and FIRST studies were funded by grants from US National Institutes of Health (NIH). Kirby Institute, UNSW Australia, is funded through the Australian Government Department of Health and Ageing. No other disclosures.

O21.4 DECREASED CELLULAR ENERGY IN THE BRAIN FRONTAL WHITE MATTER IS ASSOCIATED WITH PAST IMMUNOSUPPRESION IN CHRONIC HIV INFECTION

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Background Long-term brain neurochemical changes are not clearly understood in HIV-infected adults who are ageing and are otherwise clinically stable.
Methods Forty men (mean age = 54 ± 7), 20 HIV-infected (70% with historical AIDS, nadir CD4 ≤350, all on antiretroviral treatment and virally suppressed), and 20 demographically comparable HIV-uninfected controls were enrolled into a prospective observational cohort study. All underwent standard neuropsychological testing to determine the level of neurocognitive performance over an 18-month period, and a proton magnetic resonance spectroscopy scan of the brain frontal white matter to assess *in vivo* neurochemical information. Clinically relevant neuropsychological change over the study period was determined using neurocognitive norms for change. Major brain metabolites: Creatine, N-Acetyl Aspartate, Choline, Glutamate/Glutamine and Myo-Inositol were fitted in jMRUI in reference to water. Brain metabolites' change was determined using linear regression with a time effect, a group effect and a time*group interaction effect. Data were randomly selected from the larger baseline cohort (N = 120) for this preliminary analysis.
Results Over the 18 months period, neurocognitive performance change did not differ between HIV-infected and controls. Creatine significantly decreased in the HIV-infected compared to the controls ($p < 0.03$). Myo-Inositol and Glutamate/Glutamine increased as a function of time ($p < 0.0001$) but equally in both groups. When adjusting our analyses for age, we corroborated an age*group effect ($p < 0.03$) on reduced N-Acetyl Aspartate in the HIV-infected participants, while the decreasing Creatine

results were maintained. Among the HIV disease biomarkers including viral load blips over the study period, only a lower nadir was associated with decreasing Creatine (Spearman Rho r = -.49, p < 0.03).

Conclusions Chronic HIV infection is associated with subclinical cellular energy abnormalities (Creatine) linked to past levels of immunosuppression and acceleration of neuronal integrity (N-Acetyl Aspartate). This preliminary study further reinforces the need for longer-term follow-up in chronic HIV-infected ageing persons to determine the prognostic value of these findings.

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O22 - Ending hepatitis C in populations

O22.1 AUSTRALIAN HIV/HEPATITIS C CO-INFECTED PATIENTS FALL BEHIND HIV MONO-INFECTED PATIENTS IN MOVE TOWARDS EARLY HIV TREATMENT INITIATION

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Introduction One in eight people living with HIV (PLHIV) in Australia are estimated to be co-infected with Hepatitis C (HCV). In the light of clinical guideline changes with regard to antiretroviral therapy (ART) initiation, we examine the impact of co-infection status on uptake of treatment, and highlight population-specific differences relative to HIV mono-infected patients.

Methods Ipsos Healthcare's HIV Therapy Monitor is a patient chart audit study, which monitors trends in the treatment of PLHIV in Australia. Demographic and treatment data are collected bi-annually from a panel of 25+ HIV-treating clinicians. The data in this report is based on a sample of 4331 patient records collected between 2008- 2014, of which 412 were co-infected with HCV.

Results While the proportion of HIV mono-infected patients receiving ART has steadily increased from 67% in 2008 to 84% in 2014 (p < 0.0001), the opposite trend is observed in the HIV/HCV co-infected population. The rate of treatment in the co-infected cohort has dropped from 84% in 2010/2011 to 66% in 2014 (p = 0.003), with co-infected patients experiencing an average delay of 42 months between HIV diagnosis and initiation of ART, compared with 25 months for mono-infected patients (p = 0.013). Patient's lack of support network was most frequently cited by clinicians as the reason for delaying treatment for co-infected patients, followed by patient choice and expected non-compliance.

Conclusion Increasing evidence is now available to support early initiation of ART, both in terms of clinical benefits as well as in preventing disease transmission. However, despite encouraging results among HIV mono-infected patients, outcomes for the HIV/HCV co-infected population reveal a growing disparity between these groups in Australia. The increasing delay to treatment supports the need to consider this patient group a priority population, and indicates that further action is required to address the complications involved in treating these patients.

Disclosure of interest statement There are no conflicts of interest to declare.

O22.2 DETECTION OF HEPATITIS C VIRUS (HCV) IN SEMEN FROM HIV-INFECTED MEN WHO HAVE SEX WITH MEN (MSM) DURING ACUTE HCV INFECTION

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Introduction The mechanism(s) and bodily fluid(s) involved in the recently identified epidemic of sexually transmitted HCV in HIV-infected MSM are unclear. HCV is present only intermittently and at low levels in semen from men with chronic HCV-infection, however little is known of the dynamics of seminal HCV during acute HCV-infection.

Methods HIV-infected MSM with acute and chronic HCV-infection were prospectively enrolled into an IRB-approved study. Three paired semen and blood specimens were collected at 2-week intervals. HCV viral load (VL) was quantified using an automated RT-PCR assay platform (Abbott).

Results Paired semen and blood specimens were obtained from 33 HIV-infected MSM (21 with acute-HCV and 12 with chronic-HCV). Sixteen (27%) of 59 semen specimens had detectable HCV VL, with 11 (33%) men having at least one positive specimen. Semen specimens with detectable HCV had a significantly higher median blood HCV VL (P = 0.002). There were no differences between men with acute or chronic HCV in either the proportion of semen specimens positive for HCV (8/38 [21%] and 8/21 [38%], respectively; P = 0.159), or in the median seminal HCV VL (1.32 log IU/ml and 1.77 log IU/ml, respectively; P = 0.163).

Conclusion This study, although identifying no differences in the magnitude or proportion of seminal HCV during acute HCV-infection, provides valuable insights into the dynamics of seminal HCV during this period. It is unknown whether the levels of seminal HCV identified in this study are sufficient for the sexual transmission of HCV in HIV-infected MSM. However, it is plausible that HCV in semen deposited in the rectum after the friction of receptive anal intercourse, could enter the blood stream and infect the liver. Future research should focus on establishing the infectivity of seminal HCV, and the analysis of seminal HCV levels during the `ramp-up' period of early acute HCV-infection, where blood HCV levels are highest.

Disclosure of interest statement There are no competing or financial interests to disclose.