MONTRÉAL

CONFERENCE
CAHR 2017

26th Annual Canadian Conference on HIV/AIDS Research

April 6-9, 2017
Montreal, Quebec

CONGRÈS DE
L'ACRV 2017

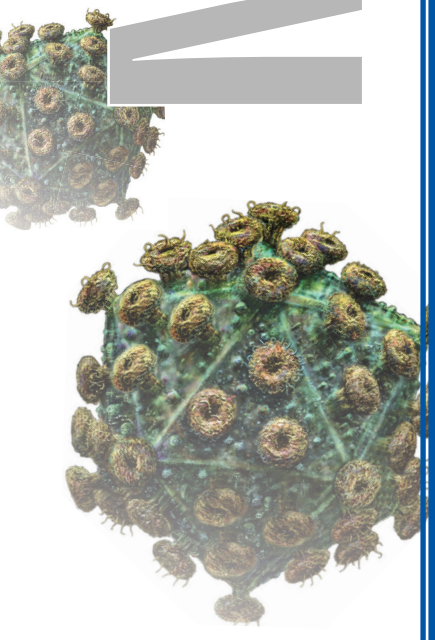
26e Congrès annuel canadien de recherche sur le VIH/sida

Du 6 au 9 avril 2017
Montréal (Québec)

WE'RE NOT DONE YET

NOUS N'AVONS PAS ENCORE FINI

ABSTRACTS
ABRÉGÉS



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Canadian Association for HIV Research
L'association canadienne de recherche sur le VIH

CAHR 2017

We're Not Done Yet

26th Annual Canadian Conference on HIV/AIDS Research

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Abstracts / Abrégés

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Montréal, Québec

Message from the CAHR President / Message du président de l'ACRV

Welcome to the 26th Annual Canadian Conference on HIV/AIDS Research (CAHR 2017).

The Canadian Association for HIV Research (CAHR) is proud to be part of the consortium of researchers and community groups working tirelessly together in the global fight against HIV. With a membership of more than 2,000 researchers and others interested in HIV research, CAHR is the leading organization of HIV/AIDS researchers in Canada.

As highlighted by the theme of CAHR 2017, We're Not Done Yet, many advances have made inroads in tackling the disease – from greater insight into the biomedical complexities of the virus, to the vastly improved clinical approaches to treat HIV as well as the new and diverse strategies to reduce risks for individuals and communities. However, thousands of new infections continue to occur each year in Canada and the number of people living with HIV in Canada is rising.

That is why at CAHR 2017 in Montreal those working in all disciplines of HIV/AIDS research, as well as policy makers, persons living with HIV, and other individuals committed to ending the pandemic, will come together to share the outcomes of new research, honour new investigators, and acknowledge the achievements of major contributors to the field.

I salute the members of the 2017 Conference Planning Committee for developing a strong thematic programme that will present new scientific knowledge and offer many opportunities for structured and spontaneous dialogue on major issues facing the global response to HIV. I hope you enjoy the conference, find it to be a worthwhile learning experience, and are able to reconnect with old friends and colleagues while engaging new ones.

Thank you all in advance for your contributions, participation, and continued support.

Dr. Michael Grant

Bienvenue au 26e Congrès annuel canadien de recherche sur le VIH/sida (ACRV 2017).

L'Association canadienne de recherche sur le VIH (ACRV) est fière de faire partie du consortium de chercheurs et de groupes communautaires qui unissent sans relâche leurs efforts dans la lutte globale contre le VIH. Comptant plus de 2 000 chercheurs et autres personnes intéressées à la recherche sur le VIH, l'ACRV est l'organisme chef de file des chercheurs sur le VIH/sida au Canada.

Tel que le rappelle le thème de l'ACRV 2017, Nous n'avons pas encore fini, nombre de progrès ont eu lieu dans la lutte contre la maladie, d'une meilleure connaissance des complexités biomédicales du virus jusqu'aux approches cliniques grandement améliorées pour traiter le VIH, en passant par les stratégies nouvelles et diverses pour réduire les risques pour les personnes et les collectivités. Toutefois, le Canada recense chaque année des milliers de nouvelles infections et le nombre de personnes vivant avec le VIH au Canada continue d'augmenter.

Voilà pourquoi, à l'ACRV 2017, à Montréal, les personnes qui travaillent dans toutes les disciplines de la recherche sur le VIH/sida, de même que les responsables de l'élaboration des politiques, les personnes vivant avec le VIH et autres personnes engagées à mettre fin à la pandémie, se rassembleront pour partager les résultats des recherches nouvelles, rendre honneur à de nouveaux chercheurs et reconnaître les réalisations des principaux intervenants du domaine.

J'adresse mes cordiales salutations aux membres du comité de planification du Congrès de 2017, qui nous ont préparé un programme thématique solide qui nous apportera des exposés sur les nouvelles connaissances scientifiques et de nombreuses possibilités de dialogue structuré et spontané sur les grands enjeux présents dans la réponse globale au VIH. J'espère que vous aimerez le Congrès, que vous y trouverez de belles expériences d'apprentissage et que vous pourrez renouer avec de vieux amis et collègues tout en vous en faisant de nouveaux.

Merci d'avance de votre contribution, de votre participation et de votre soutien indéfectible.

Dr Michael Grant

Message from the Conference Co-Chairs / Message des coprésidents du congrès

It is with great enthusiasm that we welcome you to Montreal for CAHR 2017. The realizations that were achieved since the discovery of HIV are absolutely remarkable. Accessibility to treatment, survival, and the quality of life that people living with HIV enjoy in 2017 were unthinkable not that long ago. As a community engaged in the fight against HIV/AIDS, we can be proud of these successes. However, people living with HIV, health care workers, community members, and researchers in Canada and elsewhere around the world also agree that many challenges remain. Indeed, we still need to improve HIV care and services, expand accessibility to treatment everywhere, decrease the burden and impact of co-morbidities and co-infections associated with HIV/AIDS, facilitate parenthood for people living with HIV, and ease the transition to adulthood for HIV-infected children. Combat stigma. End the pandemic. Cure HIV/AIDS. Hence the theme of this year's conference, "We are not done yet." The "We" reflects the fact that we always fight as a team, and that most of our past successes were achieved through broad collaborations and selfless collegiality. The challenges that remain prompt us to pursue the fight until we are "done," while "yet" is meant to remind us that we are inching ever closer to final success.

Canadians have made - and continue to make - key contributions to HIV/AIDS research. This is reflected in the record number of abstracts (525!) that were submitted to CAHR 2017. This impressive scholarly output allowed us to assemble a scientific program of exceptional quality, richly diverse, and well-balanced. As was done in the past, particular emphasis was placed on multidisciplinary and community-based research. Special sessions on HIV cure research, on aging and transitioning, and on marijuana will showcase outstanding speakers, as will all plenary sessions. The program was designed to facilitate movement of participants between sessions on various topics, underlining the fact that the fields of HIV/AIDS research and care are ones where cross fertilization and translational research have made the difference.

We hope that this gathering will provide you with opportunities to learn, will provide inspiration, will refuel your commitment, and will enable you to socialize with your peers in vibrant, delightful, and always enchanting Montreal.

Dr. Alexandra de Pokomandy

Dr. Hugo Soudeyns

C'est avec un vif enthousiasme que nous vous accueillons à Montréal pour l'ACRV 2017. Les réalisations obtenues depuis la découverte du VIH sont des plus remarquables. L'accessibilité aux traitements, la survie et la qualité de vie dont bénéficient en 2017 les personnes vivant avec le VIH étaient impensables il n'y a pas si longtemps. En tant que collectivité engagée dans la lutte contre le VIH/sida, nous pouvons nous enorgueillir de ces succès. Toutefois, les personnes vivant avec le VIH, les travailleurs de la santé, les membres de la collectivité et les chercheurs, au Canada et ailleurs par le monde, reconnaissent également que de nombreux défis demeurent. En fait, les soins et services dans le domaine du VIH ont besoin d'amélioration, il faut élargir l'accessibilité aux traitements partout dans le monde, réduire le fardeau et les répercussions des comorbidités et coinfections associées au VIH/sida, faciliter le rôle de parent des personnes vivant avec le VIH et adoucir la transition vers la vie adulte pour les enfants infectés par le VIH. Il faut aussi combattre les stigmates, extirper la pandémie, trouver un remède contre le VIH/sida. Voilà pourquoi le thème du congrès de cette année est « Nous n'avons pas encore fini ». Ce « Nous » rend compte du fait que nous luttons toujours en tant qu'équipe et que pour la majorité, nos succès antérieurs ont été obtenus grâce à de vastes collaborations et à une collégialité altruiste. Les défis qu'il reste à relever nous incitent à poursuivre la lutte jusqu'à ce que nous ayons « fini », tandis que « encore » veut nous rappeler que nous progressons petit à petit vers le succès final.

Les Canadiens ont apporté et continuent d'apporter une contribution clé à la recherche sur le VIH/sida. Il suffit pour s'en rendre compte de voir le nombre record d'abrégés (525!) présentés pour l'ACRV 2017. Cette impressionnante production scientifique nous a permis de concocter un programme scientifique d'une qualité exceptionnelle, d'une riche diversité et bien équilibré. Tout comme nous l'avons fait par le passé, nous avons particulièrement insisté sur la recherche multidisciplinaire et communautaire. Dans les séances spéciales portant sur la recherche d'un remède contre le VIH, aussi bien que sur le vieillissement et la transition, ainsi que la marijuana, nous avons réuni des conférenciers exceptionnels, et nous pouvons en dire autant des plénières. Le programme a été conçu pour faciliter le mouvement des participants entre séances sur divers thèmes, en rappelant le fait que les domaines de la recherche sur le VIH/sida et les soins afférents s'ensemencent mutuellement et que la recherche translationnelle a fait la différence.

Nous espérons que cette rencontre vous offrira d'amples possibilités d'apprendre, de trouver de l'inspiration, de raviver la flamme de votre engagement, et qu'elle vous permettra de socialiser avec vos pairs dans cette métropole montréalaise dynamique, agréable et toujours enchanteresse.

Dre Alexandra de Pokomandy

Dr Hugo Soudeyns

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Oral Presentations – Exposés oraux

Clinical Sciences: Lifecourse Management (Maternity, Co-morbidities, Aging)

Sciences cliniques : Gestion de la vie (maternité, comorbidités, vieillissement

CS1.01

Development of a self-report measure of cognitive ability for HIV: The Communicating Cognitive Concerns Questionnaire (C3Q)

Sorayya Askari, Lesley Fellows, Marie-Josee Brouillette, Nancy Mayo

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Background: 20-70% of people aging with HIV report cognitive difficulties that affect daily life, including medication adherence, household management, and employment. Existing HIV-specific cognitive measures are not sensitive to detect milder forms of HIV-associated cognitive disorder. Most with HIV are competent to report on their cognitive symptoms, but no HIV-specific questionnaire exists motivating the aim here of developing an HIV-specific measure of cognitive concerns.

Methods: Food and Drug Administration (FDA) guidelines for the development of patient-reported outcomes were applied. Methods included semi-structured web survey, qualitative interviews, and analyses of quantitative data. Rasch analysis was used to estimate the extent to which these items form a true measure. The final version of the Communicating Cognitive Concerns Questionnaire (C3Q) was tested for convergent validity through the strength of the correlation between the C3Q and other standard measures of cognitive ability, emotional function, and other downstream health outcomes.

Results: 817 people with HIV participated in the different phases. Out of 930 unique text threads about cognition, 125 unique concerns emerged, 60 prevalent and important items were chosen, and 18 items fit the Rasch model. The final version of the C3Q formed a measure with good internal reliability (PSI=0.84) and covering a wide spectrum of cognitive ability (n=321). On the validation sample of 97 people, the C3Q showed a strong to moderate correlation with cognitive ability measured using computerized tests (BCAM: r=0.55) and through a self-report questionnaire (PDQ: r=-0.82). C3Q was also moderately correlated with measures of emotional function, and moderately to weakly correlate with downstream health outcomes.

Conclusion: C3Q is a brief self-report questionnaire that reflects cognitive concerns of people living with HIV. It has satisfactory psychometric properties and can be administered and scored in less than 20 minutes. It should facilitate communication between HIV+ people and the clinical team about cognitive concerns.

CS1.02

Infant Feeding in HIV in Canada: Clinical and Research Priority Meeting

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Background: The dichotomy of infant feeding recommendations for women living with HIV (WLWHIV) in resource rich compared to resource poor settings is confusing to many mothers and providers. There is growing need for consensus on clinical management, research and advocacy in regards to infant feeding in the HIV context in Canada.

Materials and Methods: Canadian Physicians (pediatric, adult, and obstetrician), basic scientists, social workers, social scientists, nurses, community agencies, and peer research assistants were invited to attend a Priority Setting meeting on Infant Feeding in HIV. Sessions included: (a) Provincial description of resources available and challenges faced; (b) HIV stigma and criminalization research findings; (c) Community based research on lived experiences; (d) Basic science of transmission, and systematic review results on transmission risk in women on cART; (e) laboratory and feasibility aspects of breastmilk research. Priority topics were determined in advance using an online modified Delphi model. Using a 'World Café' model future clinical and research priorities were determined by consensus.

Results: Regional differences in affected populations and care models included the availability of resources, the depth of counselling, infant formula accessibility, and multidisciplinary supports available to affected communities. Formula programs exist in 5 of 10 provinces and no territories. Breast milk suppressant (Cabergoline) is offered at 3 clinics. The Canadian Infant Feeding in HIV Network was formed, with 6 working groups; National Formula Access, Basic Science Research, Breast Care and Cabergoline Guidelines, Knowledge Translation, Consensus Clinical Management, and Community Engagement. Next steps include literature review to inform Consensus Clinical Guidelines, a National Community Advisory Board for KT development, and advocacy for National formula access.

Conclusions: Gaps in the science and risk of breastmilk transmission, knowledge translation to the community and consensus clinical management guidelines when a mother is breastfeeding are key priorities moving forward.

CS1.03

Cancer mortality among HIV-positive adults in British Columbia, Canada from 1996 to 2013: Implications for HIV-related care in the modern cART era

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Background: In the modern combination antiretroviral therapy (cART) era, AIDS-related mortality among people living with HIV/AIDS (PLWH) has significantly declined, making way for a rise in comorbid conditions such as cancer. This study investigates the burden of cancer-related mortality among PLWH in British Columbia (BC), Canada.

Methods: The Comparative Outcomes and Service Utilization Trends (COAST) study is a retrospective cohort study that is inclusive of all PLWH in BC between April 1996 and March 2013. It utilizes demographic and HIV clinical data from the BC Centre for Excellence in HIV/AIDS provincial Drug Treatment Program (DTP) and administrative data from Population Data BC (vital statistics). We conducted a bivariate analysis of PLWH and a 10% general population sample that died of cancer in the same follow-up period. We calculated cancer-related mortality rates overall, as well as for AIDS-defining malignancies (ADM), non-AIDS defining malignancies (NADM), and system-specific cancers.

Results: Of 1121 PLWH diagnosed with cancer in BC, 555 individuals died with 233 (42.0%) deaths attributed to cancer [mortality rate of 51.7 per 1000 PY]. The mortality rate was 2.4 (1.4- 4.4) and 49.3 (42.6- 57.3) per 1000 PY for ADM and NADM, respectively. Digestive and respiratory cancers had the highest system-specific mortality rates [15.3 (12.0-19.6) and 14.9 (11.6-19.1) deaths per 1000 PY, respectively]. Of 233 cancer-related deaths, 8.2% were among women, 13.3% Indigenous, and 27.0% had a history of injection-drug use. Compared to the general population, PLWH who died of cancer were more likely to have a Hepatitis-C diagnosis (30.0% vs <1%, p<0.0001) and be younger (median age: 51 vs 74, p<0.0001).

Conclusions: Cancer-related mortality was elevated among PLWH and notably higher than rates observed in the general population. The overwhelming majority of cancer-related deaths among PLWH in the modern cART era are attributed to NADM, such as digestive and respiratory cancers.

CS1.04

Evaluation of Cabergoline for Lactation Suppression in Women Living with HIV

Melissa Roy[1], Rosie Thibaudeau[2], Karen Tulloch[3], Ema Ferreira[4], Nancy Sheehan[5], Deborah Money[3], Marc Boucher[1, 7, 8], Isabelle Boucoiran[1, 7, 8]

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Background: In Canada and in the USA, exclusive formula feeding is recommended for all infants who are born to women living with HIV (WLWH) to prevent HIV perinatal transmission. Data regarding the use of cabergoline, a dopaminergic ergot derivative inhibiting lactation, is very limited. The objective of this study is to evaluate the acceptability and efficacy of a single 1 mg oral dose of cabergoline in WLWH.

Methods: This is a multicenter prospective cohort study in 2 Canadian centers. In both centers a 1 mg single dose of cabergoline is offered within the first 48 hours postpartum to inhibit lactation in WLWH. Recruited women filled out a questionnaire regarding symptoms of lactation and cabergoline adverse effects on Day 2 and Day 15 postpartum. On Day 15, they also completed a questionnaire about their satisfaction towards the cabergoline treatment.

Results: To date, 18 WLWH who delivered after 37 weeks have been recruited. All were on combination antiretroviral therapy at delivery and in the postpartum period. All received cabergoline within 24 hours postpartum. While 9 (50%) had a previous live birth, 5 of them had breastfed after a previous pregnancy (prior to HIV diagnosis or prior to immigration to Canada). Within 14 days after delivery, none of the women reported breast engorgement, but 3 (17%) women reported nipple discharge and breast pain which was easily tolerable. Mild non-specific adverse effects were experienced by 7 (39%) women (dizziness, nausea, vomiting, headache, hand or foot numbness) and lasted 48 hours or less. All women found cabergoline easy to use, were satisfied with its ability to prevent postpartum lactation symptoms and would recommend this treatment to a woman in a similar situation.

Conclusion: In this interim analysis, it appears that cabergoline is a well-tolerated and accepted medication for lactation suppression in WLWH.

CS1.05

An Evaluation of Cardiovascular Disease Risk Scores in HIV-Positive Male Patients

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Background: Patients with HIV have been shown to be at increased risk of developing cardiovascular disease (CVD) due to complex interactions between traditional CVD risk factors, antiretroviral therapy and HIV infection itself. Therefore, prevention of CVD in HIV-positive patients through accurate risk stratification is essential.

Methods: We conducted a retrospective case-control study within the HIV-positive cohort at Spectrum Health Clinic in Vancouver, British Columbia, Canada. We identified 74 cases who presented with an incident CVD event (myocardial infarction, stroke, or new diagnosis of coronary artery disease) from January 2004 to December 2015, matched for age and sex to 74 controls with no known CVD history. We calculated and compared the Framingham Risk Score (FRS), D:A:D (Data Collection on Adverse Events of anti-HIV drugs) and ASCVD (Atherosclerotic Cardiovascular Disease). Discriminative and predictive ability was calculated using the chi-square test and area under the receiver curve (AUC). Additional covariates, including HIV-specific factors, were examined as potential risk factors for CVD. Statistical significance was determined by the t-test for continuous variables and chi-square test for binary variables.

Results Our cases had, on average, significantly higher scores for all three CVD risk scores examined, compared with our controls. The D:A:D and ASCVD demonstrated similar discriminative ability as per the chi-square test ($p<0.05$), whereas the FRS demonstrated generally poorer discriminative ability ($p=0.076$). All three demonstrated poor predictive ability as per the AUC with c-statistics ranging between 0.60-0.68. Our cases had significantly higher rates of smoking, lower HDL cholesterol, higher triglycerides, higher rates of renal impairment, lower CD4 counts, and higher protease inhibitor use.

Conclusion: Both the D:A:D and ASCVD demonstrated a similar predictive ability for CVD, and both demonstrated superiority to the FRS. Overall, our study supports the use of the D:A:D or ASCVD for CVD risk stratification in HIV-positive patients.

CS1.06

Psychiatric disorders among HIV infected Adolescents in Montreal

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Background: The incidence of psychiatric disorders among children who are on effective antiretroviral therapy (ART) is not well known, despite the neurotropic effects of the virus, and concerns about the potential ART associated neurotoxicity. The objective of this study was to document the incidence of psychiatric disorders among perinatally HIV infected children in Montreal.

Methods: Clinical records and the database of the Centre Maternel et Infantile sur le SIDA (CMIS) (Montreal) cohort (1988-2015) were reviewed to identify all children who were diagnosed with a psychiatric disorder according to DSM IV criteria. Patients were excluded if they were followed at CMIS less than 5 years, were non-perinatally infected, were less than 13 years of age, or died before the age of 18.

Results: Out of a total of 184 HIV infected children followed at CMIS, 93 met the inclusion criteria. Of these, 8.6% were diagnosed with a psychiatric disorder (psychoses with hallucinations=2, psychosis without hallucinations=1, major depression with suicide attempt=2, major depression without suicide attempt, n=3). Mean age at psychiatric diagnosis was 14 (range 10-17 years). The majority (62.5%) were on effective ART at the time of their diagnosis, with sustained viral suppression. There was a higher proportion of psychiatric diagnosis among children born during the era of cART availability (2000-2014), vs. those for whom only sequential ART was available (1980-2000) (14% vs. 8.2%), though not statistically significant. The overall incidence of psychosis (4.3%) and suicide (2.1%) was higher that reported in the general Canadian population of adolescents (0.5% and 0.001% respectively).

Conclusions: In this cohort of perinatally infected children, the incidence of psychiatric disorders was 8.6% in adolescence, and appears significantly higher than among the general population of Canadian adolescents. These findings and specific causative factors need to be confirmed in larger studies.

Epidemiology and Public Health: Administrative Data and Surveillance

Épidémiologie et santé publique : Données administratives et surveillance

EPH1.01

Evolving trends in age at diagnosis among new HIV diagnoses in Ontario (1996-2015): Identification of a birth cohort effect among men born in the 1960s

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Objective: To better understand the evolving HIV epidemic in Ontario we examined trends in two temporal components: age at diagnosis and decade of birth among new HIV diagnoses from 1996 to 2015.

Methods: In Ontario, the vast majority HIV diagnostic testing is performed by the public health laboratory system. Data on individuals in Ontario ≥ 15 years at the time of their first-time HIV-positive test during the period 1996-2015 were analyzed. Diagnoses were grouped into 5-year age at diagnosis and 10-year birth cohorts and trends were explored over 5-year time periods by sex and priority population.

Results: From 1996 to 2015 in Ontario 18,909 persons aged 15 or older were diagnosed with HIV. Over the discrete 5-year time periods, the highest proportion of cases in females was consistently in the 30-34 year age group, with a slight shift towards older age at diagnosis over time. A birth cohort effect was observed among males, with the greatest proportion of cases consistently among those born in the 1960s over time: 30-34 years of age in 1996-2000, 35-39 in 2001-2005, and 40-44 in 2006-2010. This cohort effect was present for both men who have sex with men and other males. The most recent time period (2011-2015) was the first where this pattern changed. Instead, a bimodal distribution has emerged, with the largest proportion of new HIV diagnoses among men born in 1980s, and a smaller peak in the 1960s cohort.

Conclusions: We identified a birth cohort effect among new HIV diagnoses in Ontario for males born in the 1960s. These effects could be due to multiple factors including generational differences in prevalence, testing, attitudes towards HIV or changes in sexual behavior and require further research. Data indicating increased HIV diagnoses in the cohort of men born in the 1980s will require careful monitoring.

EPH1.02

Linking to Care among People Diagnosed with HIV during Hospital Admission: A population-based Study in Ontario, Canada

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Background Linking people newly diagnosed with HIV to care is critical to improve health outcomes and reduce onward HIV transmission. We aimed to assess the timeliness of linkage to care for people diagnosed with HIV and determine factors associated with delayed linkage.

Methods: We conducted a population-based study using Ontario's health administrative databases. The cohort included all individuals newly diagnosed with HIV during hospital admission between April 1, 2007 and March 31, 2015. We used competing risk models to examine the cumulative incidence of linkage to care by 90 days following hospital discharge and to identify characteristics associated with linkage to care while considering death as a competing risk. We applied sensitivity analyses to examine differences between people having HIV as the primary versus any diagnosis during admission.

Results: Among 393 patients who received a primary HIV diagnosis, cumulative probability of linkage to care was 66.4% within 30 days and 82.5% within 90 days. After 365 days, 89.2% of people had linked to care. Following multivariable adjustment, people with moderate (HR 1.96, 95% CI 1.08-3.54) and high (HR 2.17, 95% CI 1.07-4.42) numbers of comorbidities were more likely to link with care. People living in low-income neighborhoods were less likely to link with care (HR 0.68, 95% CI 0.47-0.98). In our sensitivity analysis of 509 patients with HIV as primary or other diagnosis, linkage was more likely for immigrants from countries with generalized HIV endemics (HR 1.50, 95% CI 1.06-2.12), but less likely among women (HR 0.56, 95% CI 0.34-0.94) and people with mental health diagnoses (HR 0.66, 95% CI 0.54-0.80).

Conclusion: Among those diagnosed with HIV during hospital admission, delayed linkage to care was associated with lower income, and potentially women and mental health illness. Future work should evaluate mechanisms to promote linkage to care among these populations.

EPH1.03

Factors determining HIV Risk among HCV infected individuals: The British Columbia Hepatitis Testers Cohort (BC-HTC)

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Background: Hepatitis C Virus (HCV) and HIV infections co-occur in certain population groups because of shared risk factors. Understanding differences in HIV incidence among HCV infected individuals can help inform strategies to prevent HIV infection. We estimated the time to HIV diagnosis among HCV infected individuals and evaluated factors that could affect HIV infection risk.

Methods: The BC-HTC includes all individuals (~1.5 million) tested for HCV or HIV from 1990 to 2013 and links medical visits, hospitalizations, cancers, prescriptions and deaths. All HCV positive and HIV negative individuals were followed for a positive HIV test to estimate adjusted hazard ratios (aHR) for factors associated with HIV infection using Cox proportional hazards regression.

Results: Of 36,163 individuals who were HCV positive and HIV negative at cohort entry, 2255 (6.2%) acquired HIV over 266,010 years of follow-up for an overall incidence rate of 8.5/1000PY (person years). The HIV incidence rate among HCV seroconverters was 10.7/1000PY versus 8.2/1000PY among those with prevalent HCV infection at diagnosis. Overall median [IQR] time to HIV infection was 3.36 [4.96] years, shorter for seroconverters than prevalent HCV infections (2.78 vs 3.52, p =0.003). In Cox regression, people who injected drugs (aHR: 1.42, 95% CI: 1.29-1.57), Hepatitis B Virus (HBV) infection (aHR: 1.37, 95% CI: 1.19-1.58), men who have sex with men (MSM) (aHR: 5.91, 95% CI: 4.21-8.29), and urban residence (aHR: 1.40, 95% CI: 1.19-1.65) were associated with higher risk of HIV infection after adjusting for number of HIV tests. Opioid Substitution Therapy (OST) (aHR: 0.39, 95% CI: 0.33-0.45) and psychiatric counseling (aHR: 0.48, 95% CI: 0.44-0.54) were associated with lower risk of HIV infection.

Conclusions: Injection drug use, HBV coinfection, MSM, and urban residence increased risk of HIV; while engagement in OST and mental health counseling reduced the risk of HIV infection among HCV infected individuals.

EPH1.04

A BC Provincial Database Analysis of Long Term Developmental Outcomes in HIV-Exposed Uninfected (HEU) Children Born to Mothers Living with HIV

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Background: Worldwide, >1.4 million children are born to HIV-infected mothers each year (within Canada there are >200 HEUs born per year), with an increasing proportion exposed to maternal ARVs. Immunological, neurodevelopmental and mitochondrial concerns exist on the possible long-term effects of ARVs; however, sociodemographic factors and adverse childhood experiences may also play a role. We previously reported high prevalence of autism spectrum disorder in HEU children within the CARMA cohort. Our objective was to assess the frequency of neurodevelopmental disorders among all HEU children born between 1990 and 2012 in British Columbia.

Methods: Data on 446 HEU children and 1332 HIV-unexposed uninfected (HUU) children (matched ~1:3 for age, sex and geocode) born between 1990 and 2012 were collected from Population Data BC. Neurodevelopmental disorders were based on Medical Services Plan physician billing diagnostic codes (ICD9 and ICD9-CM).

Results: Preliminary descriptive statistics for this cohort reveal that compared to HUUs, HEU children have significantly higher relative risks of several developmental disorders including autism spectrum disorder (RR=2.97, p=0.02), disturbance of emotions (RR=2.90, p<0.0001), hyperkinetic syndrome (RR=2.97, p<0.0001), and developmental delay (RR=3.04, p<0.0001), but no increased risk of medical conditions such as asthma (RR=1.01, p=0.89) or neoplasms (RR=0.68, p=0.06). The HEU cohort shows significantly higher proportions of maternal smoking and alcohol consumption during pregnancy, as well as higher proportions of fetal alcohol syndrome and exposure to noxious substances compared to HUUs.

Conclusions: Our data suggest HEU children in BC may be at a nearly three-fold higher risk for several neurodevelopmental disorders compared to matched HUUs. Further analysis is underway to examine confounders including sociodemographic factors and maternal substance use during pregnancy, and to examine ARV exposure. Regardless of the underlying mechanism, these results suggest that HEUs should have careful developmental monitoring and access to early intervention to optimize neurodevelopment.

EPH1.05

Enhanced Surveillance of Infectious Syphilis and the Cascade-of-Care among HIV-Positive and HIV-Negative Men who have Sex with Men in British Columbia

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Introduction: From 2010 to 2015, the incidence of infectious syphilis (primary, secondary, and early-latent) has increased 5-fold in British Columbia (BC). In response, the BC Centre for Disease Control (BCCDC) enhanced surveillance for syphilis to characterise sexual/social networks driving the epidemic, and to monitor the risk of HIV transmission. Here we communicate indicators developed from the provincial enhanced surveillance system.

Method: In BC, management of syphilis – including partner notification – is centralized, and coordinated by the BCCDC. In January 2016, a new workflow was implemented to systematically collect and analyze data on HIV co-infection, viral-load and partners. New indicators were developed along a cascade-of-care framework for case and partner care.

Results: From January to September 2016, 581 syphilis cases were diagnosed in BC; 491 (84%) were among men who have sex with men (MSM). Of these, 201 (41%) were HIV-positive and 268 (55%) were HIV-negative. Three-quarters of HIV-positive MSM had undetectable viral loads. 149 (74%) of HIV-positive MSM and 137 (51%) of HIV-negative MSM were diagnosed during the early-latent stage. For both groups, 96% of cases were treated within 30 days of syphilis testing. Of the 201 HIV-positive MSM, 141 (70%) discussed partners with public health nurses and together reported 1,270 partners (65% anonymous, 35% notifiable) or 9.0 partners/case (range:0-214). Of the 268 HIV-negative MSM, 215 (80%) discussed partners and reported 1,806 partners (51% anonymous, 49% notifiable), or 8.4 partners/case (range:1-200).

Conclusion: A greater proportion of HIV-positive MSM were diagnosed with syphilis during the asymptomatic early-latent stage, suggesting routine syphilis screening. However, a lower proportion of HIV-positive MSM with syphilis co-infection were engaged with public health for partner notification, and report a lower proportion of notifiable partners, compared to MSM with syphilis only. Strategies to engage HIV-positive MSM in partner care would strengthen the public health response to syphilis.

EPH1.06

Economic evaluation of HIV pre-exposure prophylaxis: A systematic review

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Background: Data consistently support the efficacy and real-world effectiveness of antiretroviral pre-exposure prophylaxis (PrEP) in preventing HIV acquisition. However, coverage among those in need remains limited by uncertainties in the necessary health care-related financial and human resource investments and ultimately the cost-effectiveness of PrEP.

Methods: We systematically reviewed economic evaluations of PrEP implementation strategies published until October 31, 2016 using peer and non-peer reviewed sources. We included studies that assessed both costs and consequences of PrEP. We summarized incremental cost-effectiveness ratios (ICER) and identified sources of heterogeneity in outcomes. We converted all costs to 2016 USD.

Results: Of 41 studies, 33 captured onward HIV transmission using dynamic models; 14 were conducted in high-income settings; and 15 included men who have sex with men (MSM). Of 105 strategies examined across all studies, 64 evaluated oral emtricitabine-tenofovir with effectiveness ranging from 44-99% among MSM in high-income settings. Compared with no PrEP, universal PrEP strategies for MSM in high-income settings ranged widely from $34,000 to $570,273 per quality-adjusted life years (QALYs) gained. ICERs were lowest when PrEP was focused on a subset of the highest-risk MSM (those with greater than a 4-fold higher HIV incidence than overall incidence among all MSM), ranging from cost-savings to $51,000/QALY. Across all strategies, settings, and formulations, PrEP was more cost-effective with greater effectiveness (adherence); longer analytical time-horizons; and when impacts included the prevention of onward transmission. No studies explored variability in duration of HIV risk; individual and temporal heterogeneity in uptake and adherence; duration and speed of scale-up.

Conclusions: The costs per anticipated benefit of PrEP implementation strategies depend on various factors, including analytic techniques and the HIV incidence. Future economic evaluations should explore the influence of individual, temporal, and epidemic heterogeneity by incoming data from real-world implementation.

Social Sciences: New Approaches in Indigenous Health Research

Sciences sociales : Nouvelles approches en recherche sur la santé des Autochtones

SS1.01

An Indigenous HIV Research Feast: New Directions for HIV Research with Indigenous Communities

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Background: The Canadian Aboriginal AIDS Network partnered with Indigenous and non-Indigenous stakeholders to develop a research response to HIV in Indigenous communities that is grounded in community concerns and relevant across scientific disciplines. The *Indigenous HIV Research Feast* is a culturally-grounded and evidence-based guiding document for community members, academics, and decision-makers to ensure their research interests are aligned with the interests of Indigenous communities.

Method: All feasts involve protocols, planning, preparing, sharing, and take aways. Our *Feast* was wrapped in and infused with protocols to ensure that we worked 'in a good way'. Planning for our *Feast* was underscored by Indigenous worldviews, decolonizing methodologies and two-eyed seeing. Preparing our *Feast* included a comprehensive literature review, 25 face-to-face consultations, and an online questionnaire with a total of 285 participants.

Sharing Results: Understanding and addressing racism and HIV-related stigma and discrimination remain top priorities for Indigenous people living with and affected by HIV. These concerns are amplified for northern, rural or remote communities. Access to and engagement in healthcare is equally important, including care for intersecting and complex needs such as mental health, addictions, co-morbidities, and unequal access to social determinants of health. HIV prevention, testing, treatment and care continue to be areas of concern, as do engagement and retention in vaccine and clinical trials research. A clear preference emerged, for research approaches to these issues that are strengths-based, Indigenous-led, community-based, and that build capacities in the community. For example, research into culture and healing, harm reduction, colonization, and systems also emerged as important.

Take Aways: 1) There is always room at the table. Addressing HIV in Indigenous communities requires collaborative and multi-disciplinary efforts by multiple stakeholders at multiple levels; and 2) HIV research with Indigenous communities must be: Indigenous-led, action-oriented, grounded in community-concern, and inclusive of Indigenous approaches and world-views.

SS1.02

Storying Change: The Impacts of Indigenous Youth Sharing HIV Prevention Digital Stories in Community

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Background: Digital storytelling is an increasingly popular public health strategy that engages communities in public health research and practice. The literature has predominantly focused on the process of creation or the content of the stories. Far less attention has been paid to their potential uses as HIV prevention tools. This paper reflects on the impact of sharing digital stories created from the *Taking Action Project: Using Arts-Based Approaches to Develop Aboriginal Youth Leadership in HIV Prevention* (TA2).

Methods: *Taking Action II is* a national community-based participatory action research project engaging Indigenous youth in HIV activism. Eighteen Indigenous youth leaders created digital stories about HIV. They each planned and executed screenings of the work in their home communities to foster dialogue about HIV in Indigenous communities. Here we reflect on the impacts of sharing stories publically. Data is drawn from individual semi-structured interviews with the youth leaders, audio-recordings of audience reflections, and the field notes of the research team.

Results: Many youth storytellers reflected on how the process of creating and sharing their story was an empowering and meaningful experience that contributed to personal growth and transformations. In addition, the stories were used to spark important new dialogue around HIV prevention and sexual/reproductive health in many communities. Community members and relatives demonstrated immense pride and support for young leaders and expressed how inspirational and compelling they found the stories for opening up new conversation. Several public health practitioners and bureaucrats shared how the stories helped them think differently about HIV prevention in Indigenous communities.

Discussion Conclusion: Digital stories can be powerful catalysts for personal, interpersonal and community mobilization. Firmly situated within Indigenous youth's experiences and worldviews, the stories challenged dominant silo approaches to thinking about HIV prevention and opened up new possibilities for dialogue and programming.

SS1.03

Peer- Support Efforts Promote Health Access for Indigenous Sex Workers: Critical Need for Self-Determination in Indigenous Sex Worker-Led HIV Prevention and Care

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Background: Structural inequities of violence, criminalization, racism, and stigma and the ongoing impacts of colonial policies has led to significant overrepresentation of Indigenous sex workers within the most visible aspects of sex work in Canada. Indigenous street-involved women continue to face the heaviest burden of HIV, violence, and barriers to health access. With increasing adoption of peer-based models in HIV and support services (e.g. peer navigators, peer support groups), and calls for culturally-safe and Indigenous-led programming, understanding how peer support may reduce gaps in health care remains critical.

Methods: Analysis draws on a longitudinal CBR project (AESHA, An Evaluation of Sex Workers Health Access) in partnership with 15+ community organizations, including experiential team. Bivariate and multivariable logistic regression using generalized estimating equations (GEE) were used to examine the independent effect of engagement in peer support on access to health services.

Results: Among 724 women sex workers, 36% (n=261) were Indigenous women. In longitudinal GEE analysis, peer support increased access to health services by 31% among all sex workers. In a longitudinal GEE confounder model restricted to Indigenous sex workers, engagement in peer support had the largest independent effect, with a 52% increased odds of accessing health care services (OR=1.52, 95%CI 1.00-2.33), even after adjusting for age, homelessness, living with HIV, substance use, and police harassment.

Discussion: In adopting decolonizing practices in mainstream healthcare models, and redressing the legacy of violence and colonial practices, Indigenous communities, and the Truth and Reconciliation Commission have called for cultural-safety and self-determination in health and HIV services. This research highlights the critical role of peer models for building resiliency and strength among Indigenous sex workers and mitigating barriers to healthcare. Community-based and Indigenous-led research remains critical to understanding how models of peer engagement foster culturally safe spaces for Indigenous sex workers and other marginalized populations.

SS1.04

Experiences of Indigenous youth engaging in an intergenerational participatory filmmaking and HIV/AIDS education workshop

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Background: Arts-based approaches are becoming increasingly popular strategies for HIV/AIDS prevention and education with Indigenous youth. However, little research has examined the experiences of youth participating in these arts-based initiatives. This presentation explores the experiences of Indigenous youth attending a participatory filmmaking and HIV/AIDS education workshop.

Methods: 11 youth and 5 Elders representing the diverse groups of Indigenous people in Labrador attended a 3.5 day filmmaking workshop hosted as part of a community-based research project examining the use of arts in HIV/AIDS education and prevention with Indigenous youth. Participatory filmmaking was used to engage youth and create dialogue about HIV/AIDS, sexual health and health in general. The youth and Elders created 4 films. Following the workshop, youth and Elders were interviewed about their experiences making films and working together. Thematic analysis was used to analyse interview transcripts and the films produced.

Findings: i) the youth found participatory filmmaking to be an acceptable and engaging strategy for HIV/AIDS education; ii) participatory filmmaking allowed the youth to create an environment in which they learned; iii) the process of participatory filmmaking facilitated the development relationships between youth and between youth and Elders; iv) participatory filmmaking facilitated the development of the youth as HIV/AIDS educators.

Conclusion: The findings of this research project suggest participatory filmmaking is a promising arts-based approach for HIV/AIDS education and prevention with Indigenous youth, providing a good platform for constructive dialogue and engagement among youth and between youth and Elders as well as contributing to the development of knowledge, skills and the desire to be educators amongst the youth who participated. Further research is required to examine the use of participatory filmmaking as a strategy for developing peer leadership in the context of HIV/AIDS education and prevention.

SS1.05

Family Matters: Informing a family-based model of care with Aboriginal families affected by HIV – The Findings

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Background: The Canadian Aboriginal AIDS Network membership has consistently identified the importance of understanding the effect of HIV on Aboriginal families, and implications for providing culturally adequate and appropriate supports and services.

Methods: Within a CBR framework that embraced GIPA and MEPA principals , from conception through to dissemination, the research team applied Indigenous and two-eyed seeing approaches to engage with families across Canada. An online survey gathered details regarding programs and policy; story telling circles gathered data from family members and APHAs; collaborative team analysis prepared coding for a National gathering to fully review and reflect on the data informing the final report.

Findings: The *Family Matters* team's Indigenous CBR approach has led to rich contextual data on the complex realities of living with HIV as an Aboriginal family and family-oriented care, treatment and support service needs. Family members living with HIV – those living positive and those affected – agreed that 6 major themes are central to their experience: Meaning of and types of families; Family experiences; Impact on family; Children; Trauma, Loss and Resilience; and Family Supports. Both the on-line survey and Storytelling circles provided clear insight into what is working and what is needed. Family members affected by HIV felt invisible because supports are focused on the family member living with HIV. Many of the storytellers shared their desire to have programs they could participate in as a family. Positive parents spoke of how programs for children were needed to help them understand HIV and have a safe and supportive space they could go to learn from each other.

Conclusions: Family is constructed in many ways. Culturally responsive, confidential and inclusive services with resources for the WHOLE family. Recommendations include the need for case management, subsidies to access activities, housing, and enhanced advertising of existing resources.

SS1.06

Reimagining Housing for Indigenous Peoples living with and affected by HIV across Canada: Lessons Learned from Stable Homes, Strong Families

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Background: The connection between housing and health is well established. Stable Homes Strong Families (SHSF) investigated the connections between HIV, housing and Indigenous cultures among Aboriginal People living with HIV (APHAs). This critical policy sub-analysis seeks to provide recommendations for improving housing programs and policies.

Methods: Semi-structured interviews were conducted with managers and frontline workers (n=12) from non-profit and supportive housing organizations within Indigenous and HIV housing sectors in BC, SK, and ON. Informants highlighted programs and organizational and legislated policies specific to APHAs. Interviews were transcribed and coded. SHSF team members conducted reflexive thematic analysis and collaborative writing to refine recommendations.

Results: Informants from Indigenous and HIV communities highlighted the compartmentalization of housing funding and management across Canada. Effectively creating silos, this has introduced restrictive criterion for clients seeking support and inhibited cross-sectoral dialogue and collaboration. As a result, APHAs in need of housing can fall through the cracks. To cut across silos and reduce housing instability, policy solutions in planning and providing services should be integrated with culturally responsive and spiritually inclusive interventions to 'indigenize' housing and health services for APHAs. Consulting with Indigenous communities can enrich housing development to reflect community needs and priorities. The utilization of health liaison workers could straddle the gap between HIV/health and housing sectors and facilitate access to cultural and spiritual resources. Ensuring physical space for ceremonial practices can also strengthen Indigenous peoples' sense of home and connectedness.

Conclusions: Housing providers will benefit from integrating Indigenous approaches to health and well-being including self-determination, non-hierarchical governance, and social and community integration. Organizational policies are urgently needed that operationalize these principles in order to reduce housing instability among APHAs. In light of the Truth and Reconciliation Commission's Calls to Action, the time is now to champion and enforce such policies.

Multidisciplinary: HIV Cure

Multidisciplinaire : Remède contre le VIH

MD1.01

From Treatment Possibilities to Treatment as Prevention: HIV and biomedicalisation in UK qualitative datasets

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Two decades of highly effective anti-retroviral treatment (ARV) have undoubtedly transformed the global HIV epidemic. As social scientists engaged with the impact of biomedical treatment and prevention throughout this period, we identified number of questions that have been de-prioritised or neglected. For example, how has lived experience alongside ARVs changed over time?; how have identities been shaped by the increasing biomedicalisation of HIV?; and how have social and structural inequalities impacted on or been reinforced by these developments?. We took an innovative approach to addressing these questions through the secondary analysis of a sample from 12 qualitative datasets ranging from 1997-2013 involving over 600 participants. In order to engage with this large body of data, the presenting authors analysed a subset of datapoints from each project, focusing on discourses of treatment literacy and engagement with (or rejection of) expert knowledges related to ARVs.

This pilot work generated significant insights which we will discuss under three main headings: questions of hope, disappointment and uncertainty; biocitizenship and bioeligibility; and a consideration of whose experiences are being captured within such research, and who is absent.

Secondary data analysis and data sharing brought diverse projects, time periods and participant groups into conversation with each other. In this presentation, we will share with international colleagues the opportunities that this approach has afforded as well as the ways of tackling technical challenges that this approach is perceived to present.

Given the mixed outcomes of ARVs as treatment, this interrogation has been vital in the current era in which the prevention possibilities of these technologies now rest at the centre of current and future HIV policy-making (in the UK, as well as in Canada and elsewhere).

MD1.02

The Early Pediatric Initiation, Canada Child Cure Cohort Study (EPIC4): Successes and Failures of Early Combination Antiretroviral Therapy (cART) Initiation

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Background: The EPIC[4] study is a multicenter prospective study involving 9 major pediatric HIV care centers across Canada. Study objectives are to investigate the impact of early initiation of combination antiretroviral therapy (cART) on HIV reservoirs, HIV-specific immune responses and chronic inflammation in children with perinatally-acquired HIV infection. The purpose of this report is to describe the baseline characteristics of the cohort with a focus on those who initiated cART during the first year of life.

Methods: Cross-sectional analysis of baseline characteristics of all children enrolled in the EPIC[4] cohort as of December 2016.

Results: Of 211 children enrolled, 185 have collated partial baseline data. Mean age 12 years (0.4-25 years); 52% female; 55% foreign born, most being from Africa (63%), Asia (19%) or the Caribbean (12%). Viral load (VL) was undetectable in 84% (112/132). Forty-six (22%) initiated cART prior to 1 year of age (≤72 hours, n=9; 72 hours-30 days, n=3; 31-90 days, n=10; 3-12 months, n=14). Overlapping reasons for cART initiation within 72 hours of birth included poor maternal adherence (n=7), unknown maternal HIV status (n=3), high risk behaviour or event (n=7), detectable VL at end of pregnancy (n=7), routine neonatal prophylaxis protocol (n=12), and other (n=11). At least one period of poor adherence was noted in 43% of children. Among those initiated on cART prior to one year of age, 43% had excellent adherence in infancy, 28% had occasional missed doses, and 30% had frequent missed doses. Only 4 of the 9 initiated on cART within 72 hours of birth maintained virologic suppression into late childhood.

Conclusions: Early initiation of cART in children, as a strategy for limiting HIV reservoir size, is hampered by poor adherence to treatment. Further conclusive evidence of viral remission following early cART could encourage better adherence in resource rich settings.

MD1.03

Single cell characterization of viral translation-competent reservoirs in HIV-infected individuals

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HIV cure efforts are hampered by a limited characterization of the cells that support active HIV replication *in vivo,* and inadequate quantification methods for latent viral reservoirs in persons receiving antiretroviral therapy (ART). Here we combine fluorescent *in situ* hybridization for viral RNA with detection of HIV protein by antibody staining and flow cytometry. By simultaneously detecting both HIV RNA and protein, the CD4+ T cells (CD4) harbouring translation-competent virus are identified with a detection limit of 0.5-1 *gag-pol* mRNA$^+$/Gag protein$^+$ infected CD4 per million. In the peripheral blood of untreated individuals, active HIV replication correlated with viremia and preferentially occurred in CD4 expressing T follicular helper cell markers and the inhibitory co-receptors PD-1, CTLA-4 and TIGIT. In virally-suppressed subjects receiving ART, the approach identified latently infected cells capable of producing HIV mRNA and protein after stimulation with PMA/ionomycin or latency reversing agents (LRA). The size of this translation-competent latent reservoir correlated with integrated HIV DNA levels, but not with the replication-competent reservoir as measured by QVOA. While ingenol-induced reactivation mirrored the effector and central/transitional memory CD4 contribution to the pool of integrated HIV DNA, bryostatin-induced reactivation occurred predominantly in cells expressing effector memory markers. In summary, we define the major reservoir of cells harbouring translation-competent HIV at a single-cell level. Our data indicate that CD4 differentiation status affects LRA effectiveness; this suggests that a detailed understanding of the cellular factors influencing the reactivation of latent HIV is essential to guide the development of successful cure strategies.

MD1.04

Sensitization of HIV-1-infected cells to ADCC

Jonathan Richard, Andrés Finzi

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Antibodies recognizing conserved CD4-induced (CD4i) epitopes on HIV-1 Env and able to mediate antibody-dependent cellular cytotoxicity (ADCC) have been shown to be present in sera from most HIV-1-infected individuals. These antibodies preferentially recognize Env in its CD4-bound conformation. CD4 downregulation by Nef and Vpu dramatically reduces exposure of CD4i HIV-1 Env epitopes and therefore reduce the susceptibility of HIV-1-infected cells to ADCC. Importantly, it has been shown that this viral mechanism of immune escape could be circumvented with small CD4-mimetics (CD4mc) which are able to "push" Env into this conformation and sensitize HIV-1-infected cells to ADCC mediated by HIV+ sera. However, in addition to CD4 downregulation, HIV-1 developed additional mechanisms to avoid ADCC including limiting the overall amount of Env present at the cell surface. We developed new approaches to circumvent this evasion strategy. By combining these new approaches to CD4mc, we were able to greatly enhance ADCC responses against HIV-1-infected cells. The combination of these newly-developed approaches to the use of CD4mc holds promise in the efforts aimed at HIV eradication.

MD1.05

Expression of Integrins α4β7, αEβ7 and α4β1 on CD4+T cells Isolated from the Cervix, Rectum and Blood and Their Degree of Immune Activation and CCR5 Expression

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Background: α4β7 expression on CD4$^+$T-cells has been associated with HIV acquisition and blockade with a monoclonal antibody has recently been shown to improve viral control, although the mechanisms remain elusive. Other integrins such as αEβ7 and α4β1 may also contribute to HIV infection of CD4$^+$T-cells presenting potential targets for mAb therapies directed towards HIV treatment. In this study we characterized α4β7, αEβ7 and α4β1 expressions on CD4$^+$T-cells and their co-expression with CCR5 and canonical markers of immune activation in blood and in cervical and rectal mucosa of healthy Kenyan women.

Methods: This study is part of KAVI-VZV001 trial (ClinicalTrials.Gov: NCT02514018). CD4$^+$T-cells were isolated from blood, cervix and rectum at baseline and were analyzed by flow cytometry for α4, αE, β7, CCR5, CD69, HLA-DR, CD38, and Ki67 expressions (n=45). Friedman and Wilcoxon matched-pairs tests were performed using SPSS. P-values were adjusted for multi-comparisons using a step-down procedure. Medians and IQR are reported here.

Results: α4β1 is preponderant on systemic and cervical CD4$^+$T-cells (24.0% [17.9-28.5%] and 15.8% [11.1-22.2] respectively), followed by α4β7 (13.9% [11.6-18.0%] in blood and 4.9%, [2.8-10.3%] in cervix). α4β7 is predominant in rectal CD4$^+$T-cells (11.8% [9.1-15.8%]) followed by αEβ7 (5.6% [3.8-9.8%]). αEβ7 CD4$^+$T-cells exhibit the highest frequencies of CCR5 expression among the integrin populations analyzed at all three sites (54.2% in blood, 98.2%

in cervix, and 89.2% in rectum) (p<0.0001). αEβ7 CD4+T-cells in both cervix and rectum also displayed the highest levels of CD69 expression (57.1% and 49.7% respectively) (p<0.0001). Systemic αEβ7 CD4+T-cells were rare (0.1% [0.05-0.15%]) but exhibit strikingly high expression of HLA-DR and Ki67 (19.2% and 13.8% respectively).

Conclusion: Integrin expression on CD4+T-cells and the activation status of these cells were shown to be tissue-dependent. In addition to α4β7, α4β1 and αEβ7 CD4+T-cells were frequent and activated, especially at the mucosa, encouraging their investigation in HIV pathogenesis.

MD1.06

Identification of Small RNAs for Use in Combination Gene Therapy to Functionally Cure HIV

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Hematopoietic stem cell (HSC) transplant has the potential to functionally cure HIV infection. Several clinical trials have been initiated to insert a combination of antiviral genes into an infected person's HSCs by an autologous transplant. Due to their limited potential to elicit immune responses, genes expressing small RNAs are the most appropriate for HSC therapy and HIV RNA represents one of their main targets. To identify optimal target sites for small RNAs, we screened HIV RNA for highly conserved and accessible ribozyme target sites. We identified a target site in the Gag coding region that was particularly accessible to a ribozyme. The target site was also highly accessible to RNA interference mediated by a short hairpin RNA (shRNA), with anti-HIV potency comparable to an shRNA in clinical trials.

The design of molecules targeting HIV RNA is complicated by the sequence diversity of circulating HIV strains as well as the structure of the RNA in cells. We show that the target site we identified in Gag RNA is highly conserved across circulating HIV strains. We also demonstrate that the shRNA we designed is effective against diverse HIV subtypes, suggesting that the structural accessibility of the target site is also highly conserved. To optimize the format of RNA interference molecules targeting Gag RNA, shRNAs and small interfering RNAs (siRNAs) with different lengths were evaluated for anti-HIV effects. In the absence of cellular toxicity, the optimal stem length for shRNAs was 20 to 21 base pairs, while for siRNAs it was 27 to 29 base pairs. Our results highlight the importance of optimizing the format of therapeutic RNA interference molecules and provide a set of optimal candidates for use in combination gene therapy to functionally cure HIV.

Basic Sciences: Immunology and Pathogenesis

Sciences fondamentales : Immunologie et pathogénèse

BS1.01

Influence of the Envelope Gp120 Phe 43 Cavity on HIV-1 Sensitivity to ADCC Responses

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HIV-1-infected cells presenting envelope glycoproteins (Env) in the CD4-bound conformation on their surface are preferentially targeted by antibody-dependent cellular-mediated cytotoxicity (ADCC). HIV-1 has evolved sophisticated mechanisms to avoid exposure of Env ADCC epitopes by downregulating CD4 and by limiting the overall amount of Env on the cell surface. In HIV-1, substitution of large residues such as histidine or tryptophan for serine 375 (S375H/W) in the gp120 Phe 43 cavity, where Phe 43 of CD4 contacts gp120, results in the spontaneous sampling of an Env conformation closer to the CD4-bound state. While residue S375 is well-conserved in the majority of group M HIV-1 isolates, CRF01_AE strains have a naturally-occurring histidine at this position (H375). Interestingly, CRF01_AE is the predominant circulating strain in Thailand where the RV144 trial took place. In this trial, which resulted in a modest degree of protection, ADCC responses were identified as being part of the correlate of protection. Here we investigate the influence of the Phe 43 cavity on ADCC responses. Filling this cavity with a histidine or tryptophan residue in Envs with a natural serine residue at this position (S375H/W) increased the susceptibility of HIV-1-infected cells to ADCC. Conversely, replacing His 375 by a serine residue (H375S) within HIV-1 CRF01_AE decreased the efficiency of the ADCC response. Our results raise the

intriguing possibility that the presence of His 375 in the circulating strain where the RV144 trial was held contributed to the observed vaccine efficacy.

BS1.02

Altered IFN1 Signalling Facilitates OV Infection of HIV-Infected Monocyte-Derived Macrophages

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Introduction: Impairment of the type 1 interferon (IFN1) response is common to multiple diseases, including HIV-1 infection. In cancer, novel oncolytic viruses (OV) have been designed to selectively kill tumor cells with impaired IFN1 responses. Similar strategies may prove useful for the eradication of HIV-infected cells *in vivo*. However, IFN1 signalling in the context of persistent infection, such as that seen in myeloid cells, remains poorly understood.

Hypothesis: IFN1 responses are impaired within HIV-infected macrophages, and may serve as a target for OV.

Methods: Monocyte-derived macrophages (MDM) were infected *in vitro* with the reporter virus, HIV NL4-3 BAL-IRES-HSA. The IFN1 response was assessed by measuring the induction of two IFN-stimulated genes (ISG), PKR and ISG15, following stimulation with IFNα or the synthetic RNA, 5'ppp, by flow cytometry. The ability of OV to target HIV-infected MDM was evaluated via quantification of p24 release by ELISA, total and integrated HIV DNA by RT-PCR, and HSA expression by flow cytometry.

Results: IFNα- or 5'ppp-induced PKR expression was greater in uninfected MDMs, when compared to HIV-infected (HSA^+) MDM. Similar differences in ISG15 induction were observed following 5'ppp, but not IFNα stimulation. OV infection of HIV-infected MDM prevented the accumulation of p24 in culture supernatants. A decrease in total and integrated HIV DNA, and number of HSA^+ MDMs, was also observed following OV infection.

Conclusion: IFN1 responses were found to be altered in HIV-infected MDM. This was associated with a decrease in HIV-1 production following OV infection, which may represent the specific, OV-mediated killing of HIV-infected MDM.

BS1.03

HIV Subtypes Display Differential Receptor Binding and Entry Rates: Contributions to Pathogenesis

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Background: Progressive depletion of $CD4^+$ T Cells is the defining feature of HIV-1 infection and the primary driver of immunodeficiency and the onset of AIDS. Previous work has demonstrated varying degrees of pathogenicity between HIV-1 subtypes, though the causes of these differences are unknown. The predominant viral subtypes of the epidemic in Sub-Saharan Africa are A, D and C, with subtype C causing ~80% of regional infections alone. Unfortunately, despite their importance in global health, these subtypes understudied relative to subtype B. This study seeks to compare Env binding affinity, viral entry rates and their impacts on disease progression between diverse viral isolates (subtypes A, C and D) from a cohort of women in Uganda and Zimbabwe.

Methods: Primary viral isolates were utilized from previously published cohorts (HC-HIV and GS Studies). Receptor and coreceptor binding was measured via SPR of recombinant gp120s and a novel competitive binding assay to measure CD4 affinity was developed to compare primary gp120s. In vitro models of HIV-1 Env cellular engagement and entry were developed to investigate cell-free and cell-cell transmission modes. Linear models (GEE and GLM) were employed to identify major contributors to the rate of $CD4^+$ T Cell decline and the role of Env function.

Conclusions: These data showed HIV-1 subtype-dependent patterns of Env function. Subtypes A and D displayed the greatest affinities for CD4 and CCR5, demonstrated the most rapid cellular entry and the most rapid rate of disease progression relative to subtype C. Linear models built with this data uncover highly significant impacts of Env diversity on disease progression ($p>0.001$). These data suggest that the diminished virulence of subtype C relative to other HIV-1 subtypes stems from weaker Env/entry-receptor affinities and slowed rates of cellular entry. Future work will focus on flow cytometric assays to measure Env-induced apoptosis between viral subtypes.

BS1.04

Post translational modifications of barrier proteins in the female genital tract and their relationship with the vaginal microbiome

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Background: Diverse non-Lactobacillus bacterial communities in the female genital tract are associated with bacterial vaginosis, poor reproductive health outcomes and increased HIV infection. Our previous studies indicate epithelial wound healing impairment with diverse bacterial communities, but the mechanisms are not wellunderstood. Post translational modifications (PTMs) can affect the structural strength of epithelial barriers. Here, we evaluated the relationship between phosphorylation and other PTMs to vaginal bacteria in the mucosa of women at high risk of HIV infection.

Methods: 688 CVL samples from South African women analyzed by tandem MS were searched for the presence of PTMs using a spectral library based method. The relative level of each modification was quantified by spectral counting of modified peptides with highly confident identifications (P > 90%). Major community state types measured previously include Lactobacillus dominant (LD, > 50% Lactobacillus species), and non-Lactobacillus dominant (nLD, ≤ 50% Lactobacillus species). Two-sample t-tests, Spearman rank correlations, and hierarchical clustering were used for analysis.

Results: Twenty-one major PTMs from 11,443 unique sequences were identified including phosphorylation, methylation, and glycosylation (0.53%, 0.55%, and 0.09% of total unique sequences respectively). LD women showed increased phosphorylation, glycosylation, and decreased methylation ($p < 0.0001$, 95% CI 0.72-3.7%) of two epithelial barrier proteins. Cluster analysis shows a clear relationship between decreased phosphorylation and increasing bacterial diversity, where Prevotella and Mobiluncus were the strongest negative correlates ($r \sim -0.3$, $p < 0.0001$).

Conclusion: This shows for the first time a relationship between bacteria and PTMs of vaginal epithelial barrier proteins. Given the importance of PTMs in barrier structure and function, this demonstrates one possible mechanism for barrier damage in individuals with high bacterial diversity. The mechanism behind these changes remains to be explored and may help better understand mucosal barrier function and HIV susceptibility in women.

BS1.05

Activating NK Receptor Ligand Expression Profile of HIV-1 Infected CD4+ T Cells

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Background: Natural Killer (NK) cells suppress HIV replication in autologous HIV infected CD4+ T cells (iCD4) cells by secreting chemokines that can block HIV entry into new targets. NK cells sense HIV infection through receptor-ligand interactions that initiate signals through inhibitory and activating NK receptors (iNKR and aNKR). The consequence of HIV infection on the expression of ligands to iNKR is well defined. Less is known regarding the HIV infection-related changes in ligands for aNKR on iCD4. Here, we compared the aNKR ligand profiles of HIV iCD4 to uninfected CD4 T cells.

Methods: CD4 T cells isolated from 17 HIV seronegative donors were infected with $HIV_{JR\text{-}CSF}$ for 7 days. iCD4 T cells were stained with antibodies to CD3, CD4, ULBP-1, ULBP-2/5/6, ULBP-3, MIC-A, MIC-B, CD48, CD80, CD86, CD112, CD155, ICAM-1, ICAM-2, and intracellular p24, which is a marker of HIV infection. Samples were acquired on an LSRFortessa X-20 and the frequency and mean fluorescence intensity of ligand expression was assessed. Wilcoxon and Friedman tests with Dunn's post-tests were used to determine the significance of differences between matched groups.

Results and Conclusions: Two subsets of iCD4 T cells were identified, one that maintained cell-surface CD4 expression ($iCD4^+$) and one with downregulated CD4 ($iCD4^-$). Compared to $iCD4^+$, $iCD4^-$ demonstrated a greater intensity of p24 staining and expressed lower levels of aNKR ligands. HIV infection increased the expression of ULBP-1, ULBP-2/5/6, ULBP-3, MIC-A, CD80, and ICAM-1 on $iCD4^+$ to levels greater than those observed on uninfected cells. Expression levels of MIC-B, CD48, CD112, CD155, and ICAM-2 on $iCD4^-$ was below that of uninfected cells. We speculate that reduced expression of aNKR ligands on $iCD4^-$ may confer a survival advantage to NK-mediated anti-HIV responses.

BS1.06

Expression of HIV Dependency Factors in CCR6+CD4+ T-Cells Infiltrating the Colon of Individuals Receiving Antiretroviral Therapy

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Background: HIV preferentially persists in colon CCR6+ Th17-polarized CD4+ T-cells during antiretroviral therapy (ART). Migration of Th17 cells into gut mucosal sites is mediated *via* CCR6-CCL20 and integrin α4β7-MadCAM interactions. In a SIV model of infection inhibition of CCL20-mediated cell trafficking prevents SIV dissemination during vaginal transmission, while the administration of anti-α4β7 antibodies favors mucosal restoration and viral control upon ART interruption. Most recently, we identified mTOR as a HIV permissiveness factor modulated by the gut-homing inducer retinoic acid. Herein, we investigated the expression of CCR5 and integrin α4β7, and the intracellular expression of phosphorylated-mTOR in blood and colon CCR6+ *versus* CCR6- T-cells in a cohort of ART-treated individuals.

Methods: Experiments were performed on matched blood and colon biopsies from chronically HIV-infected subjects with undetectable plasma viral load under ART (n=7). Cells were extracted from colon biopsies by enzymatic digestion. Memory CCR6+/CCR6- T-cells were analyzed for the expression of CCR5, integrinβ7, and phosphorylated mTOR using multicolor flow cytometry (BDAria II). HIV-DNA levels were measured by ultrasensitive PCR in sorted CCR6+/CCR6- T-cells.

Results: Blood CCR6+ compared to CCR6- T-cells expressed similarly low level of CCR5, integrin β7 and phosphorylated

mTOR. In contrast, CCR6+ *versus* CCR6- T-cells infiltrating the colon expressed significantly higher levels of CCR5 (p=0.0026), integrin β7 (p=0.0025) and phosphorylated mTOR (p=0.021). These differences coincided with superior HIV-DNA levels in CCR6+ *versus* CCR6- T-cells (p=0.0014) isolated from the sigmoid colon.

Conclusion: This work reveals preferential expression of CCR5, integrin β7, and phosphorylated mTOR, in colon CCR6+ *versus* CCR6- T-cells, thus providing a molecular explanation for the increased HIV permissiveness of gut-homing CCR6+ T-cells and their contribution to HIV reservoir during ART. These results support a potential therapeutic benefit of integrin α4β7 blockade, as well as mTOR inhibitors, in reducing the size of HIV reservoirs in gut-homing CCR6+ T-cells during ART.

BS1.07

Mucosal Proteome Alterations in Acute HIV Infection

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Mucosal damage in gastrointestinal (GI) tracts during HIV infection is associated with chronic immune activation and increased morbidities. Current HIV therapies do not restore mucosal health as the mechanism is unknown. Although epithelial disruption is evident in late stages of acute infection, early molecular kinetic studies and proteome alterations during early acute infection are lacking and may help better understand mechanisms of how these dysfunctions occur. Colon tissue biopsies were obtained prior to and after SIV infection from 6 rhesus macaques (days 3, 14, 28, 63 and necropsy). A total of 1650 proteins were identified, and differential protein expression was performed using paired t tests (p<0.05 w/ 5% FDR) relative to baseline (-56, -21). IPA and DAVID pathway software (p<0.05, BH) were used for analysis.

Compared to baseline, 293 proteins were significantly altered, 167 of which have never been described in HIV infection. Early (Day 3, 14) biological functions affected included interferon signaling pathway (p<1E-5) and the mitochondrion (p<9E-5). Later in infection (Day 28, 63), viral processes and transcription (p<3E-3), leukocyte migration (p<7E-4), keratin and cytoskeletal organization (p<2E-4) were altered. Several novel proteins consistently downregulated are involved in wound healing and epithelial structure. These negatively correlated with viremia (p<0.05), proliferation/activation of CD4+ and CD8+ T cells, and positively with neutrophils, Th17 and Th22 cells, suggesting a relationship with virus replication and immune activation. Immunofluorescence microscopy co-localization identified wound healing factors with tight junctions in vitro in intestinal epithelial cells. Novel transcription factors (n=49) involved in poly(A) RNA binding and viral transcription (p<6E-28) prior to epithelial dysfunction were identified. This study identifies new factors involved in wounding of gut tissue associated with acute infection and immune activation. Deeper investigation of their role in GI mucosal barrier disruption and immune activation may identify new targets for therapeutic interventions.

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BS1.08

Identification of a public TCR clonotype against the HIV-1 Gag A2-FK10 epitope

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Background: T cell receptor (TCR) repertoire diversity determines the breadth and specificity of an individual's cytotoxic T lymphocyte response against HIV infection. A better understanding of features associated with highly active antiviral TCR may inform strategies to reduce or eliminate latent HIV-1 infection, particularly in the context of diverse or "escaped" epitopes.

Methods: Tetramer+ CD8 T cells against Gag FS8 (FLGKIWPS) were isolated by FACS from HLA-A*02+ HIV non-progressors. Paired TCR alpha and beta CDR3 sequences were determined using single-cell RT-PCR. Full-length TCR genes were reconstructed and transfected into Jurkat cells along with CD8 alpha and NFAT-driven luciferase reporter. TCR+ Jurkat "effector" cells were co-cultured with A*02+ "target" cells pulsed with FK10 peptide or variants and TCR-mediated signaling was quantified by luminescence.

Results: A dominant TCR clonotype reactive against A2-FK10 was observed in two unrelated individuals. In one case, clone 1A9 was observed at ~60% frequency in tetramer-sorted cells. In the second case, clone 4A4 was observed at 100% frequency. 1A9 and 4A4 encoded identical alpha and beta Variable genes (TRAV12-1, TRBV7-2). Furthermore, their alpha CDR3 sequences differed by 1 amino acid, and their beta CDR3 sequence differed by 4 amino acids. 1A9 and 4A4 showed similar antigen sensitivity to FS8 (EC50: 0.29 ng/μL and 0.23 ng/μL, respectively) and FK10 (EC50: 2.1 ng/μL and 0.97 ng/μL) in a TCR signaling assay. Analysis of FS8 variants indicated that positions 4, 6 and 7 were critical for signaling by both TCR, and a natural polymorphism at peptide position 4 (Gag K436R) similarly abrogated their activity.

Conclusions: We have identified a novel "type 2" public TCR clonotype against A2-FK10 with nearly identical sequences, signaling capacities and peptide cross-reactivity profiles. Our results indicate that the T cell response

elicited towards this HIV epitope may be highly restricted, but nevertheless effective once generated.

Epidemiology and Public Health: HIV co-infections and Prevention Among Key Populations

Épidémiologie et santé publique : Coinfections VIH et prévention dans les populations clés

EPH2.01

Shift in disparities in Hepatitis C treatment from interferon to DAA era: A population-based cohort study

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Background: We evaluated the shift in the characteristics of people who received interferon-based Hepatitis C (HCV) treatments and those who received recently introduced direct acting antiviral agents (DAAs) in British Columbia (BC), Canada.

Methods: The BC Hepatitis Testers Cohort includes 1.5 million individuals tested for HCV, HIV, reported cases of hepatitis B, and active tuberculosis in BC from 1990-2013 linked to medical visits, hospitalization, cancer, prescription drugs and mortality data. This analysis included all patients who filled at least one prescription for HCV treatment until July 31, 2015. HCV treatments were classified as older interferon-based treatments including pegylated interferon/Ribavirin (PegINF/RBV) with or without Boceprevir or Telaprevir, DAAs with RBV or PegINF/RBV, and newer interferon-free DAAs.

Findings: Of 11,886 people treated for HCV between 2000 and 2015, 1,164 (9.8%) received interferon-free DAAs (Ledipasvir/Sofosbuvir: n=1,075; 92.4%) while 452 (3.8%) received a combination of DAAs and RBV or PegINF/RBV. Compared to those receiving interferon-based treatment, people with HIV co-infection (adjusted odds ratio [aOR]: 2.96, 95% CI: 2.31-3.81), cirrhosis (aOR: 1.77, 95% CI: 1.45-2.15), decompensated cirrhosis (aOR: 1.72, 95% CI: 1.31-2.28), diabetes (aOR: 1.30, 95% CI: 1.10-1.54), a history of injection drug use (aOR: 1.34, 95% CI: 1.09-1.65) and opioid substitution therapy (aOR: 1.30, 95% CI: 1.01-1.67) were more likely to receive interferon-free DAAs. Socioeconomically marginalized individuals were significantly less likely (most deprived vs. most privileged: aOR: 0.71, 95% CI: 0.58-0.87) to receive DAAs.

Conclusion: There is a shift in prescription of new HCV treatments to previously excluded groups (e.g., HIV-co-infected), though gaps remain for the socioeconomically marginalized populations.

EPH2.02

Epidemiology and Risk Factors of Lymphogranuloma Venereum in British Columbia from 2011-2015

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Background: Lymphogranuloma venereum (LGV) continues to be difficult to diagnose and can lead to significant sequelae. Since 2011, all rectal specimens testing positive for *Chlamydia trachomatis* were tested for LGV serovars, leading to a greater number of LGV cases (mean=21 cases/year). In 2015, case reports of LGV doubled to 42 cases. We sought to characterize LGV cases reported in BC since 2011, and assess possible reasons for the 2015 increase.

Methods: Demographic and behavioural information about all LGV cases reported in BC from January 1, 2011 to December 31, 2015 were identified. Provincial laboratory data were reviewed for potentially missed cases. LGV cases were categorized by reporting year (i.e., 2011-2014 and 2015) and analyzed using the chi-square test or Fisher's exact test. LGV percent positivity was calculated as the number of LGV cases over the number of positive rectal chlamydia.

Results: From 2011-2014, 83 cases were reported versus 42 in 2015. All were among men who have sex with men (MSM). The median age for cases was 46 years and 44 years for 2011-2014 and 2015, respectively (p=0.26). HIV co-infection was similar in both periods (54/83 vs. 25/42, p=0.61) and the majority had undetectable viral loads (34/54 vs. 18/25, p=0.38). There was a decrease in the proportion of cases who identified as Caucasian (p=0.004) and increase in proportion of asymptomatic cases, although not statistically significant (p=0.06). Percent positivity was 7.1% and 7.2% in 2011-2014 and 2015, respectively.

Conclusion: The similar case characteristics and percent positivity during both periods, and increase in proportion of asymptomatic cases, suggest that increased screening for rectal sexually transmitted infections may be the reason for the observed increase in LGV cases. Further evaluation is needed to understand LGV trends, particularly among HIV-positive MSM who are disproportionately affected by LGV.

EPH2.03

Role of opioid substitution therapy and mental health counseling in preventing hepatitis C reinfection

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Background: People remain at risk of reinfection following clearance of primary hepatitis C (HCV) infection. We identified factors associated with reinfection risk in a large population-based cohort study, and examined the role of opioid substitution therapy (OST) and mental health counseling on HCV reinfection.

Methods: British Columbia Hepatitis Testers Cohort includes all individuals in BC tested for HCV during 1990–2013. Individuals with ≥1 valid HCV-PCR test after spontaneous clearance or sustained virologic response (SVR) were included in this study (n=5,915). Incidence rates were calculated assuming a Poisson distribution, and multivariable Cox proportional hazards (PH) model was used to examine reinfection risk factors, and the effect of OST and mental health counseling on HCV reinfection among people who inject drugs (PWID).

Results: The incidence rate of reinfection (n=452) was 1.27 (95% CI: 1.15-1.39) per 100 person-years, with significantly higher rates in the spontaneous clearance group than the SVR group. In adjusted Cox PH model, the spontaneous clearance group (adjusted Hazard Ratio [aHR]: 2.71, 95% CI: 2.0-3.68), those co-infected with HIV (aHR: 2.25, 95% CI: 1.78-2.85), and PWID (aHR: 1.53, 95% CI: 1.21-1.92) had higher reinfection risk. Among PWID, engagement with OST (aHR: 0.73, 95% CI: 0.54-0.98) and mental health counseling services (aHR: 0.71, 95% CI: 0.54-0.92) was significantly associated with lower HCV reinfection risk.

Conclusions: The incidence of HCV reinfection is higher among HIV co-infected individuals, those who spontaneously cleared HCV infection, and in PWID. HCV treatment complemented with OST and mental health counseling could reduce HCV reinfection risk among PWID.

EPH2.04

The Diverse Ways Stigma Impacts the Lives of Trans Women Affected by HIV

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Background: Trans women have previously identified the ways stigma, marginalization, and violence often restrict their access to HIV information, support, and education. Despite this, the experiences of trans women affected by HIV and stigma remains under-researched.

Methods: In March-June 2016, 78 focus groups and interviews were conducted with trans women affected by HIV in Vancouver, Edmonton, Winnipeg, Toronto, and Montreal, including Indigenous, and African, Caribbean and Black (ACB)-specific groups. Data were analyzed using deductive content analysis and discourse analysis. In this presentation we explore one of the key themes identified during data analysis: HIV stigma.

Results: Average age of participants was 40 years (SD 10.5, range 18-65). 38% identified as Indigenous, 26% white, 18% Latin American, 12% ACB, and 4% South Asian or SE Asian. 78% had exchanged sex for money or other goods, and 72% had used drugs in the past year or less. Within this group, stigma plays a complex role in silencing trans women affected by HIV. Trans women described diverse and nuanced forms of stigma including interconnected stigma, internalized stigma, victim blaming, intracommunity difficulties between community members related to stigma, and fear of stigma and its impact. Stigma was described both as a reason for why people found it difficult to talk about HIV, but also as a consequence of talking about HIV *too much*. For example, some participants felt that by highlighting trans women as a vulnerable group for HIV, researchers were associating trans women with disease and inadvertently increasing stigma for trans people.

Conclusion: Researchers, service providers, and community leaders need to attend to the multifaceted complexities of HIV stigma facing trans women and to consider how to better support trans women affected by HIV without further stigmatizing trans communities by explicitly positioning them as a vulnerable group.

EPH2.05

Two patterns of viral spread sustain the HIV epidemic among men having sex with men (MSM) in Quebec from 2002 to 2015

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Objective: HIV-1 epidemics among men having sex with men (MSM) remain largely uncontrolled despite advances in treatment as prevention. In this study, population-level phylogenetics deduced temporal trends sustaining the MSM epidemic in Quebec (2002-2015).

Design and Methods: Phylogenetics assessed evolutionary dynamics (cluster frequency, size, periodicity) of genotyped MSM (n=6135), intravenous drug user (IDU, n= 1517), and non-B subtype heterosexual (n=1094) populations. Transmission clustering was related to recency of infection, virological and behavioural variables.

Results: Phylogenetics infer that 65% of onward spread of the MSM epidemic is attributable to co-clustering of recent infections, identified in primary HIV infection (PHI, 0-6 months, n=1384) or chronic untreated infection (CUN, n=2249). There were declines in cluster sizes of 1, 2--4, 5-9, 10-19 from 2004-2015. In stark contrast, thirty large cluster outbreaks (median cluster size 48) sustained the MSM epidemic, rising from 23% of new infections in 2004 to 43% in 2015, concomitant with declines in singleton transmissions (n-1236). Early infection (0-0.44% diversity) disproportionately accounted for 24%, 43.5%, 50.9%, 52.8% and 59% of transmissions having cluster sizes of 1, 2--4, 5-9, 10-19 and 20+, respectively (odds-ratio, 1, 2.3, 2.5, 3.2, and 3.9). Large 20+ clusters arose in significantly younger populations, with 37% in persons under 30 years (odds-ratio 3.7). Despite similarities in distributional patterns of reported sexual partnerships amongst the five cluster groups, half of persons at the SPOT rapid testing site (n=1745, 2009-2011) reported poor testing habits that were inversely related to numbers of partners.

Conclusions: Timely diagnosis is the cornerstone to control the MSM epidemic and to avert the adaptive advantage that favours large clusters.

EPH2.06

Prevalence and Reasons for Not Testing for HIV among Gay, Bisexual, and Other Men Who Have Sex with Men in a TasP Environment

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Background: HIV testing guidelines in BC recommend that everyone knows their HIV status and that gay, bisexual, and other men who have sex with men (GBM) test for HIV more frequently than the general population. We examined prevalence of HIV testing and factors associated with not having a recent test among GBM in Vancouver.

Methods: We recruited sexually active GBM age ≥16 years using respondent-driven sampling (RDS). Participants completed a computer-assisted self-interview and clinical assessment. We used multivariable logistic regression to examine factors associated with not testing for HIV within the past 2 years. All analyses used RDS weighting.

Results: We enrolled 719 GBM, of whom 184 diagnosed with HIV >2 years before participation were excluded from the analysis. Among the analytic sample (n=535), the median age was 30 years and the median number of male partners in the past 6 months was 5 (Q1,Q3: 3,12). 20.1% had not tested for HIV within the past 2 years. Reasons for not testing included: considering oneself to be low risk (51.3%), wanting to test but just not having done it yet (43.6%), reporting always having safer sex (38.5%), and not having had sex with an HIV-positive partner (38.5%). Factors associated with not testing are shown in Table 1.

Conclusions: Approximately 20% of GBM in our study had not tested for HIV in the previous two years. Further efforts should be made to engage GBM in HIV testing, particularly for bisexual and older MSM, and those living outside of Vancouver.

Table 1. Univariable and multivariable analyses of likelihood of no recent (>2 years) or never testing for HIV.

		Univariable		Multivariable	
		OR	95% CI	aOR	95% CI
Sexual Identity	Gay	Ref		Ref	
	Bisexual	3.54	2.09, 6.00	13.21	4.47, 39.01
	Other	1.11	0.41, 2.97	2.18	0.71, 6.72
Ethnicity	White	Ref		Ref	
	Asian	0.49	0.49, 1.10	0.54	0.22, 1.33
	Aboriginal	0.51	0.51, 1.29	0.39	0.13, 1.12
	Latino	0.22	0.06, 0.77	0.21	0.05, 0.79
	Other	2.47	1.04, 5.91	3.80	1.31, 11.012

		Univariable		Multivariable	
		OR	95% CI	aOR	95% CI
Born in Canada	No	Ref		Not selected	
	Yes	1.99	1.18, 3.34		
Neighborhood	Downtown Vancouver	Ref		Ref	
	Not Downtown Vancouver	1.35	0.82, 2.25	1.57	0.85, 2.90
	Outside City of Vancouver	2.12	1.26, 3.56	2.64	1.41, 4.91
Age Group (years)	<30	Ref		Ref	
	30-44	0.88	0.54, 1.44	1.26	0.685, 2.34
	45+	1.74	1.01, 3.00	2.29	1.16, 4.52
# of Male Anal Sex Partners, p6m	(Continuous)	0.88	0.82, 0.94	Not selected	
Unprotected Anal Sex with	No	Ref		Not selected	
Opposite/ Unknown Status Partner, p6m	Yes	0.41	0.24, 0.70		
Viral Load Sorting Prevention Practice, p6m	No	Ref		Ref	
	Yes	0.14	0.03, 0.65	0.22	0.05, 0.98
Tested for STIs, p6m	No	Ref		Ref	
	Yes	0.26	0.16, 0.43	0.23	0.13, 0.40
Being Out	No	Ref		Ref	
	Yes	0.73	0.46, 1.14	3.58	1.39, 9.23
Told Family Doctor that you have Male Sex Partners	No	Ref		Not selected	
	Yes	0.55	0.31, 0.96		
	N/A (no family doctor)	0.50	0.29, 0.87		
HAD Depression Score	Normal/Mild	Ref		Not selected	
	Moderate/Severe	1.67	0.70, 4.03		
Frequency of Asking about Partners' HIV Statuses	<50%	Ref		Ref	
	>50%	0.70	0.46, 1.07	0.59	0.36, 0.97
Perceived Risk of HIV	Very unlikely	Ref		Ref	
	Unlikely (11-39%)	0.56	0.35, 0.89	0.45	0.26, 0.78
	Likely (>40%)	0.52	0.26, 1.02	0.89	0.40, 1.99
	Already HIV+	1.03	0.31, 3.47	3.66	0.87, 15.41

Note: p6m = past 6 months

EPH2.07

A Syndemic Approach to Assess the Effect of Substance Use and Social disparities on the evolution of HIV/HCV infections in British Columbia

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Background: Co-occurrence of social conditions (addictions, mental illness, socioeconomic deprivation) and infections (hepatitis B virus [HBV], tuberculosis and sexually transmitted infections) may affect HIV/HCV disease risk and progression. We examined the changes in relationship of these social conditions and infections on HIV and hepatitis C virus (HCV) infections over time in British Columbia during 1990-2013.

Methods: The BC Hepatitis Testers Cohort (BC-HTC) includes ~1.5 million individuals tested for HIV or HCV, or reported as a case of HCV, HIV, HBV, or tuberculosis linked to administrative healthcare databases. We classified HCV and HIV infection status into five combinations: HIV-/HCV-, HIV+ monoinfected, HIV-/HCV+ seroconverters, HIV-/HCV+ prevalent, and HIV+/HCV+.

Results: Of 1.37 million eligible individuals, 4.1% were HIV-/HCV+ prevalent, 0.5% HIV+ monoinfected, 0.3% HIV+/HCV+ co-infected and 0.5% HIV-/HCV+ seroconverters. Overall, HIV+ monoinfected individuals lived in urban areas (92%), had low injection drug use (IDU, 4%), problematic alcohol use (4%) and were materially more privileged than other groups. HIV+/HCV+ co-infected and HIV-/HCV+ seroconverters were materially most deprived (14%, 12%), had higher IDU (34%, 53%), problematic alcohol use (15%, 17%) and major mental illnesses (12%, 21%). IDU, opioid substitution therapy, and material deprivation increased in HIV-/HCV+ seroconverters over time. In multivariable multinomial regression models, overtime, the odds of IDU declined among HIV-/HCV+ prevalent and HIV+ monoinfected individuals but not in HIV-/HCV+ seroconverters. Declines in odds of problematic alcohol use were observed in HIV-/HCV+ seroconverters and co-infected individuals overtime.

Conclusions: These data show confluence of addiction, mental illnesses, co-infections and socioeconomic disparities which varied across HIV and HCV infection groups. These findings could inform prevention, care and support services for HIV and HCV infected populations based on the evolving syndemic epidemiology, disparities and risk profiles of these groups.

EPH2.08

Monitoring the impact of innovations in biomedical HIV prevention on the sexual behaviour of gay and bisexual men in Australia

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Background: PrEP and TasP are changing the sexual behaviour of gay and bisexual men. In this new era of HIV prevention it is essential that we continue to monitor the changing use of HIV risk reduction strategies among this key population. We report on monitoring of sexual risk behaviour among studies of gay and bisexual men in Australia.

Methods: Data was analysed from the Australian Gay Community Periodic Surveys (GCPS) and from the Following Lives Undergoing Change (FLUX) study, a national online cohort study of drug use among gay and bisexual men in Australia. Proportions of gay and bisexual men not practicing any form of risk reduction were estimated and characteristics associated with these men were determined. A profile of current HIV risk reduction practices was developed to graphically represent the use of different strategies. The characteristics of "high risk" men not on PrEP were also analysed.

Results: Data from the GCPS indicates overall 6% of gay and bisexual men do not practice risk reduction, from FLUX the proportion was 8.4%. Among casual male partners in the Sydney GCPS 2016, the susceptible/at-risk group (HIV negative/untested men not on PrEP and engaging in any condomless anal intercourse) comprised 30.9% of participants. Analysis of men in this group shows high levels of sexual activity, risk practice, drug use and STI diagnoses.

Conclusion: In Australia few gay and bisexual men used no form of risk reduction and there were few differences between gay and bisexual men who did and did not practise risk reduction. Almost all HIV-positive men practised HIV risk reduction. Understanding which gay and bisexual men take up PrEP is essential in ongoing PrEP implementation efforts as is understanding how PrEP uptake will impact on the use of condoms and other HIV risk reduction strategies.

Social Sciences: Experiences of Gay and Bisexual Men

Sciences sociales : Expériences des gais et des hommes bisexuels

SS2.01

The PrEP-Stigma Paradox: Learning from Canada's first wave of PrEP users

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The emergence of daily oral TDF/FTC-based pre-exposure prophylaxis (PrEP) use in Canada represents a timely opportunity to address unresolved questions about how best to deliver this HIV prevention technology. Questions also remain concerning the impacts of PrEP on gay men's everyday social and sexual lives. We sought to inductively learn from the lived experiences of gay men who were part of the 'first wave' of PrEP users in Canada. We conducted a combination of small focus groups and individual qualitative interviews with 16 gay men in Toronto who had been on PrEP for at least one year as part of PREPARATORY-5, a demonstration project which ran from November 2014 to June 2016. An additional 10 participants in Toronto were interviewed who had been on PrEP for at least 6 months. Interviews were structured to understand participants' experiences with PrEP over time. Interviews were digitally audiotaped, transcribed verbatim, and interpreted through narrative analysis. While the experiences of PrEP use were described as overwhelmingly liberating and empowering overall, sex-stigma emerged as a complex theme in the accounts of PrEP users. We considered how stigma related to men's: (1) *initial decisions to start PrEP*, (2) *experiences of getting PrEP access*, (3) *sex lives and sexual decision-making on PrEP*, (4) *challenges in relation to PrEP use*, (5) *decisions about continuing to use/not use PrEP*; and (6) *recommendations related to PrEP use and access*. Gay men's accounts of PrEP vary in complex ways, including their experiences of PrEP and sex-related stigma. Paradoxically, some men said that PrEP use both led them to experience stigmatizing reactions from friends and prospective sexual partners while also being described as helping to remove stigma, shame, and fear related to HIV and sexuality. Structural stigma associated with gay sexuality was also discussed as a pervasive barrier to PrEP access.

SS2.02

"It's Liberating to be Honest with You": A Qualitative Study of the PrEP Readiness Continuum among Gay and Bisexual Men in Toronto, Canada

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Background: This exploratory qualitative study sought to understand decision-making processes about whether or not to use PrEP among ethnically diverse gay, bisexual and other men who have sex with men (GBM) in Toronto, and PrEP-users' experiences in their intimate and social worlds.

Methods: We conducted in-depth, semi-structured interviews to explore PrEP awareness, decision-making around uptake, access, sexual behaviors/relationships and health. Interviews were audio-recorded, transcribed and reviewed using thematic content analysis.

Results: From Oct 2015-Mar 2016, 29 participants (15 PrEP-users/14 non-users; mean age=36 yrs; 27 gay, 2 bisexual), completed 45m-90m interviews. Most reported sex with multiple partners and inconsistent condom use, with an emphasis on personal responsibility and self-care. Trust and concern about HIV-infection were pervasive themes: non-users made trust-based decisions about when to use condoms; PrEP-users indicated they could only trust themselves. Non-users expressed concerns about long-term safety, needing to use condoms for other STIs, and barriers due to out-of-pocket cost and inadequate insurance coverage. PrEP-users indicated uptake due to inconsistent condom use, decreased anxiety after condomless or serodiscordant sex, and no longer using condoms unless requested by partners. PrEP-users reported no barriers or stigma from healthcare providers, but inadequate support for navigating post-PrEP challenges in sexual and social relationships. Some disclosed PrEP-use to friends, sexual partners, family, and online PrEP-user forums; others disclosed very selectively due to anticipated stigma.

Conclusions: Rather than a dichotomy, we identified a continuum of readiness to use PrEP among GBM in Toronto. Among non-users, some considered PrEP a future option, others wanted to use PrEP but couldn't afford it; among users, some considered terminating PrEP or taking a break. All hoped for an HIV vaccine. Future research should explore the PrEP readiness continuum among GBM, with attention to user-identified professional and social support needs, stigma, geographic differences, and barriers in access due to cost.

SS2.03

Undetectable Optimism: HIV-Negative Gay Men, Serostatus Uncertainty and Undetectable Viral Load

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Background: : Treatment optimism is an epidemiological hypothesis that correlates a belief in the risk reduction associated with undetectable viral load (UVL) with an increased likelihood to have "unprotected" anal intercourse (UAI). Empirically demonstrating treatment optimistic behaviour among gay men has been difficult. Despite equivocal evidence, recent research has led to further speculation that gay men will use UVL to justify condomless sex.

Methods: : I conducted 33 in-depth interviews with young HIV-negative gay men living in Montréal and Toronto. Interviews focused on experiences of serostatus uncertainty (an inability to resolutely confirm one's HIV-negative status). To broaden perspectives beyond those commonly included in qualitative research, interviewees hadn't previously participated in a HIV related interview or hadn't worked for an ASO. The data was analyzed using: sexual practice theory, institutional ethnography and interpretative phenomenological analysis.

Results: : UVL affected HIV-negative gay men in multiple ways beyond condomless sex. Men experiencing anxiety over serostatus uncertainty were less likely to accept UVL as a prevention tool than those more tolerant to serostatus uncertainty. Serostatus related anxiety was determined by: (1) *Sexual Health Literacy*; (2) *Socio-Sexual Context and Consent; (3) Sexual Confidence* (4) *Health Care Access*; (5) *Socio-Economic Vulnerability*; and (6) *Ethics and HIV Stigma*. Many HIV-negative gay men remained critical of UVL, especially those strongly reliant on serosorting. Decisions to serosort remained ethico-politically complex. Many lacked an operational understanding of UVL. Men who incorporated UVL into their sexual practices still used condoms and did so after building rapport with HIV-positive partners. UVL was not used to justify condomless sex.

Conclusion/Discussion: Awareness of UVL is not enough to alter sexual practices. Improving UVL health literacy can reduce HIV stigma and the anxiety associated with serostatus uncertainty and serovariant sex. A focus on treatment optimism may obfuscate how men are processing complex and uncertain HIV prevention knowledge.

SS2.04

Desire, risk, and surveillance: Governing gay, bisexual, and other men who have sex with men in the age of pharmacological panacea

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In this presentation we explore a range of surveillance implications related to HIV treatment and prevention

technologies in the form of 'treatment as prevention' (TasP) and 'Pre-exposure Prophylaxis' (PrEP) in North America. TasP involves scaling up HIV testing and antiretroviral therapy to improve health outcomes and reduce further transmissions. PrEP is targeted at people deemed 'at-risk' of acquiring HIV and involves prescribing the same HIV antiretroviral therapy—but to prevent infection. Together, they constitute what the US Centers for Disease Control and Prevention have termed 'high impact prevention,' an approach that uses 'combinations of scientifically proven, cost-effective, and scalable interventions targeted to the right populations in the right geographic areas.' Our work elaborates how these new pharmacological interventions are shaping the lives of gay and bisexual men and other men who have sex with men in urban centres where they have been targeted through both official public health and community-initiated health promotion messaging. Those living with HIV are urged to start treatment and maintain an undetectable viral load while those at risk of HIV are urged to take control of their health and sexuality by initiating PrEP. While these pharmacological approaches have great promise for increasing access to HIV testing, treatment, and prevention, they have also enabled new forms of medical and public health surveillance that we argue need to be interrogated. Specifically, both TasP and PrEP require greater healthcare utilization and in the case of TasP have legal and criminal justice implications. Drawing on critical insights from Michel Foucault and Roberto Esposito we explore these implications and examine how HIV -/+ men are engaging public health, clinical care providers, and each other in new ways that promote their governance organized under the auspices of notions of care, but which increasingly seem to be revealed as forms of control.

SS2.05

Community mobilisation to optimize access to combination HIV prevention for MSM in Montreal: initial results from the MOBILISE! project

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Background: Using multiple prevention options and services together ("combination prevention") could significantly reduce HIV infections among MSM, but a coordinated, synergistic strategy is needed to achieve this. MOBILISE! is a community-based research project initiated in Montreal that aims to develop a strategy for optimizing access to combination prevention for MSM through participatory evaluation and community mobilization.

Method: A coalition of 33 partners has collaborated to implement peer-led community discussions and an online survey to gather data on: 1) what MSM across Quebec know about combination prevention; 2) their experiences accessing health services in Montreal. Qualitative data from discussions were gathered using logbooks and analyzed thematically. Descriptive analyses of means and proportions were generated for quantitative data from survey responses. A deliberative process was used to leverage this data to identify priorities for action.

Results: Between November 2015 and October 2016, 20 peer researchers were recruited to lead small-group discussions with a total of 83 MSM, and 394 respondents completed the survey. Over 70 participants attended a community forum to discuss key findings including: 1) barriers in access to PEP and PrEP; 2) discrepancies in attitudes and knowledge about serosorting and undetectable viral load depending on HIV status; 3) the need for better coordination between medical and non-medical care providers. MSM unaware of their HIV status were identified as a priority group that knows less about and makes less use of risk reduction strategies. Structural change within the health care system, capacity building, and psychosocial interventions were identified as potential solutions.

Conclusion: Results from the forum will be used to develop a community consensus statement. The mobilization strategies used in Montreal are being adapted by partners in Toronto, Ottawa, and Vancouver and a framework is being developed to evaluate the impact of structural interventions on access to services and health outcomes.

SS2.06

We're here: Subjugation and resistance in older HIV-positive gay men's experiences of seeking and receiving care across health care settings

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Despite the prominent role of systemic discrimination in impeding equitable access to health care among older HIV-positive gay men, this population's subjective accounts of subjugation in health systems remain underrepresented in the literature on aging gay men. This qualitative study sought to investigate experiences of subjugation among older HIV-positive gay men in health settings, and to examine this population's accounts of resistance to these expressions of marginality. To this end, 16 Toronto-based HIV-positive gay men over age 49 underwent semi-structured interviews in which they were asked to reflect on their cumulative experiences of seeking and receiving care in health settings. Drawing on a poststructuralist tradition of grounded theory known as situational analysis to inform conceptualizations of the interview data, these accounts were used as an empirical basis from which to infer discursive processes of subjugation and resistance that may be most salient for older HIV-positive gay men

interacting with systems of care. Participant accounts revealed, among other findings, (1) complex intersections of gay identity, HIV history, and aging experience as potential targets of subjugation and sources of resistance across health settings, and (2) the role of informal and formal HIV care networks in both reinforcing historical conditions of marginality and catalyzing opportunities for change in the social conditions of this population. These findings suggest the need for researchers and practitioners to recognize and address the highly intersectional nature of subjugation and resistance experienced among older HIV-positive gay men across contexts of care, and to capitalize on this population's existing care networks as potential sources of emancipatory change.

SS2.07

Sexual and Drug-Related Risks for HIV Seroconversion among MSM: Findings from Toronto's Party-n-Play Study

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Background: 'Party-n-Play' (PNP) is condomless sex between MSM that occurs under the influence of drugs. Some scholars have suggested that PNP is a major public health concern for MSM. This qualitative study sought to examine the sexual and drug-related risks for HIV seroconversion that may occur during PNP.

Methods: In-depth 1 hour interviews were conducted between October and November 2016, with 44 self-identifying gay, bisexual, two-spirit, queer men (MSM) who lived in the Greater Toronto Area, and who used various substances (e.g., crystal methamphetamine, GHB/GBL, cocaine, ketamine, MDMA/ecstasy, poppers) before or during sex with another man during the previous month. MSM were recruited through social media, online postings, venue-based ads, and community organizations. Interviews were transcribed verbatim and the data were subjected to thematic analysis.

Results: The findings from interviews with 44 MSM (mean age = 37; 55% HIV-positive, 68% gay, 82% single, 40% men of colour; 78% born in Canada) show that these men used a variety of rationales to engage in PNP. Drug use during sex was frequently identified as a significant influence on participants' risk-taking practices, although the extent to which drugs shaped these practices varied considerably. While some participants directly attributed sexual risk practices (e.g., increased number of sexual partners, reduced condom use) to drug use, others suggested that they were able to navigate and explore boundaries often considered 'risky' without acquiring or transmitting HIV, or other harms. Some men also suggested that they maintained strict personal rules about condom use with casual partners, and demonstrated significant knowledge of HIV and STD transmission, safe injection practices, and harm reduction techniques.

Conclusions: The findings illustrate a range of relationships between PNP and HIV/STD risk. Recommendations are provided to facilitate the development of HIV, harm reduction, and sexual health educational initiatives, health promotion and care for PNP-involved MSM.

SS2.08

Ethnicity, Immigration and HIV Status among Men Who Have Sex with Men: Findings from Ontario's Cruising Counts Study

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Background: African, Caribbean and Black (ACB) and Latino/Hispanic, Brazilian and South American (LHBSA) men who have sex with men (MSM) are disproportionately affected by HIV in Canada. Given Canada's complex immigration policies and the effects of racism upon health, our aim was to examine the relationship between ethnicity, immigration and HIV status among MSM.

Methods: MSM aged>15 years were recruited across Ontario from 12/2013-1/2014 through websites, mobile-apps and community-based organizations to complete an anonymous online questionnaire. HIV status (outcome) was categorized as self-identified HIV-negative/unknown compared with HIV-positive. Immigration status was categorized as 'Canadian citizen', 'permanent resident', 'landed immigrant', 'refugee', 'student/work permit' and 'non-status'. Ethnicity was categorized as 'ACB', 'LHBSA' and non-ACB/non-LHBSA ('other'). Descriptive statistics, Pearson's chi-square tests and multivariable logistic regression analyses assessed the relationship between ethnicity, immigration and HIV status while controlling for age, education, sexual orientation and STI status.

Results: Of 1825 MSM, 42 (2.3%) self-identified as ACB, 66 (3.6%) as LHBSA and 94% as 'other' ethnicities. HIV-negative/unknown LHBSA MSM were more likely to be permanent residents and hold student/work permits while HIV-negative/unknown ACB MSM were more likely to be landed immigrants compared with MSM from 'other' ethnicities ($p<0.001$). HIV-positive LHBSA MSM were more likely to be non-status immigrants while HIV-positive ACB MSM were more likely to be permanent residents or landed immigrants ($p<0.001$). Non-status immigrants were significantly more likely to be HIV-positive than Canadian citizens (AOR=37.6, 95%CI:3.5-398.5). Compared with 'other' ethnicities, self-identifying as ACB was significantly associated with an increased odds of being HIV-positive (AOR=4.0, 95%CI:1.5-10.8) while self-identifying as LHBSA was not (AOR=1.7, 95%CI:0.63-4.5).

Conclusions: A better understanding of the specific needs of non-status and ACB/LHBSA communities is required. Online and anonymous data collection and health out-

reach may facilitate easier and more comfortable interactions with these marginalized communities and should be contextualized within Canada's immigration policies.

Multidisciplinary: Community-based Research and Participative Approaches

Multidisciplinaire : Recherche communautaire et approches participatives

MD2.01

Comparing Antiretroviral Therapy Use and Viral Suppression between Young Women Engaged in Pediatric Care and their Peers in Adult Care

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Background: There were 584 perinatal HIV cases between 1984 and 2011. Optimal transition from pediatric to adult care is essential for ideal antiretroviral therapy (ART) use. We assessed ART use and viral suppression between young women (<30) vs. older women and the differences between young women receiving pediatric and adult care.

Methods: The Canadian HIV Women's Sexual and Reproductive Health Cohort Study (CHIWOS) is a prospective study of women with HIV aged >16 years in BC, Ontario and Quebec. Enrolment occurred between October 2013 and June 2015. Descriptive analysis of socio-demographic variables [frequencies, means, standard deviations (SD)] was presented for each variable. Multivariable logistic regression models estimated adjusted risk ratios and confidence intervals (CI) for current ART use and viral suppression with age. We assessed differences between those in pediatric and adult care.

Results: Among 1425 women, 137 were <30 years (mean age 24.4 years, SD=3.4). The 1288 older women had a mean age of 44.8 years (SD=9.1). Multivariable logistic regression revealed that younger women were 2.1 times (95% CI=1.31-3.34) less likely to be on ART than older women adjusting for socio-demographic factors. Younger women were also 2.4 times (95% CI=1.15-2.75) more likely to have detectable viral load than older women adjusting for socio-demographic factors. For young women with pediatric vs. adult care, there was no significant difference in current ART use (92% vs. 90%; p=0.41) and no difference in reported medication adherence (95% in both groups). Young women receiving pediatric care, however, were more likely to have undetectable viral loads compared to young women receiving adult care (84% vs. 58%; p<0.05).

Conclusions: Younger women were less likely to be currently using ART or have a suppressed viral load compared to older women. However, this was driven by those not receiving pediatric care, all/most of whom acquired HIV in adulthood.

MD2.02

Engagement in Maximally-Assisted Therapy and Adherence to Antiretroviral Therapy among a Cohort of Indigenous People who use Illicit Drugs

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Background: In Canada and elsewhere, individuals of Indigenous ancestry experience a disproportionate burden of HIV infection and there is an urgent need to improve HIV/AIDS treatment outcomes. Maximally-assisted therapy (MAT) is an interdisciplinary care intervention that includes antiretroviral therapy (ART) dispensation to support individuals with a history of addiction and homelessness. This study sought to longitudinally evaluate the relationship between engagement in a MAT-based programme and achieving optimal adherence to antiretroviral therapy among Indigenous individuals who use illicit drugs.

Methods: Data were obtained from the AIDS Care Cohort to Evaluate Exposure to Survival Services (ACCESS), a community-recruited cohort of HIV-positive individuals who use illicit drugs in Vancouver, Canada. Longitudinal cohort data was confidentially linked to comprehensive HIV clinical monitoring records and ART dispensation records in a setting of no-cost HIV/AIDS treatment and care. To estimate the effect of engagement in a MAT-based programme on achieving ≥95% ART adherence, we used generalized mixed-effects (GLMM) as well as, marginal structural modeling to account for the nonrandomized nature of our study design.

Results: Between December 2005 and May 2014, 321 HIV-positive Indigenous participants had ≥1 day of ART dispensation and were included in these analyses. In both multivariable analyses, engagement in MAT was independently associated with optimal adherence to ART (GLMM: Adjusted Odds Ratio [AOR] = 5.23, 95% confidence interval [CI]: 3.07 – 8.91; marginal structural model: AOR = 7.46, 95% CI: 4.16 – 13.39).

Discussion: We observed that engagement in a MAT-based programme was strongly associated with achieving

optimal adherence to HIV treatment among Indigenous people who use drugs independent of drug use patterns and addiction treatment. MAT-based programmes could be a part of a renewed evidence-base to elevated levels of preventable HIV/AIDS-associated morbidity, mortality and onward viral transmission among Indigenous peoples in Canada.

MD2.03

Incarceration Associated With Reduced Odds of Viral Suppression Amongst Women Living With HIV: Critical Need to Address Gaps in HIV Cascade

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Background: Despite continued gender gaps and sub-optimal treatment outcomes for women along the HIV cascade both in BC and across Canada, there is limited longitudinal community-based research with Women Living with HIV (WLWH) examining the potential impact of incarceration on HIV care outcomes.

Methods: Data is drawn from SHAWNA *(Sexual health and HIV/AIDS: Women's Longitudinal Needs Assessment),* a community-based research cohort with WLWH (trans inclusive), aged 14+ who live or access HIV services in Metro Vancouver, Canada (2010-2016). Baseline and semi-annual questionnaires are administered by trained community and WLWH interviewers alongside a clinical visit with viral load (VL) and CD4 monitoring, sexual health education and required referrals. Multivariable logistic regression using generalized estimating equations (GEE) was used to longitudinally model the effect of incarceration on viral suppression (HIV plasma VL < 50 copies/mL).

Results: Amongst 266 WLWH, the majority (76%) had been incarcerated in their lifetime and 65% were virologically suppressed at baseline. Over the follow-up period, 16% were incarcerated. The median age was 43, 61% were Indigenous, 32% white and 5% Afro-Canadian/ Black, with no differences in VL suppression by ethnicity. In multivariable GEE analyses, after adjusting for age, drug use, homelessness, and gender-based violence (GBV), exposure to recent incarceration was independently correlated with reduced odds of VL suppression (AOR: 0.48, 95% CI 0.25-0.92). Of concern, GBV was a confounder of incarceration. In sub-analysis, ART adherence mediated the relationship between incarceration and viral suppression.

Conclusions: This research suggests critical need for research and interventions to better address factors shaping ART adherence and retention in care for WLWH, both within prisons and key transition periods (i.e., entry/ release). The confounding role of gender-based violence on incarceration further points to an urgent need for women's trauma-informed HIV care, and a better understanding of how GBV shapes HIV care experiences.

MD2.04

Trans Women's Experiences of Participating in HIV Research: A Reflection on Process and Community-Based Research

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Background: Trans women in HIV research have commonly been excluded, miscategorized as men who have sex with men (MSM), or narrowly defined through public health outputs (e.g. as 'vectors of disease' or a 'high risk population'). In recent years, there has been a demonstrated interest in understanding the experiences and impacts of HIV amongst trans women in Canada. It is important to examine how research is being conducted within a community that has a complex relationship with academia and research.

Methods: Focus groups and interviews with 78 trans women were conducted in Toronto, Montreal, Edmonton, Winnipeg, and Vancouver, and analyzed using deductive content analysis and discourse analysis. Study design and data collection were led by trans women on the research team, and research participants were recruited by peers in each of the cities. Analysis of results is underway, and aims to centre the involvement and leadership of trans women from the research team and amongst the local peer workers.

Results: Trans women shared their reasons for involvement in research including opportunities to educate others, financial compensation, to contribute to social change, for its therapeutic value, and to connect with others. Respondents stated that they did not participate in some research projects because they were concerned that they may be potentially misrepresented, or that their experiences could be ignored. Participants also identified the need for enhanced diversity in research and more focus on Indigenous lives.

Conclusion: There is a need for critical reflection on the involvement of trans women affected by HIV in community-based research. As trans women are increasingly included in calls for research and service provision funding, this project offers an important case study to better consider strengths and limitations of current community-based HIV research models, and to reflect on ways researchers can work to overcome oppressive research practices.

MD2.05

Using poetic narrative inquiry in HIV-research with, for and by African, Caribbean, and Black (ACB) communities

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Background: Social scientists are developing research methodologies grounded in the ways people living with HIV make meaning of their social worlds. ACB scholars have incorporated culturally responsive approaches to knowledge production, including performance-based methods that are reverential to emotive, embodied expression.

Description: The *Because She Cares stud*y used poetic narrative inquiry to gather, interpret and share stories of work that resonated with ACB women participants' (the Narrators) experiences of HIV-related employment. Informed by transnational feminist and decolonizing thought, this methodology draws upon ethnopoetics, performance methods, narrative research, and the poetic arts. Oral narratives were transcribed to integrate paralanguage and emotive expressions. Narratives were interpreted for emotional, theoretical or political "resonance" and "re-told" using poetic devices (i.e., metaphor, repetition, rhythmic inflection) to embody the emotive resonance of the original telling and evoke the theoretical and political relevance of the sharing. Poems were performatively workshopped with each Narrator.

Lessons Learned: This process was non-linear, reflexive, participatory and dialogic: poems were reshaped through conversations between The Narrators and researcher, and from resulting reflections arising from the interpretive process. Concerns about using poetic narrative inquiry include matters of confidentiality and anonymity, the tensions of authenticity, control and ownership, and the potentially painful emotional resonance of poetry. This method challenged the researcher to recognize her ethical responsibility to narrators and the broader ACB HIV communities represented in these poems.

Conclusions: The researcher is currently working with ACB HIV communities to develop KTE activities (i.e., spoken word performance). Using arts-informed methodologies creates an opportunity to reflect critically on knowledge production in HIV research: who produces knowledge, what ways of knowing are valued, and what messages are conveyed through knowledge production and dissemination. These methods challenge researchers to consider creative ways to interpret, represent and share research knowledge such that it fosters discussion, reflection, contemplation, and action.

MD2.06

Digging Deep: Promoting the Health of Aboriginal Women through Community-based, Culturally-safe Research

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Background: Aboriginal Women in Canada face a higher rate of HIV/AIDS. Social determinants of health are contributing factors to higher rates of IDU, HIV/AIDS, and HCV among Aboriginal women. There is a startling lack of gender-specific (LGBTQ community), Aboriginal-specific, HIV/AIDS resources and services. This research is working towards understanding and identifying powerful forms of resilience within the Aboriginal community. Our focus is to support Aboriginal women through developing community-based solutions as part of a culturally safe model of care, as well as increasing educational tools that build capacity with Aboriginal women, and the All Nations Hope Network (ANHN) organization in Regina.

Methods: Each interview began by gifting the women with a tobacco tie, water, and honorarium; over 175 women participated in interviews. We are now beginning key informant one-on-one video narratives interviews. We are building capacity with community partners and researchers by providing training for interviewing, literature review research, data analysis, and coding. NVivo software is used for the qualitative data analysis, and SPSS software captures quantitative analysis. Indigenous methodology guides all aspects of our research, and the Collective Consensual Data Analytic Procedure (CCDAP) is used throughout the data analysis process.

Results: The Digging Deep Project began with ceremony led by Elder Betty McKenna, and we continue with ceremony throughout all aspects of the project. We recruited peer researchers called "Willow Warriors," a name given by the Elder symbolic of strength, resiliency, and courage. We have been successful in building capacity by developing respectful relationships with the participants and community partners.

Conclusion: Our presentation will share key lessons learned in this research, some preliminary data, and valuable insight from the women's stories. These stories highlight Aboriginal women's resilience and the importance of community-based solutions in strengthening the health of Aboriginal women and their communities.

MD2.07

Emancipatory Participation: Active Change Agents in the Fight Against Stigma

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Introduction: The People Living with HIV Stigma Index is an international tool aimed at identifying the intersections of society where HIV stigma persists. The study has been implemented in over 60 countries to date. British Columbia will be the first region to implement this study in Canada with the goal of providing evidence that can be used as an advocacy tool for effecting change.

Methods: People living with HIV (PLHIV) are at the center of all Stigma Index processes: as research team members, core staff, interviewers and interviewees and as drivers of how the information is collected, analyzed and used. The methodology and research design, conceptualized by and for PLHIV, was built on a core commitment to the ethical process, rigor, and CBR sensitivity, which champions the support of each individual Peer Research Associate (PRA) and not "Peers" as an amorphous group.

Results: Early anecdotal information suggests the benefits of the Index, for PRA go further than just collecting this much sought after evidence. Interviewer PRA's have reported they feel empowered, able to make choices, suggestions, and this has translated into a better experience for both interviewee and PRA. Supporting the individual needs of PRA's has encouraged them to talk more openly about their individual interviewing experiences, allowing them to self-assess their own capacitates and opportunities for growth. Moreover, they are meaningfully engaged in collecting rich fulsome data.

Conclusion: The Stigma Index is not designed merely to collect information on HIV stigma, although this is the main objective, but also to be part of a process of empowerment for the interviewees and PRA. It is intended to embrace a participatory spirit for all those involved. When efforts are made to include the unique and specific needs of individual PLHIV, PRA's can become active change agents for their communities and themselves.

MD2.08

Screening for Anal Cancer in HIV-infected MSM: Early results from the HPV-SAVE Study

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Background: Malignancy is the commonest cause of death in HIV and anal cancer is the commonest malignancy. Anal cancer rates in HIV+ MSM are about 100x higher than the rates in the general population. Screening for anal cancer and pre-cancers can be done using similar techniques that are widely used for cervical cancer screening. However, anal cancer screening with treatment of precancerous lesions is less widely known, there are no universally accepted guidelines and it is not publically promoted or funded.

Methods: Our aim was to determine the acceptance rate to invitations for anal cancer screening and the factors determining acceptance or refusal. Using mailed or hand-delivered letters, we invited HIV+ MSM in Toronto, Vancouver and Ottawa to have anal Pap testing in their personal physician's office. Those with abnormal Pap tests were referred for High Resolution Anoscopy (HRA) and anal biopsy. If the biopsy indicated high-grade histology (HSIL), they were randomly allocated to electrocautery ablative therapy or to active surveillance.

Results: To date, there have been 1161 invitations and 286 subjects (25%) have agreed to have Pap testing. Overall acceptance rates of the subjects varied widely by the physicians' office: (8-87% acceptance rate, median = 27%). Cytology results from satisfactory Pap tests were: Normal (50%), ASCUS (31%), LSIL (13%), HSIL (6%). Of 23 subjects referred for HRA, 14 (61%) had high-grade histology and have been offered the treatment options. The probability of high-grade histology increased with progressively higher grade cytology. HSIL cytology had high specificity (90%) for detection of high- grade histology.

Conclusions: HIV+ MSM had moderate acceptance of invitations to have anal Pap testing. Abnormal anal Pap tests were a very sensitive screening test for detection of pre-cancerous anal histology.

This study is supported by a CIHR grant.

Basic Sciences: Antivirals, Reservoirs and HIV Cure

Sciences fondamentales : Antiviraux, réservoirs et remède contre le VIH

BS2.01

HIV persists in CCR6+CD4+ T-cells from colon and blood during antiretroviral therapy

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Background: Peripheral blood CD4+ T-cells expressing the gut-homing marker CCR6 are highly permissive to HIV. Retinoic acid (RA), a gut-homing inducer, increases HIV integration/replication preferentially in CCR6+ T-cells; this further supports the role of the gut in HIV disease progression. Herein, we investigated the contribution of CCR6+ T-cells from the colon and blood to viral persistence during antiretroviral therapy (ART) and tested the ability of RA to reactivate latent HIV in these cells.

Methods: Matched sigmoid biopsies and blood samples (n=13) as well as leukapheresis (n=20) were collected from chronically HIV-infected individuals receiving ART. Subsets of CD4+ T-cells with distinct differentiation/polarization profiles were identified using surface markers as follows: memory (T_M, CD45RA-), central memory (T_{CM}; CD45RA-CCR7+), effector ($T_{EM/TM}$; CD45RA-CCR7-), Th17 (CCR6+CCR4+), Th1Th17 (CCR6+CXCR3+), Th1 (CCR6-CXCR3+), and Th2 (CCR6-CCR4+). We used polychromatic flow cytometry for cell sorting, nested real-time PCR for HIV-DNA quantification, ELISA and flow cytometry for HIV p24 quantification. HIV reactivation was induced by TCR triggering in the presence/absence of all-trans RA.

Results: Memory CCR6+ compared to CCR6- T-cells isolated from the blood and colon biopsies were highly enriched in integrated HIV-DNA. Among the T_M pool in the blood, CCR6+ T_{CM} showed the highest levels of integrated HIV-DNA. Among blood T_{CM}, Th17 and Th1Th17 contributed the most to the pool of cells harboring integrated HIV-DNA despite their reduced frequency compared with Th2, which were infected the least. HIV reactivation was induced by TCR triggering and/or retinoic acid exposure at higher levels in CCR6+ versus CCR6- T_M, T_{CM}, and T_{EM}.

Conclusion: CCR6 is a marker for colon and blood CD4+ T-cells enriched for replication-competent HIV-DNA. The finding that RA promotes HIV latency reversal indicates an important contribution of the intestinal environment to viral persistence and reactivation. Novel eradication strategies should target HIV persistence in CCR6+CD4+ T-cells from various anatomic sites.

BS2.02

HIV-1 Resistance to Dolutegravir is Modulated by Epigenetic Signals

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Background: Integrase strand transfer inhibitors (INSTIs) act by inhibiting the HIV integrase enzyme (IN). The INSTI raltegravir (RAL) selects for drug resistance substitutions within the catalytic site of IN. The R263K dolutegravir (DTG) INSTI resistance substitution, however, is located in the C-terminus of IN and has an unknown resistance mechanism. The C-terminus is post-translationally modified by the acetylation of three lysine residues by the histone acetyltransferase enzyme (HAT) p300. We hypothesized that the R263K substitution interferes with some function of IN through dysregulation of the acetylation of nearby residues.

Results: Treatment of cells with HAT inhibitors (HATi) after infection resulted in a decrease in the 50% inhibitory constant (IC_{50}) for DTG for NL4.3 wild-type ($NL4.3_{WT}$) but not $NL4.3_{R263K}$. However, no change in IC_{50} was seen for RAL or Lamivudine and experiments are currently underway with the novel INSTIs Cabotegravir and Bictegravir. $NL4.3_{WT}$ and $NL4.3_{R263K}$ produced in the presence of HATi or histone deacetylase (HDAC) inhibitors (HDACi) displayed different parameters over the course of infection. HDACi reduced the peak of replication for $NL4.3_{WT}$ but not $NL4.3_{R263K}$, whereas HATi had no effect on $NL4.3_{WT}$ but greatly enhanced the peak replication for $NL4.3_{R263K}$. Using co-immunoprecipitation, we were also able to show that IN_{R263K} binds with a higher affinity to KAP1 (a component of the HDACI complex) as compared to IN_{WT}.

Significance: This is, to our knowledge, the first report of the influence of post-translational modifications on HIV drug resistance. Both the replication and resistance to DTG of $NL4.3_{WT}$ and $NL4.3_{R263K}$ are differentially affected by acetylation, likely through altered interactions with the HDACI complex. Many "shock and kill" strategies to eradicate HIV employ HDACi to reactivate latent HIV; however our results suggest that some drug resistant viruses may differentially respond to HDACi, which may complicate the advancement of this concept.

BS2.03

A heterologous activator vector (ACT-VEC) induces HIV-1 latency reversal in human CD4+ T cells

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Background: The existence of transcriptionally silent HIV-1 within cell reservoirs represents a substantial roadblock to a viable cure. Therapeutics designed to eliminate latent virus have thus far failed, and will require a bold and innovative approach. We have designed an activator vector vaccine (ACT-VEC), using virus like particles (VLPs) to target the resting CD4 T cell reservoir, and induce HIV latency reversal. Here we describe data from our *in vitro* latency reversal studies using ACT-VEC stimulated human PBMC.

Methods: Nine HIV^+ volunteers, at acute stage of infection, were recruited and their lymphocytes used for *in vitro* studies. DCs were pulsed with ACT-VEC before co-incubation with autologous CD4+ T cells. T cell activation

was determined by IFN-g ELISpot and Flow cytometry. Viral latency reversal was measured by qRT-PCR and Illumina sequencing. ACT-VEC latency reversal was compared to Flu, Tetanus and CMV (FTC), PMA/Ionomycin, a host of clinically relevant latency reversal agents (LRAs) (Bryostatin, Romidepsin, Panabinostat, Vorinostat) as well as TLR ligands.

Results: Here we show, ACT-VEC is immuno-stimulatory, but less so than FTC and PMA/Ionomycin. Interestingly, ACT-VEC is a significantly stronger LRA than either of these control stimuli, with more viral RNA detected in culture supernatants. Furthermore, ACT-VEC demonstrated to be a superior LRA to clinically relevant 1-drug and 2-drug pharmacologics. Finally, we demonstrate that ACT-VEC mediated immunogenicity and latency reversal can be augmented when used in the presence of TLR1/2, 5, 2/6 and 7/8.

Conclusion: Here we show that ACT-VEC latency reversal is a safe vaccine platform. We provide evidence that HIV preferentially establishes a latent reservoir within HIV-specific CD4 T cells and that ACT-VEC is a more robust LRA compared to PMA/Ionomycin and other clinically relevant single and 2-drug latency reversal regimens. In conclusion ACT-VEC signifies a promising "Shock" therapy, to purge the latent viral reservoir and facilitate cure.

BS2.04

Assessment of double negative T-cells and HIV reservoirs within the lungs of ART-treated HIV-infected adults

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Introduction: Both cellular and anatomical reservoirs of HIV remain the primary barrier to viral eradication. The lungs constitute relatively unexplored anatomical reservoirs. Meanwhile, double negative (DN) CD4-CD8- T-cells have been recently described as cellular HIV reservoirs. Consequently, we assessed DN cells in the lungs *versus* the peripheral blood of ART-treated HIV-infected individuals.

Methods: Fifteen successfully ART-treated individuals (suppressed viral load for ≥ 3 years and CD4 count ≥ 350 cells/mm^3) without any active respiratory symptoms were recruited. Bronchoscopies were performed to obtain bronchoalveolar lavage (BAL) fluid, and matched peripheral blood samples were collected. T-cell subsets were characterized by flow cytometry and the frequency of infected cells was measured by ultrasensitive PCR.

Results: Participants with detectable levels of total HIV DNA in both PBMCs and BAL cell pellets displayed greater frequencies of infected cells in the lung compared to blood (p=0.04). A substantial increase in frequency of effector memory and a substantial decrease in naïve CD4 and CD8 T-cells were observed in lungs *vs.* blood (p<0.001). Interestingly, a massive increase in CD3+CD4-CD8α-CD8β- DN T-cells (23.7±17.6% *vs.* 8.6±4.3%, p=0.007) and CD3+CD4-CD8-TCRαβ-TCRγδ- (14.8±10.6% *vs.* 4±2.4%, p=0.007) was observed in BAL *vs.* blood. Furthermore, higher levels of immune activation (HLA-DR+) were observed in pulmonary DN T-cells compared to blood (p<0.02). Finally, pulmonary DN T-cells were characterized by decreased expressions of immunosuppressive ectonucleotidases (CD39+CD73+, p=0.005) and marker of recent thymus migration (CD31+, p=0.03) when compared to their circulating counterparts. No changes were noted in CD28-CD57+ senescent and CXCR3+ (lung epithelium homing) DN T-cells within the lungs vs blood.

Conclusion: Higher frequencies of activated DN T-cells were observed in the lungs *vs* blood of successfully ART-treated individuals. This observation, together with a higher frequency of infected cells in this compartment, suggests that the lungs may serve as a preferential anatomical reservoir for HIV during ART.

BS2.05

The Primer Binding Site as a Universal Target of CRISPR/Cas9 to Inactivate HIV-1

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One approach to cure HIV infection is to inactivate and excise the proviral DNA in the infected cells. Our lab and other groups have shown that the gene editing system, CRISPR/Cas9, is able to specifically cleave HIV DNA and cause lethal mutations in viral genome as well as excision of viral DNA fragments. One challenge to apply CRISPR/Cas9 in clinical settings is the extremely high diversity of HIV sequences, which makes it tremendously difficult to design guide RNAs that are able to effectively target and inactivate all HIV in a specific patient. In spite of the great heterogeneity of HIV sequences, there is one region that is conserved in all HIV proviral DNA, which is the primer binding site that is complementary to the first 18 nucleotides of cellular tRNALys.3 and serves as the initiation site of viral reverse transcription. We hypothesize that gRNAs targeting the primer binding site should be able to, together with Cas9, impair the majority, if not all, HIV strains. To test this hypothesis, we have designed three gRNAs that target the primer binding site and examined the replication of HIV-1 in T cell lines that stably express Cas9 and these gRNAs. The

results showed strong suppression of viral replication as a result of indels in the primer binding site that were caused by Cas9/gRNA. Therefore, the primer binding site should be considered as a valuable target in the design of Cas9/gRNA to ablate HIV infection.

BS2.06

Mechanisms of HIV Persistence in Lymph Nodes After Prolonged Antiretroviral Therapy

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Introduction: HIV may persist through residual replication in follicular helper T cells (Tfh) in lymph nodes during ART. However, no study has assessed HIV persistence in this compartment after prolonged therapy. We measured the relative contributions of residual transcription and latency in lymph nodes from virally suppressed individuals on long-term ART.

Methods: Inguinal lymph nodes (LN) and peripheral blood from 6 individuals on suppressive ART for a period ranging between 8 and 14 years (median=12 years) were obtained. From LN, Tfh-enriched cells ($CD3^+CD8^-CD45RA^-PD\text{-}1^+$), non-Tfh cells ($CD3^+CD8^-CD45RA^-PD\text{-}1^-$) and naïve cells ($CD3^+CD8^-CD45RA^+$) were sorted by flow cytometry. The frequency of cells harbouring integrated HIV DNA was measured by ultra-sensitive alu-PCR in the sorted subsets. The relative contributions of residual transcription and latency were measured by the *Tat/Rev Induced Limiting Dilution Assay (TILDA)*.

Results: Germinal center Tfh ($PD1^{high}CXCR5^{high}$) were detected at very low frequency in the LN from these individuals on long-term ART (mean = 0.68% of total CD4). The frequency of HIV infected cells was slightly higher in the Tfh-enriched subset compared to non-Tfh cells and naïve cells (2396, 1384 and 718 HIV DNA copies/million cells, respectively). However, cells producing tat/rev RNA after stimulation were rarely detected in the Tfh-enriched subset. Therefore, Tfh-enriched cells had a modest contribution (12.2%) to the overall pool of cells harbouring inducible virus. Finally, the relative contribution of latency was constantly greater than that of residual transcription in LN from all participants (mean of 89.7% VS 10.3%, respectively).

Conclusion: In individuals on long-term ART, Tfh cells were rare and not enriched in inducible HIV when compared to non-Tfh cells. More importantly, our results suggest that HIV latency, rather than residual viral replication, may be the major mechanism by which HIV persists in lymph nodes after prolonged ART and that most inducible genomes persist in non-Tfh cells.

Clinical Sciences: Co-infections

Sciences cliniques : Coinfections

CS2.01

The association of HIV-related factors and the severity of liver fibrosis measured by transient elastography (FibroScan®) in an HIV/HCV co-infected population

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Objectives: We sought to determine whether HCV/HIV co-infected patients on antiretroviral therapy (ART) are at greater risk of liver fibrosis progression than HCV mono-infected patients and whether significant fibrosis is associated with HIV-related factors.

Methods: HCV+ and HCV/HIV+ adults referred for TE were recruited from 2013-2015. Significant fibrosis ($F \geq 2$) was defined as TE score $\geq$7.1 kPa for HCV mono-infected and $\geq$7.2 kPa for co-infected patients. Clinical and demographic data were collected by patient interview and HIV/ART-related factors from the BC Centre for Excellence in HIV/AIDS Drug Treatment Program. Multivariable logistic regression modelling was selected for this dataset.

Results: The cohort comprised 295 HCV-infected adults: 231 (78%) male, median age 52 years, median HCV duration 12 years; 138 (47%) had $F \geq 2$ by TE. Among the 195 (66%) HCV/HIV co-infected, 97% were on ART, 87% had a viral load <40 copies/mL, median HIV duration was 15 years, median CD4 nadir was 130 cells/mm^3, and median current CD4 was 540 cells/mm^3. Co-infection was not associated with a greater risk of fibrosis (adjusted odds ratio [AOR] 1.02, 95% confidence interval [CI] 0.58-1.78), but longer duration of HCV was (AOR 1.05 per year, 95% CI 1.02-1.08). In the HCV/HIV+ group, previous AIDS-defining illness and HCV duration were independently associated with fibrosis (Table 1).

Conclusion: ART-treated HIV/HCV co-infected patients were not more likely to have fibrosis by TE than HCV mono-infected patients in this cohort. Fibrosis was associated with longer HCV duration and advanced HIV disease, highlighting the importance of early, comprehensive treatment.

Table 1. Logistic modeling of the probability of a TE score >F2 based on HIV related factors for the HIV/HCV+ population (n = 195)

Variable	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Age (per 10 years)	1.40 (0.99-1.95)	
AIDS defining illness (Yes vs. no)	2.27 (1.19-4.33)*	2.16 (1.10-4.23)*
CD4 nadir (per 100 cells/mm3)	0.75 (0.61-0.93)*	
Duration of HCV (per year)	1.06 (1.02-1.09)*	1.05 (1.02-1.09)*
Duration of HIV (per year)	1.06 (1.02-1.11)*	
Duration of ARV use (per year)	1.08 (1.02-1.14)*	

*$p < 0.05$

CS2.02

C-ISLE: Elbasvir /Grazoprevir plus Sofosbuvir in Treatment-naïve and Treatment-experienced HCV GT3 Cirrhotic Patients Treated for 8, 12 or 16 weeks

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Background and Purpose: Therapies for hepatitis C virus (HCV) genotype 3 infection (GT3) have been limited in treatment-experienced patients with cirrhosis. C-ISLE (PN083) was developed as a regional study of HCV GT3 compensated cirrhotic patients treated for 8-16 weeks with elbasvir/grazoprevir (EBR/GZR) + sofosbuvir (SOF) ± ribavirin (RBV).

Methods: Compensated cirrhotic patients with HCV GT3 infection were randomized to 1 of 5 treatment arms. Treatment-naïve patients were randomized to EBR/GZR + SOF + RBV for 8 weeks or EBR/GZR + SOF for 12 weeks. P/RBV treatment-experienced were randomized to EBR/GZR + SOF ± RBV for 12 weeks or EBR/GZR + SOF for 16 weeks. Presence of cirrhosis was confirmed by either liver biopsy F4 (16%) or FibroScan (84%; mean 25.44 range 12.6-69.1 kPa). The primary endpoint was HCV RNA <15 IU/mL 12 weeks after treatment (SVR12).

Results: Rates of SVR12 were >90% in all treatment arms (Table). Two patients receiving treatment for 8 weeks relapsed; however, there were no patients with virologic failure in the 12-week treatment arms, regardless of treatment history or addition of RBV. NS5A resistance-associated substitutions (RASs) were present at baseline in 51% of patients (n = 49), including 4 patients with Y93H. SVR12 was achieved by 98% (48/49) of patients with baseline NS5A RASs and 98% (46/47) of patients without baseline NS5A RASs. Five patients reported serious adverse events (cellulitis; pneumonia; chest pain; opiate overdose; transient creatinine clearance decrease).

Conclusion: High rates of SVR12 were achieved in HCV GT3-infected cirrhotic patients, regardless of prior treatment history.

	Treatment-naive	Treatment-naive	Treatment-experienced	Treatment-experienced	Treatment-experienced
	EBR/GZR + SOF + RBV 8 weeks	EBR/GZR + SOF 12 weeks	EBR/GZR + SOF 12 weeks	EBR/GZR + SOF + RBV 12 weeks	EBR/GZR + SOF 16 weeks
SVR12	91% (21/23)	96% (23/24)	100% (17/17)	94% (17/18)	94% (17/18)
Relapse, n	2	0	0	0	0
Nonvirologic failure, n	0	1	0	1	1

CS2.03

Direct acting antivirals uptake disparities in vulnerable HIV-Hepatitis C coinfected populations in Canada

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Background: Direct acting antivirals (DAAs) have revolutionized hepatitis C virus (HCV) treatment, giving hope that HCV can be eliminated. However, for DAAs to have a population-level impact on the burden of HCV, treatment uptake needs to be expanded considerably. Historically, HCV treatment rates among HIV-HCV coinfected individuals have been low, particularly among people who inject drugs (PWID). We investigated second-generation DAA treatment uptake among key HIV-HCV co-infected populations in Canada.

Methods: The Canadian HIV/HCV Co-Infection Cohort Study prospectively follows more than 1650 participants from 19 centers. We evaluated second-generation DAA initiation rates among cohort participants who were HCV RNA+ as of November 20th 2013. Participants were followed until DAA initiation or until either the end of the

study (December 31st 2015), lost to follow-up, withdrew or died. A multivariate Cox proportional hazards model was used to predict the two-year probability of initiating second-generation DAAs for 8 population profiles; a combinations of sex, Aboriginal ethnicity and active PWID. The model was adjusted for *a priori* predictors of treatment initiation.

Results: Among 812 HCV RNA+ participants, 195 initiated second-generation DAAs (181/195 interferon-free DAA regimens). Overall second-generation DAA uptake was markedly lower among Aboriginals, women and active PWID. Predicted probability of initiating DAAs varied among the 8 population profiles. For example, the probability of initiating DAAs for a female, Aboriginal, PWID, was 3% (95% CI: 1- 6) while the probability of initiating treatment for a male, heterosexual, non-Aboriginal, non-PWID was 29% (95% CI: 26- 33), 10 times higher.

Conclusion: DAAs have generated enthusiasm that HCV can be eradicated. While treatment uptake has increased with the availability of all oral DAAs, marginalized populations, are still failing to access treatment. Targeted strategies to expand treatment to these groups are needed to mitigate future inequalities, reduce HCV incidence and the overall burden of chronic liver disease.

CS2.04

Increased rate of C Trachomatis infection after being prescribed PrEP

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Background: Increasing use of HIV pre-exposure prophylaxis (PrEP) using Truvada raises concerns that resulting decreased condom use could increase sexually transmitted infections (STIs). PrEP has been offered to Men who have Sex with Men (MSM) at Clinique l'Actuel (Montreal) since 2011; as of November 2016, 1366 MSM have initiated PrEP (85% continuous, 15% intermittent regimen). PrEP may lead to a shift away from condoms as a prevention strategy, or alternatively offers a new prevention strategy for those who already engage in condomless sex.

Methods: To assess whether PrEP increases condom-preventable STIs, we enrolled patients with >1 year of follow-up before and after PrEP prescription. 133 patients were included. Patients were seen every 3 months for a physician evaluation, behavioural questionnaire, and full STI screening. The proportion of individuals infected with Chlamydia Trachomatis (CT) and Neisseria Gonorrhoea (NG) were compared before and after exposure to PrEP using two-sided chi-squared test.

Results: The proportion of individuals infected with anal, oral or urethral CT in the year prior to PrEP were 10, 2, 3%, respectively and in the year post PrEP were 20, 2, 11% in the exposure period (p-value: 0.00, 1.00, 0.01, respectively). The proportion of individuals infected with CT at any site pre and post PrEP were 13 and 26% (p=0.01). The proportion of individuals infected with anal, oral or urethral NG in the year prior to PrEP were 9, 8 and 8% respectively and in the year after PrEP were 14, 11, 6% (p-value: 0.24, 0.29, 0.62, respectively). The proportion of individuals infected with NG pre- and post-PrEP were 17 and 26% (p=0.07) respectively.

Conclusion: Increased rates of CT post-PrEP suggest a shift away from condom use. Increased rates of asymptomatic STIs (i.e. CT, but not NG) post PrEP warrant further study.

CS2.05

Prevalence and predictors of occult cirrhosis diagnosed by transient elastography in 1,658 HIV infected patients

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Background: People living with HIV are at high risk for liver cirrhosis and related death. Diagnosis of compensated cirrhosis at preclinical stage is challenging due to lack of any physical, laboratory and imaging findings. We evaluated prevalence and predictors of preclinical compensated cirrhosis, defined as occult cirrhosis (OC), diagnosed by transient elastography (TE).

Methods: Unselected HIV infected patients underwent a TE examination as a part of a routine screening program for liver disease. Patients were classified as: 1) OC (TE ≥13kPa and absence of any clinical sign of cirrhosis, including no thrombocytopenia, nor signs of advanced liver disease on ultrasound); 2) clinically evident compensated cirrhosis (TE ≥13kPa with any of the previous signs); 3) non-cirrhotic patients (TE <13kPa). Predictors of OC were investigated through multivariable logistic regression analysis.

Results: 1,658 HIV-infected patients (mean age 50.3±10.6 years, 77.3% men, mean CD4 593±266, 90% on antiretrovirals) were included. Coinfection with HCV was found in 35% of cases. Overall, liver cirrhosis was present in 11.1% of cases. OC represented 5.1% of the whole patient population and 41.2% of cirrhotic patients. In multivariable analysis, OC was independently associated with higher BMI, while black ethnicity and female gender were found to be protective (see Table).

Conclusions: OC is a frequent clinical entity in HIV infected patients. Its independence from HCV coinfection suggest the contribution of emerging etiologies of liver disease, such as fatty liver. Screening of HIV infected patients by TE may help prompt initiation of appropriate surveillance and interventions for an otherwise unrecognized condition.

Multivariable analysis of predictors of occult cirrhosis

Variable	Adjusted OR (95% CI)	p
Female sex	0.23 (0.09-0.59)	0.002
Black non-Hispanic ethnicity	0.12 (0.026-0.57)	0.008
Duration of HIV infection (per year)	1.05 (0.99-1.11)	0.09
BMI (per Kg/m2)	1.02 (1.00-1.04)	0.019
HCV	1.34 (0.56-3.20)	0.52

CS2.06

The impact of sustained virological response to HCV on long term risk of decompensated cirrhosis: The BC Hepatitis Testers Cohort

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Objectives: We evaluated the impact of sustained virological response (SVR) on long term risk of hepatic decompensation among individuals treated for HCV in a large population based cohort in Canada.

Methods: The BC Hepatitis Testers Cohort includes ~1.5 million individuals tested for HCV, HIV or diagnosed with HBV or active TB between 1990–2013, linked with data on medical visits, hospitalizations, cancers, prescription drugs and mortality. Patients who were prescribed interferon-based HCV treatments were followed from the end of last treatment to occurrence of decompensated cirrhosis(DC), death or December 31, 2012. We examined DC risk among those who did and did not achieve SVR using cumulative incidence function and multivariable competing risk regression models.

Results: Of 7940 eligible individuals who initiated treatment, 4583(58%) achieved SVR(DC=70) and 3357(42%) did not(DC=368). Each group was followed for a median of 5.6 yr[IQR: 3.1-8.1]. Cumulative incidence was 0.98% and 6.55% at 5 years and 2.96% and 17.03% at 10 years in the SVR and no-SVR groups, respectively. In the multivariable model, SVR was associated with reduced DC risk (hazard ratio (HR)=0.17, 95%CI:0.14-0.23), while cirrhosis (HR=2.81, 95%CI:2.03-3.89), older age (50-59 yr: HR=2.54, 95%CI:2.04-3.16; 60+ yr: HR=3.32, 95%CI:2.43-4.53 compared to ≤49 yr), diabetes (HR= 1.69, 95%CI:1.32-2.15), and presence of an Elixhauser comorbidity (HR=1.42, 95%CI:1.16-1.75) at the time of treatment were associated with higher DC risk. In those with SVR, cirrhosis (HR=2.97, 95%CI: 1.14-7.74), older age(50-59 yr: HR=4.04, 95%CI: 2.33-7.01); 60+ yr: HR=6.10, 95%CI: 2.91-12.76) compared to ≤49 yr), diabetes (HR=1.85, 95%CI: 0.96-3.56) and being male (HR=2.11, 95%CI: 1.17-3.82) were associated with higher DC risk.

Conclusion: SVR substantially reduces but does not eliminate the risk of hepatic decompensation, which is higher among males, those with cirrhosis, diabetes and older age at treatment initiation. To substantially reduce the burden of end stage liver disease early treatment is warranted.

Social Sciences: Impacts of HIV Criminalization

Sciences sociales : Effets de la criminalisation concernant le VIH

SS3.01

The Criminalization of HIV Non-Disclosure & Exposure: Impacts of Legal Violence on the Lives of People Living with HIV

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This presentation elaborates initial findings from an ongoing qualitative research project examining the lived experiences of people who have been criminally charged in relation to HIV non-disclosure and/or exposure in Canada, a country well known for its high rates of criminalization towards HIV. This project has been exploring the material outcomes of being institutionally marked as a 'criminal' and a 'risk to public safety' through mobilizing a critically engaged ethnographic approach that is grounded in the experiences of people directly targeted by the application of the law. This project centers the voices of people who have experienced these circumstances first-hand. As a result, outcomes provide critical insight into the forms of violence and discrimination that are made possible through how the law is currently applied. Findings from this project outline the lives of people who have experienced the most punitive aspects of the state punishment apparatus, including those who have faced aggravated charges, long sentences, incarceration in segregation units, and ongoing life-long surveillance via sex offender registration. People in this study also described a range of informal forms of violence that threaten their daily security, including sensationalistic media coverage labeling people as violent predators; as well as the inability of current social services to meet the complex supports required to address the trauma and discrimination resulting from being accused. This study elaborates the increasing precarity facing HIV-positive people, who, in this context must now live their lives in a negative relation to the law and who are subject to myriad forms of violence resulting from the law itself. Finally, this project asks what harshly punishing HIV-positive people with violent and punitive sanctions in these cases says about contemporary practices of punishment in Canadian society and addresses how actors working in the HIV sector can respond to this growing social problem.

SS3.02

'Through our own eyes' – Photo-elicitation of Gender, Stigma, Disclosure and the Impact of Criminalization of HIV

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Background: Canada has one of the strictest legal thresholds for the criminalization of HIV non-disclosure and has produced the second highest number of convictions for HIV non-disclosure. Despite frequently being represented as a law to 'protect' women, there is very limited understanding how the criminalization of HIV non-disclosure shapes the negotiation of sexuality and navigation of stigma among women living with HIV (WLWH).

Methods: We used arts-based methodology in a participatory action research project to explore the gendered role of criminalization of HIV non-disclosure. Participants for this pilot project were recruited in the context of existing peer support groups and all photovoice group meetings were co-facilitated by Peer Research Associates that reflected the strong representation of Indigenous women and woman refugees. Participants were given cameras and shared their photographs and narratives with the group to contextualize their experiences and to identify common themes.

Results: The results of this exploratory community-based photovoice study provided rich visual and narrative descriptions of the gendered reality of the criminalization of HIV non-disclosure. Many WLWH were unfamiliar with the exact legal context regarding HIV non-disclosure this contributed to profound distress over HIV status and intimate relationships. Common themes in participants' images and narratives include, fear of prosecution, social isolation, shame, trauma, and feeling trapped. However, women also depicted resilience in their care networks.

Conclusions: The findings of this exploratory community-based photovoice project elucidate how the criminalization of HIV non-disclosure exacerbates HIV related stigma and the risk for interpersonal violence for WLWH. Aligned with recommendations from international policy bodies, including the WHO, UNAIDS, and Global Commission on HIV and the Law, findings demonstrate the negative impacts of regulating HIV-prevention through the use of criminal law for WLWH. WLWH voiced that they are not criminals and want to see these laws redressed.

SS3.03

What do women living with HIV know and not know about the criminalization HIV non-disclosure in Canada? Insights from a participatory arts-based study

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Background: In Canada, people living with HIV must disclose their HIV status to partners before sex that poses a "realistic possibility" of HIV transmission, or risk a criminal charge of aggravated sexual assault. Little is known, however, about what women living with HIV (WLWH) know about HIV non-disclosure laws or how the law may affect them.

Methods: The Women, Art, and Criminalization of HIV non-disclosure (WATCH) study is a participatory arts-based study exploring the impact of HIV non-disclosure laws on WLWH. Peer Research Associates co-facilitated four Body Mapping Workshops with 30 WLWH in British Columbia, Saskatchewan, and Ontario. Prior to participating in the workshops, we provided women information about HIV non-disclosure law and opportunity to ask clarifying questions. During the workshops, however, we found that participants required additional information about the law to fully and ethically engage in the body mapping process. This required us to adapt our methodological process to incorporate a facilitated and interactive education session on the criminalization of HIV non-disclosure — including real-time access to a legal expert for legal information.

Results: Emerging from the education sessions were questions highlighting women's concerns including the legal implications of not disclosing HIV status in the context of rape or when no HIV transmission occurs, and a lack of clarity about the statute of limitations of the law. Women's questions varied by their lived experiences and access to services and support, suggesting a gap between knowledge of the law, understanding of its potential impact on women's lives, and access to legal education and support.

Conclusion: WLWH have limited knowledge and understanding about the HIV non-disclosure law in Canada. Findings highlight the need for health, social, and legal care providers to provide WLWH with accurate information in supportive and safe environments, and that addresses disclosure concerns most relevant to women.

SS3.04

The influence of the criminalization of HIV non-disclosure on intentional sexual inactivity among women living with HIV in Canada

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Background: People with HIV in Canada must legally disclose their HIV-status to sexual partners unless they use a condom *and* have a viral load <1500 copies/mL, or risk a charge of aggravated sexual assault. We assessed the influence of HIV non-disclosure laws on intentional sexual inactivity among women living with HIV (WLWH).

Methods: We analysed cross-sectional wave 2 survey data of WLWH enrolled in the peer-led Canadian HIV Women's Sexual and Reproductive Health Cohort Study (CHIWOS). We assessed the prevalence of partnered sexual inactivity (i.e., no consensual sex (oral or penetrative) in prior six months), and prevalence of and reasons for intentional sexual abstinence.

Results: At time of analysis, 585 of 1425 CHIWOS participants were included. Median age was 45 (IQR: 37-52), 86% were receiving ART, and 85% reported an undetectable viral load (<40 copies/mL). Overall, 55% of participants were sexually inactive, of whom 78% reported that abstinence was intentional. Reasons for intentional sexual abstinence included general worries about HIV disclosure (35%) and HIV non-disclosure laws specifically (23%). Additional (non-mutually exclusive) reasons included: no sexual partner (58%), satisfied without sex (38%), worries about transmitting HIV (24%) or contracting STIs (16%), reduced/absent sexual desire (30%) or sexual arousal (17%), and partner's reduced/absent sexual desire (3%).

Conclusions: Despite good HIV clinical outcomes, over half of WLWH were sexually inactive, most of whom reported intentional sexual abstinence. Over one-third cited concerns about HIV disclosure and the law as primary influencers of intentional abstinence. Laws criminalizing HIV non-disclosure have been viewed, pursued, and defended as a means of protecting the sexual well-being of women. However, some WLWH protect *themselves* from the law and against legal and social expectations of HIV disclosure by intentionally abstaining from sex. Findings underscore the need to de-stigmatize HIV, support safe disclosure, and re-appropriate the sexual rights of WLWH.

SS3.05

Awareness, understanding and perceived healthcare impacts of HIV non-disclosure case law among women living with HIV in Canada

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Background: In 2012, the Supreme Court of Canada (SCC) ruled that people living with HIV must disclose their HIV-serostatus to sexual partners unless they use a condom *and* have a viral load <1500 copies/mL. Awareness of this ruling remains undefined among women living with HIV (WLWH).

Methods: We analysed wave 2 cross-sectional data (June 2015-January 2016) from the peer-led Canadian HIV Women's Sexual and Reproductive Health Cohort Study. Participants were asked if they were aware of the 2012 SCC ruling. The law was then defined and those reporting awareness were asked how similar their understanding was to the provided definition. Existing and preferred sources of information about the law, and perceived impacts, were also assessed. Multivariable logistic regression identified correlates of ruling awareness.

Results: 584 of 1425 CHIWOS participants were included. Median age was 45 (IQR: 37-52), and 84% reported an undetectable viral load. Overall, 74% were aware of the ruling, while 204 (35%) had accurate understanding of the legal obligation to disclose. Among participants aware (n=431), 36% had discussed disclosure and the law with healthcare providers. Regular HIV physicians (61%), peer workers (25%), and community workers (25%) were the preferred providers to discuss disclosure laws. Most participants (65%) believed disclosure laws might affect the type of information WLWH would share with providers. Participation in community HIV work (AOR:1.74, 95%CI:1.10-2.76) was positively associated with ruling awareness, whereas experience of violence in adulthood (AOR:0.39, 95%CI:0.21-0.70), self-reporting a detectable/unknown viral load (AOR:0.52, 95%CI:0.30-0.90) and lack of awareness of HIV prevention benefits of ART (AOR:0.59, 95%CI:0.38-0.91) were negatively associated with awareness.

Conclusions: Awareness and understanding of HIV non-disclosure law is suboptimal among WLWH. Women less engaged with HIV care and community were least likely to be aware of the law. Efforts are needed to build knowledge and support around disclosure and the law.

SS3.06

Governing HIV/AIDS in a Neoliberal Age: The 'end of exceptionalism', criminalization and policy contradictions

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HIV/AIDS is marked by a series of new governance challenges, including (1) an emerging 'end of exceptionalism' characterized by the integration of HIV/AIDS into a broader STBBI response, and (2) continued criminalization of HIV non-disclosure. In this presentation, we draw from an upcoming edited collection to explore the tensions between, and reasons for, these simultaneous efforts to criminalize yet 'integrate' HIV, and to discuss their implications for HIV/AIDS governance in Canada. First we assess recent efforts to integrate HIV responses with other STBBIs. HIV was initially considered uniquely different from other communicable diseases; the resulting 'AIDS exceptionalism' produced policies and practices including anonymous testing, stand-alone AIDS programs and services, and concerted activist efforts to shield the HIV/AIDS response from traditional top-down public health interventions. Now, government funders are promoting an emerging model of service integration. This model, which collapses HIV into a broader STBBI response, will ostensibly provide better continuity of care, promote intersectoral collaboration, and create efficiencies by reducing program duplication. However, in a move epitomizing the contradictory nature of neoliberal governance, the continued criminalization of HIV non-disclosure reinforces HIV exceptionalism. We therefore examine how and why HIV exceptionalism is being upheld by one part of the federal system (the federal judiciary) at the same time that another component of that system (the federal bureaucracy) is seeking an end to HIV exceptionalism; we argue that the coexistence of these efforts indicates the need to theorize HIV/AIDS governance as at once more complex and less coherent than is often suggested in public policy literature.

Multidisciplinary: HIV Prevention

Multidisciplinaire : Prévention du VIH

MD3.01

POPPEE: Purchasing Online Pre-Exposure Prophylaxis (PrEP) Pills to Evaluate Equivalence

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Introduction: PrEP with oral tenofovir disoproxil fumarate and emtricitabine (TDF/FTC) is highly effective at preventing HIV. Co-formulated TDF/FTC is patent-protected in Canada, but is prohibitively expensive and not publicly reimbursed for PrEP in most Canadian jurisdictions. Highly motivated individuals are thus purchasing foreign generic TDF/FTC through online pharmacies, but product authenticity remains uncertain.

Methods: We purchased TDF/FTC from websites selling to Canadian addresses. We evaluated websites, product packaging and tablets qualitatively for trustworthiness. Samples were evaluated against U.S. Pharmacopeia (USP) standards of TDF and FTC for content uniformity and dissolution using high performance liquid chromatography, and tablet breaking force.

Results: Nine bottles of TDF/FTC representing three different generic manufacturers were procured from four online pharmacies. Websites displayed inconsistent details regarding manufacturer, brand name/generic status, country of origin, price, prescription requirements, and payment security. Security features were inconsistent, with one bottle seal opened prior to arrival. Four samples, representing three generic and the brand-name product, underwent quantitative analysis. Content uniformity analysis demonstrated that all were within the USP drug content range of 85-115% of the labeled claim, with TDF means (SD) of 96.6% (1.3%), 98.4% (0.9%), 97.2% (0.4%) and 96.8% (1.2%) and FTC means (SD) of 98.8% (1.1%), 97.9% (1.9%), 98.7% (0.4%) and 97.6% (1.2%) for generics #1, 2, 3 and brand-name respectively. Dissolution testing showed that 95%, 100%, 99% and 98% of TDF and 98%, 99%, 101% and 98% of FTC were released into solution at 30 minutes for the four products respectively. Hardness of generic #1 was lower than the other products, but all met the industry standard of >4 kiloponds.

Conclusions: Although Canadian law does not permit ordering of medications for direct delivery to Canada, and although trustworthiness of online vendors appeared vari-

able, the three generic and brand name formulations of TDF/FTC we tested met USP standards.

MD3.02

Estimating the number of gay, bisexual and other men who have sex with men (gbMSM) eligible for HIV pre-exposure prophylaxis (PrEP) in Ontario

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Background: Estimating PrEP demand based on forthcoming Canadian guidelines may inform resource allocation. Grade 1A recommendations for PrEP among gbMSM are condomless anal sex in the past 6 months PLUS any of: a) infectious syphilis or rectal gonorrhea/chlamydia in the past 12 months; b) sexual relationship with an HIV+ partner with unsuppressed viremia; c) recurrent post-exposure prophylaxis (PEP) use; d) score ≥11 on the HIRI-MSM risk index.

Methods: We estimated the number of Ontario gbMSM meeting each criterion in one year using data from Public Health Ontario Laboratories for reportable STIs and HIV testing; Hassle Free Clinic for anatomic site-specific gonorrhea/chlamydia cases; the OHTN Cohort Study for sexual behaviour and viral load; the PREPARATORY-2 study for sexual behaviour; and two Toronto PEP clinics. For each criterion, we further ascertained the number needed to treat (NNT) to prevent one HIV infection assuming PrEP effectiveness=86-100%, using Ontario HIV incidence data for criterion b) and published literature for all others; and the number of potential infections prevented. Finally, we anticipated total person-years of PrEP demand over 10 years, accounting for estimated years of risk, 55% uptake (from PREPARATORY-2), and average duration of use (from US demonstration projects).

Results: Findings are summarized in the Table. If criteria are mutually independent, up to 623 infections could be averted in one year, assuming optimal uptake and effectiveness.

Conclusions: Large numbers of gbMSM may meet criteria for PrEP. The potential number of infections averted in one year rivals the annual number of incident infections in gbMSM.

	Criterion	Number eligible in 1 year	NNT if effectiveness=86%	NNT if effectiveness=100%	Potential infections prevented in 1 year (100% uptake & effectiveness)	Anticipated person-years of PrEP demand over 10 years
a	Infectious syphilis	504	32-41	28-35	18	2884
	Rectal gonorrhea	691-1108	16-28	14-24	79	3972-6370
	Rectal chlamydia	1202-1484	20-73	17-63	87	6878-8491
b	HIV+ partner unsuppressed	56	78	67	<1	320-321
c	Recurrent PEP use	63-252	16	14	18	363-1451
d	HIRI-MSM score ≥11	29477	81 (weighted average)	70 (weighted average)	421	168665-168838

MD3.03

Using the US Centers for Disease Control guidelines for Pre-Exposure Prophylaxis in a Canadian context: are we underestimating risks?

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Background: The High-Risk Incidence Index for Men who have Sex with Men (HIRI-MSM) was introduced by the United States Centers for Disease Control (CDC) Clinical Practice Guidelines for Pre-Exposure Prophylaxis (PrEP) in 2014. The HIRI-MSM is a tool used to inform clinical decisions about which patients should begin PrEP due to high-risk for HIV infection. Quebec issued an Interim Notice for the use of PrEP in 2013 and Health Canada approved the use of Truvada in PrEP in 2016. To date, no risk index for PrEP has been approved in Canada.

Methods: Clinique médicale l'Actuel (Montreal) has offered PrEP since 2011. We systematically collected HIRI-MSM data during consultations for PrEP from June 1 – December 1, 2016. The score ranges from 0 – 45, with all scores >=10 indicating patients who should be recommended PrEP following CDC guidelines. Data also was collected in line with Quebec recommendations, whereby MSM who engage in unprotected anal sex with partners of HIV positive/unknown status should be recommended PrEP.

Results: In total, 255 patients contributed HIRI-MSM data, with a median score of 19.0 (IQR: 13– 27). 33 patients (13%) scored below 10, but presented with considerable risks including: HIV-positive partner with detectable viral load (n=1), unprotected anal sex with multiple partners of unknown HIV status (n=12) and reported a median of 10

sex partners within 12 months (IQR: 4 – 13.5). MSM scoring below 10 were older (mean 42.3, 95%CI: 39.4–46.1) as compared with those scoring from 10-45 (mean 35.1, 95%CI: 33.8–36.5).

Conclusion: Inconsistent information between the HIRI-MSM and the Quebec recommendations sends mixed messages regarding which patients should receive PrEP. The HIRI-MSM may lead to underestimation of risk and is subject to age bias. Further evidence is needed for the creation of an adapted risk assessment tool for a Quebecois/ Canadian context.

MD3.04

Population-Level Trends and Person-Level Stability Over Time in Objective and Subjective HIV Risk Measures for HIV-Negative Gay and Other Men Who Have Sex With Men

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Background: We sought to evaluate how HIV risk may change over time for gay and other men who have sex with men (MSM) at the individual- and population-level.

Methods: Longitudinal data were used from the Momentum Health Study, which enrolled MSM aged >15 years from Metro Vancouver into a prospective cohort from 02/2012-02/2016. Follow-up visits occurred every 6-months, which included self-completed behavioural surveys and optional rectal swabs for sexually transmitted infection (STI) testing. Four HIV risk outcomes were used: rectal STI diagnosis, the HIV incidence risk index (HIRI-MSM) scored at ≥10 and ≥25, and self-assessed "high" versus "low" current risk of HIV acquisition. We examined population-level temporal trends categorized into 6-month periods using generalized mixed effect modeling and person-level stability by calculating intraclass correlation coefficients (ICC).

Results: A total of 551 HIV-negative MSM contributed a median follow-up time of 2.50 years. At the population-level, there was no change over time in the proportion of MSM diagnosed with a rectal STI (mean=2%, OR=0.94, 95%CI:0.81-1.09), however, there were significant declines in the proportion of MSM who scored HIRI ≥10 (61% in late 2012 to 52% in late 2015, OR=0.92, 95%CI:0.87-0.97) and HIRI ≥25 (9% in late 2012 to 7% in late 2015, OR=0.89, 95%CI:0.81-0.97). There was no population-level change over time in proportion of MSM who reported self-assessed "high" HIV risk (mean=8%, OR=0.93, 95%CI:0.84-1.02). As an evaluation of person-level stability, the proportion of MSM who reported each risk outcome at any visit along with the respective ICC was 9.4% for rectal STIs (ICC=0.19), 79.2% for HIRI ≥10 (ICC=0.42), 23.3% for HIRI ≥25 (ICC=0.43) and 18.6% for self-assessed "high" HIV risk (ICC=0.42).

Conclusions: Despite modest to no population-level changes in HIV risk over time, these measures had poor-to-fair person-level stability over time, which has important implications for HIV prevention interventions, notably pre-exposure prophylaxis.

MD3.05

Distinct effects of the cervico-vaginal microbiota and herpes simplex type 2 infection on female genital tract immunology

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Background: Genital inflammation is a key determinant of HIV transmission, and may both increase HIV-susceptible target cells and alter epithelial integrity. Several genital conditions that increase HIV risk are more prevalent in African, Caribbean and other black (ACB) women, including bacterial vaginosis and *Herpes simplex* type-2 (HSV-2) infection. Therefore, we assessed the impact of the genital microbiota on mucosal immune cell and cytokine alterations in ACB women, and HSV-2 interactions.

Methods: Cervico-vaginal secretions and endocervical cells were collected by cytobrush and Instead Softcup, respectively. T cell and dendritic cells were assessed by flow cytometry, cytokine levels by multiplex ELISA, and the microbiota by 16S rRNA gene sequencing.

Results: The cervico-vaginal microbiota of 51 participants was composed of community state types (CSTs) showing diversity (20/51; 39%) or predominated by *Lactobacillus iners* (22/51; 42%), *L. crispatus* (7/51; 14%) or *L. gasseri* (2/51; 4%). High diversity CSTs were strongly associated with increased cervico-vaginal pro-inflammatory cytokines, but not with altered endocervical T cell subsets or dendritic cell populations. However, cervical CD4+ T cell number was associated with HSV-2 infection and a distinct cytokine profile.

Conclusions: This suggests that the genital microbiota and HSV-2 infection, both of which are very common in ACB women, may influence HIV susceptibility through independent biological mechanisms.

MD3.06

Les impacts de la PrEP à la demande sur la prise de risques d'hommes ayant des relations sexuelles avec d'autres hommes

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L'essai ANRS IPERGAY, qui offre également des dépistages réguliers et un counseling sexologique, a permis de démontrer, grâce à l'utilisation d'un placebo, que la prophylaxie pré-exposition (PrEP) prise de façon intermittente en fonction des relations sexuelles anticipées diminue les risques de transmission du VIH de façon très significative. Malgré tout, la PrEP suscite encore plusieurs inquiétudes quant à son impact sur les comportements préventifs. La présente étude vise à décrire l'impact de l'essai sur les comportements sexuels à risque de 13 hommes ayant des relations sexuelles avec d'autres hommes (HARSAH), âgés en moyenne de 37,8 ans. Ces derniers ont participé à trois entretiens individuels semi-dirigés réalisés à trois temps de mesure (moment de l'inclusion, après 6 et 18 mois). Les résultats démontrent qu'au fil des mois, un peu plus de la moitié des participants (n= 8) ont moins utilisé le condom, principalement en raison d'une diminution de leurs craintes d'avoir le VIH, et qu'à l'inverse 3 participants ont davantage eu recours aux condoms, étant plus conscients des conséquences de leurs comportements sur leur santé sexuelle et à l'aise d'en utiliser. Bien que la plupart aient mentionné avoir acquis de meilleures connaissances sur la prévention, certains après plusieurs mois ont consciemment choisi de rencontrer des partenaires plus à risque (ex. : cherchant ouvertement des relations sans condom). En contrepartie, plusieurs stratégies ont été mises en place par ceux-ci pour gérer leurs risques, dont entre autres le séropositionnement, l'augmentation du nombre de partenaires réguliers et la communication sur le sécurisexe. Pour plusieurs, l'essai a apporté aussi des bénéfices sur leur bien-être, dont un plus grand sentiment de contrôle, de sécurité et d'épanouissement sexuel. Ces données témoignent de l'importance d'offrir un suivi médical et psychosocial en complémentarité avec la PrEP, afin de favoriser l'emploi de stratégies combinées pour réduire les risques du VIH.

Basic Sciences: HIV Virology and Genetics

Sciences fondamentales : Virologie et génétique du VIH

BS3.01

Endogeneous TRIM5alpha senses HIV-1 in elite controllers

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Elite controllers (ECs) are a rare subset of HIV-1 infected subjects characterized by prolonged viremia suppression and normal $CD4^+$ T cell counts without antiretroviral therapy. Genetic factors such as specific HLA alleles partly explain the success of $CD8^+$ T cells to kill infected cells but also drives the emergence of escape mutants. Recently, it was found that approximately half of these mutants are sensitive to restriction by TRIM5alpha, suggesting the existence of a previously unknown mechanism of virus control in ECs. We hypothesize that, in addition to blocking viral replication, TRIM5alpha recognition of EC HIV-1 promotes pro-inflammatory signaling leading to an antiviral state and also stimulates HIV-1 transcription thus preventing latency establishment. We enrolled 19 patients from the Montreal Slow Progressors cohort (10 progressors and 9 ECs). We reverse-transcribed, amplified and sewed the Capsid (CA) from patient HIV-1 RNA samples into NL43-based HIV-1 plasmids, then produced VSV-G-pseudotyped chimeric viral particles, which we used to infect THP-1 and Jurkat cells previously knocked-out for TRIM5alpha or not using CRISPR/Cas9. HIV-1 vectors containing CA from ECs exhibited more CTL escape mutations (p=0.0013) and were significantly more restricted by TRIM5alpha (8.2- *vs.* 1.6-fold restriction, p=0.0240). Using RT-qPCR, we show that TRIM5alpha-sensitive HIV-1 vectors activate NF-kappaB, AP-1 and IFN-beta, and induce an antiviral state that protects cells against a second HIV-1 challenge. Finally, using J-Lat6.3 cells and pharmacological inhibitors, we demonstrate that TRIM5alpha-sensitive vectors are able to reactivate the transcription of a latent HIV-1 provirus, but only in the presence of TRIM5alpha, in a NF-kappaB-dependent fashion. In conclusion, we propose that in addition to its direct effector functions, TRIM5alpha sensing triggers an antiviral state that contributes to dampening HIV-1 and counteracts the formation of a transcriptionally latent reservoir in ECs. This study could lead to novel strategies of viral control and latency reversal.

BS3.02

HIV-1 Envelope Glycoprotein Stimulates Viral Transcription and Increases Infectivity of Progeny Virus through Manipulation of Cellular Machinery

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Introduction: During HIV infection, large amounts of progeny viral particles are produced, including infectious virus and a big proportion of the defective viral particles, both of which are critical for virus dissemination and pathogenesis in vivo. There are multiple copies of the envelope glycoprotein that are stably presented on the surface of the defective viral particles. The binding of envelope to CD4 and coreceptors is not only essential for viral entry, but also for viral infection and replication. However the impact of the virion-associated envelope glycoprotein on HIV viral transcription as well as progeny virus infectivity remain elusive. Our study investigated how virion-associated envelope (vEnv) regulate HIV transcription and progeny virus infectivity in resting CD4+ T cells and further explored the underlying mechanism.

Results and Conclusions: We first demonstrate that virion-associated envelope (vEnv) specifically activates HIV LTR promotor activity in TZMb1 cells as well as HIV-infected cells, including J-Lat 6.3 cell, resting PBMCs and PBMCs isolated from HAART-treated aviremic HIV-infected patients. This activation is through the interaction between envelope and CD4 and coreceptors (CCR5 or CXCR4) and is Tat independent. Through RNA-seq analysis, we identified more than 1,000 genes that were significantly modulated in response to vEnv treatment. Among these genes, we identified a downregulated cellular factor microRNA 181A2 (miR181A2) upon vEnv treatment, which results in increased HIV LTR histone H3 acetylation and HIV transcription. Furthermore, we found another vEnv-modulated cellular factor histone deacetylase 10 (HDAC10), whose downregulation is associated with an increased infectivity of progeny viruses. All of these findings provide evidence for the important role of vEnv playing in modulating cellular environment and facilitating HIV expression and infection in vivo.

BS3.03

Higher HIV-1 envelope sequence diversity in the female reproductive tract than in blood at acute/early phase of infection

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Background: In the majority of heterosexual HIV-1 transmission events a single infectious variant establishes a systemic infection despite the presence of a genetically diverse swarm being present in the donor. This indicates that there is a profound genetic selection of HIV-1 during the transmission process and that this so called "genetic bottleneck" results in the transmission of a single transmitted founder virus.

Methods: 80 Ugandan and Zimbabwean women were recruited during acute (0-3 months) and early (3-7 months) stages of HIV-1 infection. We analyzed the genetic diversity by 454 deep sequencing of HIV-1 isolated from endocervical swab samples and compared it to the diversity of HIV-1 isolated from blood. We were able to analyze 14 matched pairs of cervical and blood samples of the same patients at the same time points collected within three months (<90 days) and 7 matched pairs collected within seven months (<210 days) of infection.

Results: Genetic analysis of the C2-V3 env region revealed that early HIV-1 isolates within blood displayed a more homogeneous genotype (mean 2.2 clones, range 1-7), while HIV-1 clones in the female genital tract showed higher genetic diversity (mean 6 clones, range 3-16). Interestingly Env diversity slightly decreased in endocervical samples while diversity in plasma samples increased from acute to early stage of infection. We further observed that subjects with higher diversity in the blood had a greater CD4 T cell decline. No differences in Env diversity were observed between HIV-1 subtypes A, C and D.

Conclusion: We clearly show the presence of a heterogenous HIV-1 population in the female genital tract following transmission but few transmitted clones in the blood. Providing *in vivo* evidence for the existence of a genetic bottleneck from the female genital mucosa to the blood, leading to the establishment of a homogenous systemic infection.

BS3.04

HIV-1 Env antagonism of SERINC5 is conserved among variants HIV-1 strains

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HIV-1 Nef has been known to enhance the infectivity of viral particles and maintain high viral loads. The underlying mechanism has remained elusive for almost 20 years until the discovery of the antiviral activity of SERINC5. SERINC5 is a transmembrane protein that participates in incorporating serine into phospholipids to produce phosphotidylserine and sphingolipids. SERINC5 restricts HIV-1 infection by drastically impairing the infectivity of viral particles, but is antagonized by HIV-1 Nef that downregulates SERINC5 from the cell surface and prevents the incorporation of SERINC5 into viral particles. Results of this study show that the Env proteins of primary HIV-1 isolates including AD8-1 and YU-2 are able to resist ectopically expressed SERINC5 and that Env is able to counter SERINC5 without excluding SERINC5 from incorporation into viral particles. Testing a large panel of HIV-1 Env proteins from different subtypes reveals a high frequency of SERINC5-resistance, indicating that SERINC5-resistance is a conserved function in the majority of HIV-1 Env. We have also investigated why HIV-1 has evolved two mechanisms to resist SERINC5 inhibition, which involves Nef and Env, respectively. Interestingly, the virion–associated SERINC5 renders HIV-1 more sensitive to the inhibition by CCR5 inhibitor maraviroc and broadly neutralizing antibodies 4E10 and 35O22. These findings suggest that HIV-1 needs Nef to block the incorporation of SERINC5 into virions so that the functions of Env in viral particles can be protected from being affected by SERINC5.

BS3.05

The Human Immunodeficiency Virus-1 Protein Nef Interacts with Adaptor Protein-2 to Inhibit CD4+ T Cell Apoptosis

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A defining characteristic of Acquired Immune Deficiency Syndrome (AIDS) is the loss of immune function due to the steady decline in $CD4^+$ T cell counts. Here, the mechanism underlying $CD4^+$ T cell death in Human Immunodeficiency Virus-1 (HIV-1) infection was further elucidated by examining the host apoptotic pathways hijacked by the viral protein Nef. We deciphered the precise Nef interaction partners mediating apoptosis using a panel of Nef mutants unable to bind to specific host proteins and uncovered that Nef can generate pro and anti-apoptotic signals using distinct motifs. We observed an increase in apoptosis upon mutating the motifs involved in Nef:AP-1 (Nef M_{20}A or Nef $EEEE_{62\text{-}64}AAAA$) or Nef:AP-2 (Nef $LL_{164/165}AA$) interactions, implying that the above interactions are anti-apoptotic in nature. In contrast, disrupting the Nef:PAK-2 interaction motifs with Nef H_{89}A and F_{191}A mutants reduced apoptosis and generated lower levels of activated caspase-3 implicating a pro-apoptotic property for the Nef:PAK-2 interaction. To validate these findings, we measured early apoptosis after transient short-hairpin RNA knock-down of the Nef interaction partners AP-1, AP-2, as well as PAK-2. Strikingly, depleting the α adaptin subunit of the trafficking protein AP-2 enhanced early apoptosis in cells transduced with HIV-1 demonstrating a novel anti-apoptotic pathway utilized by Nef to modulate cell survival.

BS3.06

Hide and seek with HIV-1 Nef: Gaining super-resolution insights to viral immune evasion

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A major factor preventing the elimination of HIV-1 lies within the ability of the virus to hide from the immune system. This inherent ability of HIV-1 to confuse the immune system is accomplished by the small accessory protein Nef. Specifically, MHC-I downregulation by the HIV-1 Nef prevents infected cells from cytotoxic T-cell mediated killing. Nef downregulates MHC-I by modulating the host membrane trafficking machinery, resulting in the endocytosis and eventual sequestration of MHC-I within the cell. In the current report, we utilized the intracellular protein-protein interaction reporter system, bimolecular fluorescence complementation (BiFC), in combination with super-resolution microscopy to uncover the membrane trafficking route undertaken by Nef and MHC-I. We demonstrate that this interaction occurs upon Nef binding the MHC-I cytoplasmic tail early during endocytosis in Rab5-positive endosomes. Disruption of early endosome regulation inhibited Nef-dependent MHC-I downregulation, demonstrating that Nef hijacks the early endosome to sequester MHC-I within the cell. Furthermore, super-resolution imaging identified that the Nef:MHC-I BiFC complex transits through both early and late endosomes before ultimately residing at the trans-Golgi network. Together we demonstrate the importance of the early stages of the endocytic network in the removal of MHC-I from the cell surface and its re-localization within the cell, which allows HIV-1 to optimally evade host immune responses. Understanding these complex molecular pathways will aid in the development of new inhibitors targeted at crippling HIV-1's ability to evade our own immune surveillance system.

BS3.07

Putative Role of APOBEC3 Proteins in the Establishment of a Subset of the Latent HIV-1 Infected Cell Reservoir

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Combination antiretroviral therapy (cART) is extremely effective at suppressing HIV-1 viremia and extending the life of infected individuals to nearly that of those who are uninfected. The reason why cART is not a cure for HIV is because it targets actively replicating viruses. There exists in all HIV-1 infected individuals several small and elusive reservoirs of long-lived resting CD4+ cells, called latently infected cells, where integrated and genetically intact proviruses fail to express detectable levels of viral proteins. Although several factors have been identified to contribute to proviral latency, ultimately, latency is complex, multifactorial and still poorly understood.

Here we show that certain members of the APOBEC3 (A3) family of host-encoded HIV restriction factors can help the virus persist by sublethally mutating HIV-1 proviral DNA. More specifically, A3 proteins target the HIV-1 long terminal repeat (LTR) promoter, notably on transcription factor binding sites. Characterization of a library HIV-1 clones with A3 mutated promoters has revealed a broad range of effects including viruses that immediately exhibit a latent phenotype upon infection, viruses that become either completely or partially resistant to PMA/ionomycin induction, and viruses that no longer respond to Tat-mediated transactivation. Our results thereby provide the first evidence that A3 proteins may contribute to HIV-1 persistence and latency.

BS3.08

Antagonism of SERINC5 is impaired in HIV-1 Nef clones isolated from elite controllers

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Background: Nef enhances virion infectivity by downregulating host restriction factor SERINC5 from the cell surface. Mutations at several highly conserved Nef residues impair SERINC5 antagonism, but few studies have evaluated the impact of natural sequence variation on this function. Furthermore, no reports have examined Nef alleles isolated from HIV-1 elite controllers (EC) who spontaneously suppress plasma viremia in the absence of therapy.

Methods: Nef alleles from 45 EC and 46 chronic progressors (CP) were amplified from plasma viral RNA and cloned. SERINC5 levels on the cell surface were assessed by flow cytometry following transfection of CEM T cells with Nef and SERINC5-(iHA) and results were normalized to wild type Nef (SF2 strain). Natural polymorphisms associated with function were identified using statistical analyses of linked Nef genotype-phenotype data.

Results: Nef clones derived from EC displayed lower ability to antagonize SERINC5 (median 76 [IQR 38-91]%) compared to clones from CP (94 [IQR 70-101]%) (p=0.009). We identified two EC Nef clones (EC16 & EC48) that were impaired for SERINC5 downregulation (38% and 30% function, respectively) but retained their abilities to downregulate CD4 and HLA-I and to modulate T cell signalling. Reduced SERINC5 downregulation function was seen for Nef clones encoding the HLA-B*57-associated escape mutation (H116N) (H: 91% vs. N: 79%; p=0.04); however, H116N was not associated with reduced ability to downregulate CD4 or HLA-I, nor to inhibit T cell signalling (p=0.75, p=0.88 & p=0.87, respectively) Interestingly, EC16 and EC48 possessed this protective HLA-I allele and both clones harboured the N116 polymorphism.

Conclusions: Our results demonstrate that EC Nef clones are attenuated for their ability to antagonize SERINC5. Natural sequence variation in Nef, including polymorphisms selected to evade CTL pressure, could have significant impact on this function. Differences in Nef's ability to downregulate SERINC5 may contribute to improved clinical outcome in some EC.

Clinical Sciences: HIV Care, ART and Viral Suppression

Sciences cliniques : Soins liés au VIH, TAR et suppression virale

CS3.01

Smoking and Uncontrolled HIV Viremia Both Exacerbate Leukocyte Telomere Length (LTL) Attrition

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Background: Telomeres shorten over lifespan. HIV infection and smoking are both associated with shorter leukocyte telomere length (LTL) cross-sectionally, but their influence on LTL over time is unclear. This study investigated the relative contribution of HIV and smoking on LTL dynamics in people living with HIV.

Methods: All non-pregnant girls and women ≥12 years old enrolled in the CARMA cohort with available blood specimens were included. For those with >1 sampling ≥1 year apart, the latest specimens were included in longitudinal sub-analyses. LTL was measured by multiplex qPCR. Possible predictors including age, ethnicity, smoking (current, past, never), HIV/viral load (VL) status (HIV-, HIV+/detectable VL, HIV+/undetectable VL), peak VL, and Hepatitis C virus status were considered for inclusion in multivariable models.

Results: LTL was obtained for 287 HIV+ and 211 HIV- participants aged 12-78 years, including 199 HIV+ and 49 HIV- with two specimens 1.0-7.9 years apart. In a cross-sectional multivariable regression, shorter LTL was associated with older age (ß=-0.35, p<0.0001), current smoking (ß=-0.18, p=0.001) *vs.* never, and HIV+/detectable VL (ß=-0.13, p=0.004), but not HIV+/undetectable VL (ß=-0.06, p=0.17) *vs.* HIV-, after adjusting for ethnicity (n=450, R^2=0.25). These results persisted in sensitivity analyses that either excluded or restricted ethnicity to the largest group. Longitudinally, LTL attrition rates were greater with current smoking (ß=-0.20, p=0.004) *vs.* never, but not associated with baseline HIV/VL status, after adjusting for baseline LTL (n=246, R^2=0.11). HIV+ participants with detectable VL who became undetectable at follow-up were more likely to show an increase in LTL and vice-versa (n=57, Fisher's exact test, p=0.043).

Conclusions: These analyses highlight the negative impact of smoking on LTL, with an effect size larger than even uncontrolled HIV infection. These data suggest that LTL is better preserved in controlled HIV, and stress the importance of smoking cessation and controlling viremia to curb cellular aging.

CS3.02

Facilitators and barriers to participating in PrEP trials among adolescent girls and young women enrolled in a youth-centred HIV prevention study in South Africa

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Background: Global pre-exposure prophylaxis (PrEP) trials report challenges initiating, retaining, and promoting adherence among young women, a priority population for HIV prevention initiatives. We explored barriers and facilitators to future PrEP trial participation among adolescent girls and young women in South Africa.

Methods: We conducted four age-stratified (16-18yrs and 19-24yrs) focus group discussions (FGDs) among 32 HIV-negative female participants recruited from AYAZAZI, a youth-centred HIV prevention prospective cohort study in Soweto and Durban. Prior to FGDs, participants received an overview of expectations and potential risks and benefits of participating in various types of biomedical HIV prevention trials. FGDs were co-facilitated by experienced qualitative research assistants and newly-trained youth. Content analysis identified major themes.

Results: Primary **motivators** for participating in PrEP studies included a desire for primary protection against HIV; "back-up" protection when condoms failed or couldn't be used; and the opportunity to receive other priority sexual and reproductive healthcare services. Participation **facilitators** included offering free services, regular adherence reminders, being explicit that PrEP works to prevent HIV if taken, and offering PrEP without requiring (yet encouraging) young women to disclose study participation to parents, partners, or friends. Participation **barriers** included: Parents finding out and risks of secondary disclosure of "risky" sexual activity; Partners finding out and risks of secondary disclosure of her suspicions about his HIV status; Concerns about PrEP side effects and long-term consequences on overall health, HIV risk, and pregnancy; and worries about PrEP access ending after trial completion.

Discussion: Young women are motivated to participate in PrEP trials to protect themselves against HIV, however, they consider numerous contextual factors and consequences to participation. The often conflicting parental, partner, and social pressures that young women confront as they navigate their sexual lives underscore the importance of embedding PrEP programming within youth-centred and comprehensive sexual and reproductive health services.

CS3.03

Drug Resistance Pathways to Second Generation Integrase Inhibitors based on Cell Culture Selections of Large Cluster Viral Lineages

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Background: Second-generation Integrase strand transfer inhibitors {INSTIs), including dolutegravir (DTG), bictegravir (BIC), and cabotegravir (CTG), are the latest drugs recommended for long-term HIV-1 treatment and prevention. Resistance to DTG in the clinic is rare with isolated cases reported in first-line DTG monotherapy. In Quebec, half of onward spread of HIV-1 among Men having Sex with Men (MSM (2002-2015) can be ascribed to 30 viral species leading to large cluster networks (median cluster size 44). We postulated that cell culture selections on these viral species showing a transmission advantage could be exploited to characterize emergent resistance to DTG, BIC and CTG.

Methods: HIV-1 isolates from MSM, belonging to ten large clusters and five singleton/small cluster transmissions, were passaged *in vitro* in the presence of increasing concentrations of DTG, elvitegravir (EVG), and/or lamivudine (3TC) for 36 weeks, based on weekly reverse transcriptase assays. Sanger and Ultradeep sequencing monitored the development of drug resistance

Results: Large cluster HIV-1 strains showed the appearance of resistance to DTG (R263K or S153Y), EVG (T66I), or 3TC (M184V/I) within 8 weeks, as compared to unique/small cluster viruses that only started to develop resistance to DTG after 24 to 36 weeks. Of note, acquisition of R263K or S153Y (2-5 fold) with DTG impaired fitness, with no further accumulation of mutations over 36 weeks. Upon release of DTG pressure, there was no reversion of acquired R263K or S153Y over 20 weeks. In contrast, EVG selections led to sequential accumulation of mutations, including R263K, leading to high-level resistance and viral escape by week 24. Initial selection of resistance to CTG or BIC arose through S153F or R263K pathways within 8-12 weeks.

Conclusions: The low genetic barrier to R263K or S153Y/F, coupled by the severe compromise in viral replicative competence may contribute to the long-term clinical benefit of second-generation INSTIs.

CS3.04

Improving Access to and Engagement in HIV Care for Women Living with HIV: Findings from the Canadian HIV Women´s Sexual and Reproductive Health Cohort Study (CHIWOS)

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Background: Linkage and engagement in HIV care are essential to ensuring virologic suppression. The purpose of this study was to determine the proportion of Canadian women living with HIV (WLWH) who have never accessed care, report delayed linkage, or are not engaged in care, and to identify their socio-demographic, psychosocial and clinical characteristics.

Methods: We analysed baseline survey data from CHIWOS, a longitudinal multi-site, community-based research study of 1,425 WLWH from British Columbia, Ontario and Quebec. The primary outcomes were having never accessed HIV care (by self-report), delayed access to care (receipt of care > three months after diagnosis) and lack of care engagement (<1 medical care visit during the previous year). Multivariable logistic regression was used to identify independent care correlates. Penalized maximum likelihood estimation logistic regression was used to address rare event outcomes.

Results: Overall, 2.8% of CHIWOS women reported having never accessed care, 28.8% reported delayed linkage and 3.7% were not engaged in care. In multivariate analyses, Indigenous ethnicity [OR:4.30 (95% CI:1.31,14.13), p<0.05], unstable housing [OR:4.06 (95% CI:1.82,9.06), p<0.01] and racism [OR:1.04 (95% CI:1.01,1.08), p<0.05] were associated with increased odds of never having accessed care. Age at time of diagnosis [OR:1.08 (95% CI:1.101,1.15), p<0.05], Indigenous [OR:2.04 (95% CI:1.42,2.92), p<0.001] or African/Caribbean/Black [OR:2.79 (95% CI:1.95,3.98), p<0.001] ethnicity were associated with increased odds of delayed linkage to care. A self-reported detectable viral load was associated with increased odds of not being engaged in care in the past year [OR:3.00 (95% CI:1.32,6.79), p<0.01].

Conclusions: While a small proportion of CHIWOS women have never accessed and do not receive routine HIV care, a significant proportion report delayed access to care. Programmatic efforts that address access to and engagement in HIV care for WLWH in Canada should focus on several social determinants of health including housing insecurity, social exclusion and Indigenous/African/Caribbean/Black ethnicities.

CS3.05

Predictors of suboptimal antenatal treatment of pregnant women living with HIV in Canada

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Objectives: To evaluate predictors of suboptimal antenatal HIV treatment ≤ 4 weeks maternal combination antiretroviral therapy (cART)) since 2010 in the Canadian perinatal HIV surveillance cohort of births to mothers living with HIV.

Methods: 22 Canadian pediatric and HIV centres report maternal and infant data yearly. Data collected include maternal characteristics, pregnancy cART and infant outcome. Logistic regression was used to determine the association of region, maternal race and mode of maternal HIV acquisition with suboptimal treatment.

Results: There have 14 documented cases of vertical transmission (N=14, (1%) since 2010) in the prospective cohort (HIV-exposed infants identified within three months of birth) for an overall transmission rate of 1%. 6.8% of pregnant women received ≤ 4 weeks of cART prior to delivery. The percentage of suboptimally treated women declined nationally between 2010 and 2014 but there was a modest increase in 2015, consistent across regions. The percentage of suboptimally treated women was highest in the Prairies (8.7%), with similar proportions in the three Prairie Provinces. Multivariate analysis for the years 2010-2015 adjusting for race and mode of maternal infection suggested that British Columbia and Saskatchewan had lower adjusted rates (OR's of 0.03 and 0.28 respectively) compared to Ontario. Compared to white women, black women are less likely to receive suboptimal treatment (OR=0.43, p<0.01) while indigenous women are more likely (OR=1.78, p=0.1). The proportion of indigenous women receiving suboptimal treatment decreased from 38% in 2009 to 10% in 2014 to 2015.

Conclusion: While the occurrence of suboptimal maternal antenatal treatment has decreased, challenges remain in ensuring access to treatment, particularly amongst indigenous women.

CS3.06

Is Tenofovir Use in Pregnancy Associated with Preterm Delivery? A Canadian Perinatal HIV Surveillance Program Analysis

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Background: The recently published PROMISE trial found that tenofovir-based cART was associated with higher rates of preterm delivery and infant death. We assessed rates of preterm delivery according to cART components in the Canadian Perinatal HIV Surveillance Program (CPHSP).

Methods: Data collected annually from 22 pediatric and HIV centres participating in the CPHSP were reviewed for the period 1997-2015, including: race/ethnicity, maternal HIV acquisition risk category, province of birth, antiretroviral choice, and preterm (<37weeks) delivery.

Results: Among 2816 cART-treated mother-infant pairs (MIPs), 1732 (61.5%) received zidovudine, 575 received abacavir (20.4%) and 501 received tenofovir (17.8%). Tenofovir use in pregnancy increased from 0.75% in 2004 to 54.6% in 2015; this coincided with decreased zidovudine use (100% in 1997 to 14.6% in 2015). Overall preterm delivery rate was 15.8%, with a higher rate in tenofovir-treated mothers (19.2% vs 15.1%, p=0.022). No other significant differences were found in comparing mothers treated vs not treated with abacavir, zidovudine, protease inhibitors (PIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs) or integrase inhibitors (IIs). There was no difference in preterm delivery rate among women exposed to tenofovir with versus without a PI (19.2% vs. 19.5%, p=0.93), NNRTI (17.7% vs 19.5%, p=0.710) or II (17.4% vs 19.2%). Preterm delivery rates differed according to province of birth [p<0.001, with significant variation in rates across provinces from 12.4% to 28.6%], maternal race/ethnicity (p<0.001, black 12.9%, white 17.0%, indigenous 26.8%), maternal risk category (p<0.001, sexually acquired 13.6%, intravenous drug use 27.4%), and viral load closest to delivery (p<0.001, undetectable 15.5%, detectable 23.7%).

Conclusions: Rates of prematurity were higher amongst mothers treated with tenofovir in pregnancy; however, other factors which may impact antiretroviral choice and increase risk of preterm delivery could explain this finding. Further investigation to determine the safest antiretroviral treatment in pregnancy is warranted.

CS3.07

Late HIV Diagnosis and Normalization of CD4:CD8 Ratio: Results from the Ontario HIV Treatment Network Cohort Study (OCS)

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Background: Late diagnosis is detrimental to health outcomes and overall survival for persons living with HIV. CD4:CD8 normalization has been associated with chronic inflammation and premature aging. We assessed the impact of late HIV diagnoses on current CD4:CD8 among OCS participants.

Methods: Data were collected from at 9 HIV specialty clinics using medical chart abstractions and linkage with Public Health Ontario Laboratories for viral load (VL) tests. Late

HIV disease at diagnosis was defined as CD4<350 or the presence of an AIDS-defining condition within 12 months of diagnosis. Current immune status of participants diagnosed in 1997-2012 and on antiretroviral therapy (ART) was measured as CD4:CD8 ratio at the last measurement in 2013/14. A ratio >=1.2 is considered normalized, while <1.2 as inverted. Multivariable Poisson Regression with robust error variance was used to identify factors associated with prevalence ratio (PR) for CD4/CD8 normalization.

Results: In total, 835 (58%) of 1431 patients on ART with known HIV stage at diagnosis were diagnosed late (mean age: 46.2 years). The majority were males (79%) and White (55%). 32% were diagnosed in 1997-2002, 34% in 2003-2007, and 33% in 2008-2012. While 90% had an undetectable VL in 2013/2014 (84% in females vs. 91% in males, p=0.03), only 15% reached CD4:CD8 normalization, a lower proportion of those diagnosed late were normalized vs. those not late (14% vs. 18%, p=0.008). In multivariable analysis, after controlling for age, time on ART, ethnicity, injection drug use, and having an undetectable VL, only late diagnosis (PR=0.63, 95%CI:0.49-0.81) and being female was associated with normalization (PR=1.63, 95%CI:1.06, 2.51)).

Conclusion: Among those on ART, only late diagnosis and sex had an impact on CD4:CD8 normalization. While a lower proportion of females were undetectable, a higher proportion achieved normalization. This highlights a need for understanding how biological differences between sexes impact ART mechanisms.

CS3.08

Effect of Sex and Hepatitis C Co-Infection Status on Virologic and Immunologic Outcomes of Antiretroviral Therapy and All-Cause Mortality: A 15-Year Follow-up

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Background: We aimed to investigate if response to ARV differs by hepatitis C virus (HCV) co-infection and if the response is modified by sex.

Methods: Using data from the Canadian Observational Cohort Collaboration, a multi-site cohort of HIV+ adults (≥18 years) initiating ARV 2000-14, Fine and Gray models adjusted for competing risk of death estimated the adjusted subhazard ratio (aHR) and 95% confidence intervals (CI) of HCV and sex on time to virologic suppression (two consecutive viral loads <50 copies ≥3 months apart) following ARV initiation and to virologic rebound (two consecutive viral loads ≥50 copies/mL ≥3 months apart) following suppression. Cox proportional hazard model estimated time to death following ARV initiation.

Results: Of 10,400 participants (median follow-up 5.0 years), 1865 were women (38% HIV-HCV) and 3583 men (21% HIV-HCV). Cumulative incidence differed significantly (p<0.001) for (i) suppression at 48 weeks (men HIV+ 88.8%; men HIV-HCV 85.8%; women HIV+ 93.5%; women HIV-HCV 80.0%) (ii) rebound (1134 events) 12 weeks following suppression (men HIV+ 4.8%; men HIV-HCV 13.5 %; women HIV+ 11.8%; women HIV-HCV 21.1%) and (iii) for mortality one year following ARV initiation (men HIV+ 2.2%; men HIV-HCV 6.5%; women HIV+ 0.1%; women HIV-HCV 7.0%). Compared to HIV+ men, co-infected participants were less likely to suppress and at higher risk for mortality. Rebound risk was higher for HIV+ women and co-infected participants relative to HIV+ men. Sex did not modify associations.

Conclusion: Co-infected have poorer responses to ARV with greater risk of mortality. Women are at greater risk of rebound.

Table. Adjusted^ models with marginal effect of infection status within sex and HCV*sex interaction term. (^Adjusted for variables shown plus age, race, injection drug use, men having sex with men status, province, baseline viral load, CD4 cell count, AIDS defining illness, ARV class, and year of ARV initiation).

		HIV	HIV-HCV	HCV within sex	p value
Outcomes	Sex	aHR* (95% CI)	aHR* (95% CI)	aHR* (95% CI)	(HCV*sex)
(i) Virologic Suppression	Male	1.00	0.86 (0.79,0.93)	0.86 (0.79,0.93)	0.48
	Female	1.04 (0.90,1.13)	0.82 (0.79,0.98)	0.96 (0.86,1.07)	
(ii) Virologic Rebound	Male	1.00	1.57 (1.32,1.89)	1.57 (1.32,1.89)	0.42
	Female	1.35 (1.07,1.73)	1.96 (1.54,2.49)	1.44 (1.08,1.94)	
(iii) All-cause Mortality	Male	1.00	1.83 (1.44,2.33)	1.83 (1.44,2.33)	0.59
	Female	0.79 (0.52,1.20)	1.81 (1.33,2.47)	2.30 (1.46,3.64)	

Epidemiology and Public Health: Interdisciplinary Epidemiology

Épidémiologie et santé publique : Épidémiologie interdisciplinaire

EPH3.01

Correlation of objective risk of HIV infection with self-perceived risk in MSM enrolled in the Momentum Health Study

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Background: HIV risk amongst men who have sex with men (MSM) is associated with prior sexually transmitted infection (STI) or elevated HIV risk index score (HIRI-MSM). Whether MSM self-identify as being at risk is unclear. We assessed association of objective/subjective HIV risk in MSM enrolled in the Momentum Cohort, Vancouver.

Methods: MSM enrolled February 2012 – February 2016 were eligible if they were HIV-negative at baseline, had available HIRI-MSM and provided HIV risk self-assessment. Objective HIV risk was defined as rectal STI, HIRI-MSM ≥10 and ≥25. Self-perceived risk for HIV transmission was assessed using a single item on "current HIV risk" with "low" or "high" response options. Correlation between objective and subjective risk was calculated using generalized estimating equations and c-statistics.

Results: At baseline in 551 MSM, 61.5% and 10.7% of participants had HIRI-MSM ≥10 and ≥25, respectively, 2.5% had a rectal STI, while 10.7% self-classified as being high risk for HIV transmission. Individuals with rectal STI were more likely to subjectively classify themselves at high HIV risk (19.1%) than those without a rectal STI (7.3%, odds ratio [OR] 2.97,95%CI 1.37-6.46, c-statistic 0.559), as were those with HIRI ≥10 (11.8% versus 2.3%, OR 4.38,95%CI 2.47-7.79, c-statistic 0.548) and HIRI ≥25 (33.8% versus 4.9%, OR 7.86,95%CI 4.76-12.98, c-statistic 0.648). Awareness of PrEP was not significantly associated with any measure of objective HIV risk: OR 1.67,95%CI 0.88-3.18 for rectal STI, OR 1.01,95%CI 0.79-1.29 for HIRI ≥10 and OR 1.18,95%CI 0.81-1.70 for HIRI ≥25, or in subjectively high risk individuals OR 1.10,95%CI 0.74-1.65.

Conclusions: MSM with objective risk for HIV infection were more likely to subjectively classify themselves as being high risk for HIV transmission than those with low objective risk, but correlation was weak. PrEP awareness was not significantly different amongst those with high objective risk suggesting targeted PrEP education is required.

EPH3.02

Drivers of Quality of Life in 700 HIV+ Men

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Introduction: As HIV in developed countries has transitioned from an acute infectious disease with high mortality to a chronic disease that must be managed, quality of life (QOL) has emerged as an important construct. QOL cannot itself be treated but the contributors to QOL could be potential targets of intervention.

Objective: The purpose of this study is to estimate the extent to which HIV-related clinical factors and patient-centered outcomes relevant to brain health and its consequences inter-relate and impact on QOL in HIV+ men.

Methods: The data came from the men in the Brain Health in HIV Now Cohort comprising people ≥ 35 year of age from three Canadian cities. The cohort was fully characterized on the components within the Wilson-Cleary Model for health-related QOL. Structural equation modeling was used to identify the inter-relationships between and among variables using Wilson-Cleary model as the theoretical framework.

Results: 706 men were assessed. The model comprised five latent variables: QOL, health perception (HP), anxiety, depression, and sleep and 34 observed variables. 87% of the variance in QOL was explained by model variables through paths from HP, social function, depression, and environmental quality. 75% of HP was explained by paths from NadirCD4, education, depression, pain, vitality, physical function, personal worry, and environment quality.Factors related to brain health included cognitive ability which was explained by younger age, higher education, sources of stress, environment quality, and HIV progression to AIDS. Cognitive ability correlated with anxiety, depression, sleep, pain and vitality, partly explained self-reported memory, physical function, and engagement in meaningful activities, which in turn partly explained social function and roles emotional and physical. The data fit the model.

Conclusion: Overall, QOL life was explained by symptoms and impairments which have evidence-based interventions. The effects of cognitive ability were widespread contributing indirectly to HP and QOL.

EPH3.03

Incident Sexually Transmitted Infections Among a Prospective Cohort of HIV-Negative and HIV-Positive Gay and Other Men Who Have Sex With Men

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Background: We examined chlamydia (CT), gonorrhea (GC) and syphilis infection within a prospective cohort of MSM in Vancouver, Canada where HIV treatment as prevention (TasP) has been policy since 2010.

Methods: MSM aged ≥16 years were recruited and followed from 02/2012-08/2015 every 6 months Participants self-completed behavioural questionnaires, including the HIV treatment Optimism-Skepticism Scale (HOSS), provided venous blood samples for syphilis serology, and optional urine testing and/or pharyngeal, rectal or urethral swabs for CT/GC. We calculated incidence rates (IR) stratified by HIV status and used generalized estimating equations to identify predictors of CT/GC infection and syphilis infection. Multivariable models were built using backward selection, type III p-values ($p<0.05$), and QIC minimization.

Results: Of 575 MSM with a median follow-up of 1.98 years (29.4% HIV-positive), 134 (23.3%) had any incident STI.

Incident CT/GC was less likely among HIV-positive MSM (IR=9.14/100 person-years) than HIV-negative MSM (IR=15.39/100 person-years; RR=0.59, 95%CI:0.38-0.92). For HIV-positive MSM, incident CT/GC was associated with greater HOSS scores (aRR=1.07, 95%CI:1.01-1.14), younger age (aRR=0.97, 95%CI:0.94-1.00), and group sex (aRR=2.55, 95%CI:1.24-5.23). For HIV-negative MSM, incident CT/GC was associated with younger age (aRR=0.95, 95%CI:0.93-0.98), being gay-identified (aRR=2.14, 95%CI:1.12-4.10), being single (aRR=1.94, 95%CI:1.25-3.01), recent condomless anal sex with a sero-discordant/unknown status partner (aRR=2.50, 95%CI:1.50-4.17), group sex (aRR=1.98, 95%CI:1.25-3.11), and recent STI diagnosis (aRR=2.18, 95%CI:1.25-3.80), but not HOSS scores.

Incident syphilis was more likely among HIV-positive MSM (IR=7.25/100 person-years) than HIV-negative MSM (IR=1.84/100 person-years; RR=3.94, 95%CI:1.98-7.81). For HIV-positive MSM, recent escort work predicted incident syphilis (RR=3.22, 95%CI:1.40-7.41); HOSS scores did not. For HIV-negative MSM, incident syphilis was associated with being single (aRR=4.75, 95%CI:1.17-19.23), recent crystal methamphetamine use (aRR=7.02, 95%CI:2.50-19.75), sero-positioning (aRR=3.89, 95%CI:1.24-12.26) and viral load sorting (aRR=3.49, 95%CI:1.20-10.18), but not HOSS scores.

Conclusions: STI incidence was high, generally not attributable to TasP scale-up (as per HOSS scores), and prompts additional focus on primary STI prevention.

EPH3.04

Social context of chemsex in Montreal: Is Montreal the next London?

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Introduction: Chemsex is a growing phenomenon in Europe particularly in London and consist of using some specific recreational synthetic drugs to facilitate or enhance sex. The chemsex market in London is a high-tech one, the drugs (crystal, mephedrone and GHB) are purchased over Internet, and the apps and «sex parties» or «chillouts» are the main venues for encountering partners. We wonder if chemsex in Montreal followed the same path than London.

Methods: This is an exploratory study. We conducted a survey at Clinique médicale Quartier Latin, a Montreal's urban center specialized in sexual health. Data on socio-demographics, previous/current drug use, sexual practices & behaviour were collected by auto-administered questionnaire completed by patients while waiting to see a clinician. Descriptive statistics are presented and comparisons were done using X^2 for proportion or Fisher Exact test for continuous variables. Analyses were done on SPSS-20.

Results: Since October 2016, 504 patients participated to the survey. 72% were male, median age was 49y (IQR 36-60), 53% were MSM. Lifetime use of recreational drug was 75% cannabis, 44% cocaine, 36% speed, 33% ecstasy, 24% GHB, 19% ketamine, 14% crystal and only 2 patients reported use of mephedrone. Chemsexers here were younger than non-chemsexers (43y vs. 50y, $p<0.001$) but much older than Londonian ones; they were mostly men (91% vs 66%,$p<0.001$), MSM (74% vs. 50%,$p<0.001$), with higher number of sexual partners (5 vs. 0.7 during last 12months, $p<0.001$). Internet and apps were the most common way to find sex partner (50% vs. 20% in non-users, $p<0.001$). However, regarding drug acquisition, here chemsex drugs doesn't seem to be purchased over Internet (3-8% only).

Conclusion: The Montreal's Chemsex is quit distinct from the London one. Users are older, Internet purchase is not common, mephedrone is absent. Further studies are warranted for a better understanding of this epiphenomenon.

EPH3.05

HIV genetic clustering for molecular epidemiology: why it doesn't work and how we can fix it

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A genetic cluster is a group of sequences that are substantially more similar to each other than other sequences in the sample population. Genetic clustering has become a popular technique for identifying potential HIV transmission outbreaks from the sequence variation sampled through routine HIV drug resistance genotyping. However, clustering is an inherently subjective process, and the many different clustering methods that have been used to study regional HIV epidemics have seldom been validated on simulated data.We have evaluated the performance of six nonparametric clustering methods on simulated HIV sequence datasets: pairwise clustering (TN93, patristic distance); subtree clustering; Gap Procedure; Cluster Picker; and PhyloPart. Epidemics were simulated under a suscept-

ible-infected (SI) model with variation in rates of transmission and/or sampling among subpopulations. Phylogenies were generated under this model using *MASTER* and HIV sequences were evolved along each tree using *INDELIBLE*. None of the clustering methods was effective at correctly classifying sequences into clusters of rapid transmission. Instead, they were biased to detect clusters of early diagnosis (e.g., patients sampled at acute infection).Based on this result, we developed a new model-based clustering method based on a Markov-modulated Poisson process that uses maximum likelihood to reconstruct the evolution of branching rates along a tree. When applied to the same simulations, our method correctly classified sequences into rapid transmission clusters with a mean sensitivity of 92% and specificity of 99%. However, it was completely uninformative about sampling rates.There is rapidly growing interest in using genetic clustering to support public health decisions in HIV prevention. Our analysis reveals a significant and pervasive deficiency in popular HIV clustering methods, for which we provide a potential solution that takes a completely different approach to clustering. The source code for our model-based clustering program (pcbr) is available as open source at http://github.com/rmcclosk/netabc.

EPH3.06

HIV Disclosure Without Consent Linked to Increased Risk of Violence Against Women Living with HIV in Metro Vancouver, British Columbia

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Background: Canada stands out globally in its assertive approach to criminalizing HIV non-disclosure, frequently framed as a law to "protect" women. There is currently limited understanding of how forced or non-voluntary HIV disclosure shapes experiences of violence among women living with HIV (WLWH). We quantitatively examined the impact of HIV disclosure without consent (e.g., by a health provider) on experiences of violence due to HIV status amongst WLWH.

Methods: This analysis draws on baseline data from SHAWNA, a longitudinal community-based research project with WLWH (trans inclusive) aged 14+, who live or access HIV services in Metro Vancouver (2015- present). At baseline and semi-annually, participants complete questionnaires administered by trained interviewers, including WLWH and sexual health nurses. Bivariate and multivariable logistic regression were used to investigate prevalence and factors associated with physical and/or verbal violence due to HIV status amongst WLWH.

Results: Of 255 WLWH enrolled in SHAWNA, half (49.8%, n=127) had had their HIV status disclosed without consent and one-third (38.0%, n=97) had experienced violence due to their HIV status. More than half, 61.2% (n=156), were of Indigenous ancestry and 32.9% (n=84) identified as a gender/sexual minority. In multivariable analysis, non-voluntary disclosure of HIV status (e.g., HIV status "outed" without consent by housing staff/residents, prisons etc.) retained the strongest independent association with increased odds of violence due to HIV status [AOR 4.94 (2.73-8.95)].

Conclusions: WLWH who had their HIV status disclosed without consent had 5-fold increased risk of experiencing HIV-related violence. Criminalization of HIV non-disclosure may contribute to and reproduce gender-based violence, and raises concern about stigma, discrimination, and women's confidentiality rights. Canada needs to move away from the criminalization of HIV and implement urgently required trauma-informed HIV care for WLWH, alongside efforts to reduce HIV-related stigma and gender-based violence, and ensure women's rights to privacy and confidentiality.

EPH3.07

A tale of two treatment eras – Mortality outcomes of long-term versus medium-term survivors living with HIV

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Background: People living with HIV (PLWH) initiating modern antiretroviral therapy (ART) have the benefit of improved and simplified treatment regimens with fewer side effects. We compared clinical outcomes of individuals starting ART between 2000 and 2003 and those starting ART between 2004 and 2007 and to determine disparities in mortality outcomes.

Methods: The Canadian HIV Observational Cohort (CANOC) Collaborative is a pan-provincial observational study consisting of nine clinical cohort sites from British Columbia (BC), Ontario and Quebec. Accelerated failure time model determined factors associated with death. Explanatory variables included ART initiation year (2000-2003 vs. 2004-2007) as well as known confounders such as race, gender, injection drug use and co-infection with Hepatitis C.

Results: A total of 4731 PLWH with data on death or follow-up were included in this study, of which 48.7% were from BC, 31.1% from Ontario, and 20.3% from Quebec with 2090 in 2000-2003 and 2641 in 2004-2007. Among

the 676/4731 PLWH who died, 389 (57.5%) initiated ART in 2000-2003 and 287 (42.5%) had initiated in 2004-2007. The univariate analysis found higher risk of death among individuals initiating ART in 2000-2003 (HR=1.36, 95% CI: 1.16, 1.58), older individuals (HR=1.45 per 10 years, 95% CI: 1.35, 1.56), females (HR=1.26, 95% CI: 1.05, 1.50), and Indigenous individuals (HR=2.94, 95% CI: 2.31, 3.74). In the multivariate model, the strongest predictor of death was era of ART initiation between 2000-2003 (aHR=1.40, 95% CI: 1.20-1.64) and Indigenous ethnicity (aHR=2.16, 95% CI: 1.68-2.77).

Conclusion: It must be considered that the BC cohort of population-based and mortality differences may be attributed to better ascertainment of deaths. Despite this, we observed that Indigenous PLWH and those initiating ART between 2000 and 2003 had a 120% and 40% higher risk of death, suggesting that despite clinical advances, there are important social and era-related disparities in mortality outcomes.

EPH3.08

Time Trends and Factors Associated with Early ART Initiation Following Primary HIV Infection in Montreal: 1996-2015

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Introduction: Guidelines regarding ART initiation have varied over time; the WHO recently recommended ART initiation regardless of CD4 T-cell counts. Herein, we investigated time trends and factors associated with early ART Initiation in the Montreal Primary HIV Infection (PHI) Study.

Methods: The PHI study is a prospective cohort established in three private HIV clinics (PHCs) and two university medical centres (UMCs). Recently diagnosed adults were categorized as early (vs. delayed) initiation of ART if within 180 days of baseline visit. Socio-demographic and behavioral information was collected at baseline. Based on statistical significance in the univariate analyses and clinical relevance, covariates were selected for multivariate analyses using SPSS 23.0.

Results: A total of 550 participants were recruited from 1996 to 2015; 348 (63%) had a documented date of HIV acquisition of <180 days. The median (IQR) age of participants was 35 (28; 42) years and the majority was male (96%), Caucasian (89%), MSM (78%), and recruited in PHCs (52%) or UMCs (48%). Participants presented with a median viral load of 4.6 (3.7; 5.3) $\log_{10}$ copies/mL, CD4 count of 510 (387; 660) and CD8 count of 829 cells/mm^3 (600; 1232). Early ART initiation was observed in 47% of the participants; the trend followed a V-shaped curve with peaks in 1996-97 (89%) and 2013-15 (88%) with a dip in 2007-09 (22%). Multivariate analyses showed increasing age, employment, lower CD4 count, higher CD8 count, care at UMCs, and more recent calendar years were independently associated with early ART initiation.

Conclusion: Socio-demographic factors such as unstable employment may be a barrier to accessing early ART. In line with recommendations, early ART initiation was associated with poorer prognostic factors. It is unclear why care at UMCs was associated with early initiation; a better description of the attributes of these clinical settings could help explain this finding.

Multidisciplinary: Women's Health, Maternity and Paediatrics

Multidisciplinaire : Santé des femmes, maternité et pédiatrie

MD4.01

Lactobacilli enhance mucosal barrier and estradiol has anti-inflammatory effect on female genital epithelial barrier functions in presence of HIV-1

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Epithelial cells that line the female genital tract (FGT) interact closely with the mucosal microbiota and these interactions are regulated by female sex hormones. Previous studies have suggested that certain hormonal contraceptives or a dysbiosis of the vaginal microbiota may enhanced HIV-1 acquisition in the FGT. We examined the effects of female sex hormones and lactobacilli on primary genital epithelial cell (GEC) barrier functions and innate immune responses. Primary genital epithelial cells (GEC) were isolated from hysterectomy tissues obtained following patient consent. GEC cultures were grown to confluence on cell culture inserts and polarized monolayers were exposed to two probiotic strains of *Lactobacillus*: *L. reuteri* (RC-14) and *L. rhamnosus* (GR-1), in the presence or absence of the female sex hormones estrogen (E2), progesterone (P4), or MPA. Cell viability, measures of barrier integrity, and innate inflammatory factors were assessed in the presence or absence of HIV-1. Cell viability was unaltered in the presence of Lactobacilli and/or female sex hormones. Transepithelial electrical resistance (TER), a measure of the epithelial barrier function, was increased in the presence of both strains

of probiotic lactobacilli. Exposure to HIV-1 decreased epithelial TER, but when GECs were pre-treated with lactobacilli, they were able to enhance epithelial barrier integrity in presence of HIV-1. Epithelial monolayers grown in presence of estrogen showed a decrease in pro-inflammatory cytokine production (IL-1b, IL-1a, TNF-a, GM-CSF) compared to other hormone treatments and conferred an anti-inflammatory effect even in presence of HIV-1. In conclusion, probiotic lactobacilli enhanced GEC barrier functions and estrogen appeared to exert an anti-inflammatory effect on epithelial innate responses. Enhanced barrier function and decreased inflammation correlate with decrease in HIV infection and replication. These studies provide an insight into how factors in the genital microenvironment can affect HIV-1 infection in the FGT.

MD4.02

Angiopoietin-1 and endothelial quiescence are associated with early initiation of cART in vertically HIV-1 infected children

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Background: Angiopoietin-1 (Ang-1), a biomarker of endothelial quiescence, is a ligand for endothelial-specific receptor tyrosine kinase Tie-2. Ang1/Tie2 maintains the integrity of mature vascular beds by inhibiting apoptosis of endothelial cells and enhancing endothelial barrier function. Endothelial activation in acute systemic inflammatory states is associated with poor outcome and, chronically, may be a risk factor for HIV-associated neurological disorders, nephropathy, and/or atherosclerosis.

Methods: Cross-sectional study of 63 children vertically infected with HIV-1 on combination anti-retroviral therapy (cART) with sustained virologic suppression. Ang-1 levels in serum were measured by commercially available ELISA. We examined correlations between Ang-1 and age at cART initiation, duration of virologic suppression, HIV-specific serology, and HIV-specific cell-mediated immunity (CMI).

Results: Children in the cohort initiated cART at a median (range) age of 2.0 years (<24 hours to 12 years). The proportion of life on effective cART (PLEC) was 38% (2.3-97%). Median (range) plasma concentrations of Ang-1 was 18 (6.1-93) ng/mL. Younger age of cART initiation and PLEC were correlated with Ang-1 (ρ=-0.36, p=0.0062 and ρ=+0.47, p=0.0002, respectively). Among 4 HIV- infected seronegative children (all of whom initiated cART within 24 hours of birth and had sustained suppression of viral replication), Ang-1 levels were higher than 18 HIV-seropositive children who initiated treatment after 6 weeks of age: median (IQR) 66 (42-89) ng/mL *vs* 19 (15-34) ng/mL, p=0.018. Moreover, among seropositive children, lower antibody levels were associated with higher Ang-1 levels (ρ=-0.68, p=0.0005). HIV-specific CMI, expressed as the proportion of clade-specific HIV-1 Gag peptide pools leading to production of IFN-γ, was median (range) 17% (0-96%); lower CMI was associated with higher levels of Ang-1 (ρ=-0.65, p=0.0086).

Conclusions: Early treatment initiation, prolonged viral suppression, and reduced HIV-specific humoral and CMI responses were associated with elevated levels of Ang-1, a marker of endothelial quiescence.

MD4.03

Honouring Indigenous Women's Resilience and Indigeneity in the provision of HIV Care

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Background: Indigenous women in Canada and globally are disproportionately affected by HIV. Alongside gender inequalities, the intergenerational impacts of colonialism shaping Indigenous women's exposure to HIV are well known. However, we know less of the experiences of Indigenous women living with HIV in navigating HIV care and culturally safe services.

Methods: As part of SHAWNA *(Sexual Health and HIV/AIDS: Women's Longitudinal Needs Assessment),* a community-based longitudinal project, we conducted 53 qualitative in-depth interviews with women living with HIV (WLWH) in Vancouver in 2015/16, 23 of whom were Indigenous women. Indigenous women participated in the development of the interview guide, data collection and analysis. An adapted Medicine Wheel was used to identify conceptualizations of health. Indigenous women's narratives were analyzed drawing on decolonizing and feminist theories and participatory research principles.

Results: Many Indigenous WLWH shared the significance of spirituality in their conceptualizations of health and HIV care. Narratives about health conjured up the legacies of colonialism wherein women recalled how culture, community and identity were stolen from them through colonial policies like residential schools. Participants' narratives about intersecting oppression and structural racism made accessing HIV care challenging. Many identified culture and spirituality as part of treatment but women stated obstacles to cultural revitalization from limited access to urban healing ceremonies and barriers to visiting home communities. Participants wanted greater access to HIV services delivered by Indigenous peers, Elders and in groups. Ultimately, Indigenous family-centred HIV care that is responsive to women's complex realities was not available and the current care landscape further jeopardizes Indigenous WLWH's health outcomes.

Conclusion: Despite the high prevalence of Indigenous WLWH, HIV services offer limited engagement with Indigenous epistemologies, spiritualties and collective healing. These stories construct a call for HIV care to be delivered in culturally safe and holistic ways that honour Indigenous women's resilience and Indigeneity.

MD4.04

Engagement in Care Among Women Versus Men: Results from the Ontario HIV Treatment Network Cohort Study (OCS)

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Background: Men and women are affected differently by HIV. We compared socio-economic, behavioral, clinical characteristics and engagement in HIV care among women versus men participating in a HIV clinical cohort in Ontario, Canada.

Methods: The OCS is a multi-site cohort of patients at 10 HIV clinics. Data were collected from medical charts, face-to-face interviews, and via record linkage with Public Health Ontario Laboratory for viral load (VL) tests. We examined participants with follow-up data in 2008-2014 with characteristics reported among women active in OCS in 2013-2014. Generalized Estimation Equations with Poisson regression adjusted for time were used to estimate prevalence ratios (PR) for being in annual care (≥1 VL/year), on antiretroviral therapy (ART), and having suppressed VL among women versus men.

Results: In total, 4986 participants were included (17.8% were women). Compared to men, women were younger (mean age: 43.7 vs. 48.1, p<.0001) and a higher proportion: were African-Caribbean-Black (48.5% vs. 11.7%, p<0.001), were on disability (34% vs. 26%, p<.0001), had an annual household income of <$20,000 (46% vs. 26%, p<.0001), were diagnosed late (60% vs. 53%, p=0.006) and experienced mental health concerns (32% vs. 23%, p<.0001). Compared to men, fewer women were employed (26% vs. 50%, p<.0001), lived alone (29% vs. 45%, p<.0001), reported non-medicinal drug use (9% vs. 17%, p<0.001), hazardous alcohol use (20% vs. 37%, p<0.001) or smoked (46% vs. 64%). In 2008-2013, women were less likely than men to be in annual care (PR: 0.98, 95% CI: 0.97-0.99), on ART (0.96, 0.93-0.098) and virally suppressed (0.95, 95%CI:0.93-0.97).

Conclusion: We observed that women in OCS experience inequalities in socio-economic characteristics compared to men, as well as differences in behavioral, and clinical characteristics. Women performed less well than men in HIV care cascade over time, suggesting that gender-specific strategies are needed.

MD4.05

Canadian Perinatal HIV Surveillance Program (CPHSP): Demographics, Perinatal HIV Transmission, and Treatment in Pregnancy in Canada 1997-2015

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Objectives: To describe demographics of mother-infant pairs (MIP), antiretroviral (ART) treatment during pregnancy, and vertical transmission (VT) rates in the Canadian perinatal HIV surveillance cohort of births to HIV+ mothers from 1997 to 2015 in the combination antiretroviral treatment (cART) era.

Methods: 22 Canadian pediatric and HIV centres report maternal and infant data yearly. VT rates are based on the "perinatally identified cohort" defined as MIP delivered in Canada and identified within 3 months after birth. Data collected include maternal characteristics, pregnancy ART and infant outcome.

Results: There have been 3441 MIP between 1997 and 2015. 35% were identified in Ontario, 23% in Quebec, 15% in Alberta, 13% in British Columbia, 7% in Manitoba and 6% in Saskatchewan. Ontario has the highest proportion consistently, with a growing proportion in Saskatchewan, 14% of the 231 MIP in Canada in 2015. Overall, 68% of mothers acquired HIV heterosexually, 21% through injection drug use (IDU) and1% perinatally; the proportion of IDU has dropped from 40% in 1997 to 20% in 2015. 50% of mothers were black, 23% were white and 20% were indigenous Overall, the VT rate was 1.9%. It dropped steadily from 8% in 1997 to .3% in 2012-2014 but increased to 1.3% (3 cases) in 2015. Among the 13 mothers who did not receive antenatal cART in 2015, there were 2 VTs. Of mothers receiving > 4 weeks of antenatal cART throughout the period, the VT rate was 0.2% (5/2643). The overall proportion receiving ≤ 4 weeks of antenatal cART was 19.7%, but dropped steadily to 3.0% in 2014 but increased to 6.6% in 2015.

Conclusions: VT rates of HIV in Canada remain very low but increased in 2015, reflecting the increase in women

who were not optimally treated. Efforts to ensure access to optimal therapy must be sustained.

MD4.06

Elevated estradiol levels in HIV-positive pregnant women on protease inhibitor-based regimens; an association with foetal growth restriction

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Background: The use of combination antiretroviral therapy (cART) can prevent HIV vertical transmission. However, numerous studies link cART use in pregnancy with higher rates of adverse birth outcomes, and these effects may be more pronounced with protease inhibitor (PI)-based cART. The mechanisms underlying these adverse outcomes are not fully understood, but an association with steroid hormone levels, specifically progesterone, has been implicated. The sex steroid estradiol also plays an important role in pregnancy, but no data are available in the context of HIV and pregnancy. The objective of this study was to investigate the effect of cART on estradiol and its association with birth outcomes.

Methods: Sixty-three HIV-positive and 49 HIV-negative Canadian pregnant women were followed prospectively throughout gestation. Maternal plasma samples were collected at 12-18 weeks, 24-28 weeks, 34-38 weeks, at delivery, and from the cord. Birth outcomes were recorded. Levels of estradiol, DHEAS, DHEA, SHBG, cortisol, and ACTH were quantified by ELISA.

Results HIV-infected PI-cART exposed women had higher total and bioavailable estradiol levels in maternal and cord plasma compared to HIV-uninfected and HIV-infected women on PI-sparing cART ($p<0.001$). HIV-infected PI-cART exposed women had higher DHEAS levels (the precursor for estradiol) in cord plasma that correlated with both cord and maternal delivery estradiol levels. Cortisol and ACTH levels were similar between groups, providing data against a generalized hypothalamic-pituitary-adrenal axis dysfuction. In the HIV-postive women on PI-cART, cord estradiol levels correlated negatively with birth weight centile ($r=-0.47$, $p=0.0016$).

Conclusion: Our data suggest that PI-cART exposure in pregnancy is associated with elevated levels of estradiol, likely driven by higher DHEAS production. Our data caution that PI-cART use in pregnancy may be associated with foetal exposure to high estradiol levels that may contribute to foetal growth restriction and could potentially increase the risk for long-term adverse health outcomes.

MD4.07

The Association of Precarious Employment with Mental and Physical Health Outcomes among a National Cohort of Women Living with HIV: A Mediation Analysis

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Background: : As a key social determinant of health, source of income may impact physical and mental health of women living with HIV (WLWH). We explored the relationship between source of income and health (physical, mental, HIV-related), and the role of potential mediators (social support, HIV-related stigma, gender discrimination, and access-to-care) among WLWH in Canada.

Methods: : We analyzed baseline survey data from the Canadian HIV Women's Sexual and Reproductive Health Study (CHIWOS), a community-based participatory longitudinal cohort study (n=1377/1425). We used logistic and linear regression to estimate adjusted odds for self-reported viral load (HIV-related health), and overall mental and physical health (SF-12), by source of income. We conducted a path analysis to estimate direct and indirect effects of source of income on each outcome, accounting for potential mediators and adjusting for confounders.

Results: Among 1377 participants, one-fifth (22%) gained income through paid employment, two-thirds (62%) through social assistance, 2% through jobs considered illegal (selling drugs, sex work or panhandling), and one-tenth (10%) through other sources (pension/savings/loan/family). Compared to participants with paid employment and accounting for the association between social support, stigma, and barriers to access-to-care, women who received social assistance were at increased risk for detectable viral load and poorer mental and physical health; participants with income from illegal work were more likely to report a detectable viral load compared to those with paid employment. HIV-related stigma, gender discrimination, and social support mediated the relationship between source of income and viral load, mental and physical health. After adjusting for several covariates and accounting for potential mediators, source of income still affected physical and mental health.

Conclusions: : Findings highlight the need to address source of income as a determinant of health for WLWH and inform mental and physical health interventions, including

improving social support, and combating HIV stigma and gender discrimination.

MD4.08

« Plurielles »: evaluation of a Quebec program to improve the sexual health of HIV-positive women beyond HIV

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Context: Living with HIV undeniably affects the sexual health of women. However, the sexual health of women with HIV (WLHIV) is little documented and few actions and interventions to address it have been evaluated. Through a collaboration with ten community organizations involving fifteen intervention workers and peer-helpers, "Plurielles," an empowerment program to improve the emotional and sexual wellbeing of WLHIV was submitted to a cultural validation process (2013) followed by a Quebec-wide evaluation (2014-2015).

Methods: This community-based research project enlisted the participation of sixty WLHIV aged from 23 to 70 years old (M = 48 years) with diverse ethnic backgrounds. Most were mothers (79%) and had been living with HIV for 12 years on average. The sample was mostly single (70%) and a quarter reported being sexually active. A concomitant triangulated mixed-methods design served to evaluate the program's impacts on the sexual wellbeing. At each time period, pretest, posttest and follow up (at 6 months), data was collected with a quantitative questionnaire and a qualitative interview.

Results: This evaluation indicated positive effects on the women's capacity to mobilize their personal and environmental resources to improve their sexual wellbeing. In this regard, the qualitative findings suggest that the program allowed the women to demystify sexuality, to break their isolation, and to recognize and attend to their sexual health needs. The program had significant effects on the participants' capacity to build skills conducive to self-esteem, self-confidence, taking initiative, and gaining control over their sexuality.

Conclusion: The WLHIV underscored multiple challenges related to their sexual and love lives. Through close collaboration with knowledge users and different actors in this project, the creation of this innovative intervention improved understanding of and the response to the sexual health needs of WLHIV which increased the women's sense of control over their sexuality.

Poster Presentations – Présentation d'affiche

Basic Sciences

Sciences fondamentales

Antivirals, Microbicides and Mechanisms of HIV Resistance

Antiviraux, microbicides et mécanismes de résistance au VIH

BSP1.01

Identification of a Novel and Potent U1 Interference RNA Targeting the Gag Open Reading Frame of HIV-1

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HIV-1 replication is critically dependent upon RNA splicing, whereby over 35 viral mRNA species are produced. Assembly of the spliceosome begins with the recognition of 5' splice donor sites by cellular U1 small nuclear RNAs (U1 RNAs). More recently, U1 RNAs have been exploited to suppress gene expression. Modified U1 interference RNAs (U1i RNAs) have been designed to target HIV-1 RNA by inhibiting polyadenylation or inducing excessive splicing. Our lab has identified potent U1i RNAs targeting a conserved site in the Gag coding sequence of HIV-1 RNA. We evaluated the therapeutic potential of our U1i RNAs and those previously designed, by measuring production of HIV-1 in culture supernatants of cells co-transfected with an HIV-1 molecular clone and U1i RNAs. U1i RNAs targeting Gag and those that induce excessive splicing were found to be the most potent, with EC50s ranging from 1 to 5 ng/ml, compared to those that inhibit polyadenylation, with EC50s of 50 ng/ml or greater. To identify the mechanism of Gag U1i RNAs, we compared their effects on HIV RNA levels. Like U1i RNAs that inhibit polyadenylation, Gag U1i RNAs reduced RNA levels evenly, suggesting a global RNA inhibition. We also found that Gag U1i RNAs inhibit processing of Gag, similar to U1i RNAs that induce excessive splicing. Our results suggest that the Gag U1i RNAs are acting through different mechanisms compared to previously described candidates and work is in progress to characterize their mechanism(s). We also found that U1i RNAs acting through any mechanism are more potent compared to ribozyme or decoy candidates and are comparable to short hairpin RNA candidates in development. Overall, our results suggest that U1i RNAs are potent RNA interfering molecules that have the potential to be used in a gene therapy approach to cure HIV-1 infection.

BSP1.02

Impaired Human Immunodeficiency Virus Type 1 Replicative Fitness in Atypical Viremic Non-Progressor Individuals

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Background: Progression rates from initial HIV-1 infection to advanced AIDS vary significantly among infected individuals. A distinct subgroup of HIV-1-infected individuals -termed viremic non-progressors (VNP)- do not seem to progress to AIDS, maintaining high $CD4^+$ T-cell counts despite high levels of viremia for many years. Several studies have evaluated multiple host factors, including immune activation, trying to elucidate the odd HIV-1 disease progression in these patients; however, limited work has been done to characterize viral factors in viremic controllers.

Methods: Here we analyzed HIV-1 isolates from three VNP individuals and compared the replicative fitness, near full-length HIV-1 genomes and intra-patient HIV-1 genetic diversity with viruses from three typical (TP) and one rapid (RP) progressor individuals.

Results: VNP individuals carried viruses with impaired replicative fitness, compared to HIV-1 isolates from the TP and RP patients ($p < 0.05$, 95% CI). Although analyses of the near full-length HIV-1 genomes showed no clear patterns of single-nucleotide polymorphisms (SNP) that could explain the decrease in replicative fitness, both the number of SNPs and HIV-1 population diversity correlated inversely with the replication capacity of the viruses ($r = -0.956$ and $r = -0.878$, $p < 0.01$, respectively).

Conclusions: It is likely that complex multifactorial parameters govern HIV-1 disease progression in each individual, starting with the infecting virus (phenotype, load, and quasispecies diversity) and the intrinsic ability of the host to respond to the infection. Here we evaluated a subset of viremic controller patients and demonstrated that similar to the phenomenon observed in patients with a discordant response to antiretroviral therapy (i.e., high $CD4^+$ cell counts with detectable plasma HIV-1 RNA load), reduced viral replicative fitness seems to correlate with late disease progression in these antiretroviral-naïve individuals.

BSP1.03

Application of a Proteomics Platform for the Preclinical Toxicity Screening of the Anti-HIV Microbicide Candidate, Griffithsin, in a Non Human Primate Model

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Background: PREVENT (PREvention of Viral ENTry) is a preclinical trial evaluating the safety and tolerability of Griffithsin (GRFT) as a rectal microbicide to prevent HIV infection. Given that certain microbicide candidates (nonoxonyl-9) are associated with increased HIV acquisition risk, the determination of potential toxic side effects of GRFT on mucosa is critical. Mass spectrometry (MS)-based proteomics offers systems-level information of mucosal surfaces, making it an ideal tool for preclinical screening. Here, we utilized this approach to screen toxic side effects of GRFT microbicide gel in a non-human primate model.

Methods: Six Rhesus macaques were randomized 1:1 to HEC- or carbopol-formulated placebo and 0.1% GRFT gels, which were applied intra-rectally. A mid-trial crossover step allowed evaluation of both HEC and carbopol formulations. Baseline and post-gel application mucosal samples were collected and analyzed label-free by using tandem-MS. Proteome effects were measured by paired and unpaired t-tests, correcting for multiple comparisons, and interpreted by hierarchical clustering and pathway analysis.

Results: 382 unique proteins were identified. Compared to baseline, GRFT 0.1% did not elicit any significant changes in protein expression in either gel formulation (threshold: FDR<5%). Strong effects were observed 2 hours post-placebo gel application, with HEC inducing more changes (19.9%) than carbopol (8.4%) at the proteome level (FDR<5%). These included proteins involved in transport (p=1.5E-8), exocytosis (2.7E-8), secretion (p=3.6E-6), proteolysis (p=1.5E-4), and inflammation (p=1.7E-4). These changes were no longer detectable 24 hours post-gel application (threshold: FDR<5%).

Conclusions: Intra-rectal application of GRFT 0.1% gel did not elicit any significant changes in the rectal proteome. However, placebo gels triggered a strong and unexpected, transient response. These short-lived effects demonstrate that current placebo formulations may induce significant changes in the host. This study also supports the safety profile of GRFT 0.1% gel as an anti-HIV microbicide. This work was funded by NIH grant # U19 AI113182.

BSP1.04

Identification of optimal promoters for different classes of anti-HIV RNAs

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Gene therapy vectors that deliver antiviral molecules to hematopoietic stem cells (HSCs) is an alternative approach to classical treatments to reach a functional cure against HIV infection. This could be achieved by engineering HSCs to permanently produce antiviral RNAs. While there are clinical trials already in progress with this approach, improvements are necessary for gene therapy to be able to provide a cure for HIV-1 infection. Notably, increasing the efficiency of the molecules used to inhibit viral replication and decreasing their toxic effects to ensure their safety are desirable. Although several anti-HIV RNAs from different classes have been identified, differences in delivery vectors and promoters make it difficult to identify the best candidates within and between different RNA classes. Our overall goal is to compare the efficacy and toxicity of anti-HIV RNA candidates from different classes. To identify optimal promoters for different RNA candidates we have constructed delivery vectors expressing RNAs from different classes, including short hairpin RNAs, ribozymes, and decoy molecules. We have expressed them from the human RNA polymerase III promoters U6, H1 and 7SK, and evaluated their effects on HIV-1 production from strain NL4-3. We observed major differences in efficacy for all RNAs expressed from the different promoters, with the U6 and 7SK promoters producing more potent RNAs compared to the H1 promoter. Work is in progress to compare the toxicity of RNAs expressed from different promoters and the transcriptional profile of each RNA candidate in various cell types. We expect to identify optimal promoter strategies to transcribe anti-HIV RNAs. This will be used to identify the optimal combination therapy approaches for gene therapy to provide an alternative to drug therapy. This study will also be important for the use of RNA drugs in other diseases and for applications using small RNAs to investigate diverse biological processes.

BSP1.05

Determination of cell trafficking after induction of immune quiescence

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Background: Despite continual effort from the HIV prevention community, there are 2 million new HIV infections yearly suggesting new HIV prevention methods are needed. Despite intense exposure to HIV, some individuals remain HIV uninfected, this natural protection is associated with a resting immune state, termed Immune Quiescence (IQ). IQ is defined as: reduction in levels of proinflammatory cytokines/chemokines, and proportion of HIV target cells. Our lab conducted a study to induce IQ, by using anti-inflammatory drugs: acetylsalicylic acid and hydroxychloroquine. Both drugs decreased the proportion of HIV target cells in the blood, use of acetylsalicylic acid lead to additional decreased expression of target cells at the female genital tract. The mechanism of decreased target cell frequency after anti-inflammatory use remains unknown.

Hypothesis: the induction of IQ using anti-inflammatory drugs leads to an altered chemokine gradient and chemokine receptor expression on immune cells causing decreased immune cell recruitment to the female genital tract.

Methods: Peripheral Blood Mononuclear cells isolated from participants, before and at the end of the drug treatment, were stained and observed using flow cytometry. Differences in expression of chemokines will be compared before and at the end of drug treatment.

Results: Overall, there was no difference in expression levels of cytokines and chemokines before and at the end of treatment. However, decreased frequency of target cells at the genital tract and changes in the orientation of the chemokine gradient – cell recruitment shifting towards the blood at the end of treatment - suggests modifications in the cell trafficking. Additionally, T cells and MAIT cells (mucosal associated invariant T cells) will be assessed for expression of mucosal trafficking markers on the cell surface.

Significance: If this study can demonstrate that balance has been achieved, inducing IQ through anti-inflammatory drugs could be a new tool in the HIV prevention arsenal

BSP1.06

Mining microarray gene expression data to train classification models that discriminate for the host resilience to HIV-acquisition phenotype

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Background: Epidemiological observation of an HIV-exposed seronegative (HESN) subgroup in the Pumwani commercial sex worker cohort in Nairobi, Kenya, implicates that the repertoire of human diversity has the potential to confer reduced susceptibility to HIV-1 infection. Previous studies have shown that specific genetic variants and expression profiles were associated with this phenotype. However, utilization of this information to create a quantitative model to discriminate for this phenotype with gene expression data, to our knowledge, has yet to be described in literature. Here, we report on the application of statistical classification to a public microarray dataset for model generation.

Methods: The public dataset GSE33580 contains Affymetrix U133plus2.0 microarray gene expression profiles of whole blood from HESN (n=43) and unexposed individuals (n=43). Eight samples were excluded from the dataset (5 HESN; 3 controls) due to poor RNA quality. These samples had outlier values in terms of 5':3' ratios for at least 6 of 21 spike-in control genes, based on median absolute deviation (modified z-score >3.5). Probes were mapped to ensembl gene identifiers (ENSG) by a custom CDF. A panel of supervised machine learning algorithms from the scikit-learn python library was applied.

Results: The models generated by the random forest (RF) and support vector machine (SVM) algorithms had a median classification accuracy >85%. To assess overfitting, the distribution of cross-validation classification accuracies were visually compared between models trained on a subset of samples versus the entire sample set. Furthermore, feature selection robustness was evaluated by aggregating the frequency of each gene used as an influencer.

Implications: Presently, identification of new HESN individuals by epidemiological criteria is challenging. Generated prediction models may potentially be used to screen for extreme phenotypes in terms of HIV susceptibility risk, via biomarkers, from the general population for enrollment in clinical, genetic or cell-based studies.

BSP1.07

Dolutegravir resistance progressively diminishes levels of HIV-1 integrated DNA

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HIV infection and HIV drug resistance persist despite decades of active antiretroviral therapy (ART). Treatment decreases levels of plasma viral RNA but viral nucleic acid persists, mostly as integrated DNA within the host cell genome. In fact, viral DNA blood levels correlate with the extent of comorbidities and the rapidity of viral rebound following treatment interruption. To date, no intervention aimed at decreasing HIV DNA levels below those attained through ART has been successful. This includes the use of some integrase inhibitors either as part of ART or treatment intensification studies. No patient who has received dolutegravir (DTG) as part of a first-line therapeutic regimen has ever developed resistance against this drug and the most frequent substitution associated with DTG failure is R263K in integrase that is associated with diminished integrase activity both in cell-free and tissue culture assays, while H51Y has also been selected in culture. Here, we investigated how integrated DNA levels change over time during multiple cycle infections with R263K/H51Y-containing viruses.Levels of reverse transcripts were measured by quantitative PCR. We monitored replication and measured HIV-1 integration in Jurkat cells over the course of multiple cycle four-week infections using Alu-mediated quantitative PCR.The R263K substitution did not decrease reverse transcription but did lead to far less integrated HIV DNA over multiple cycles of infection in culture compared to wild-type viruses and ultimately to a loss of viral infectiousness when combined with H51Y.These results help to explain the absence of documented drug resistance and even of the R263K substitution in patients who have failed first-line DTG-based therapy. The inability of H51Y/R263K-containing viruses to successfully propagate suggests that the selection of this combination of substitution may not have negative consequences for patients

BSP1.08

Meta analysis of HIV-1 drug resistance for the past 10 years of ART treatment in Uganda

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Background: By 2015, there were 36.7 million people living with Human Immunodeficiency Virus (HIV) infection worldwide. Uganda is among one of the countries with highest burden of HIV infections with 7.1% prevalence. Of 33 million people in Uganda, 1.5 million have HIV infection and only 57% of patients are on ART

Methods: We analyzed drug resistance data of over 3000 baseline and treatment failure patients tested using an in-house technique. We looked at drug resistance profiles from 2006 up to date. We analyzed both the reverse transcriptase (RT) and the protease (PR) regions for drug resistance as well as subtypes.

Results: We show that the most frequent drug resistance mutation (DRM) to NRTIs was M184V, conferring 3TC and FTC resistance (>60% of all subtype A, C and D samples tested). The collection of mutations mostly responsible for Thymidine Analog Mutations (TAMs) were found at a low but similar frequency in both subtype A, C and D despite the fact that AZT is one of the most prescribed drugs in Uganda. Less drug resistance was associated with TDF of all NRTIs and ETR for NNRTIs. For the PR region, the most frequent mutations were M46L, I54V, I50L and V82A. We had expected to observe a decrease DRMs/sample/year with the roll out of HAART in Uganda (2005-2009). However, the level of DRMs/sample/year remained remarkably constant.

Conclusion: Even with the roll out of ART, the burden of drug resistance is still a major challenge that needs to be addressed. HIV subtype is influencing treatment outcomes.

BSP1.09

Washout of Dolutegravir and Other New INSTIs at Early Stages of HIV-1 Infection in Culture Does Not Abrogate Antiviral Activity

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Among Integrase Strand-Transfer Inhibitors (INSTIs), dolutegravir (DTG) has shown greater efficacy than raltegravir (RAL) in suppressing HIV-1 replication in treatment-experienced individuals. We previously showed that removal of DTG from HIV-1 infected cells during early phases of infection resulted in a slower increase in viral replication compared with RAL. Here, we further investigated viral rebound after drug washout by measuring viral integration and production of 2-LTR circles. This study also incorporated elvitegravir (EVG), as well as the G140S/Q148H double-substitution that confers high levels of resistance against all currently-approved INSTIs.MT-2 cells treated with DTG, RAL, or EVG were infected with HIV-1_{WT}, HIV-1 IN_{R263K} or HIV-1 $IN_{G140S/Q148H}$, and drugs were removed after 3 days of treatment. Viral replication was monitored by measuring reverse transcriptase (RT) activity in culture supernatants. Viral integration and 2-LTR circle production were measured by qPCR.Using a WT virus, viral integration did not immediately resume after DTG washout but

increased by more than 2-fold at 8 days after washout compared to the drug control when RAL was used. Similar results were observed when using the virus containing the R263K substitution, previously associated with resistance against dolutegravir. A much higher level of viral integration was measured after washout of EVG from cells infected with the R263K-containing virus. Using the highly resistant G140S/Q148H-containing virus, levels of integration were as high as with the no-drug control when either RAL or EVG were used. When using DTG, levels of integration were approximately 45-fold lower than the no-drug control at 3 days after infection. Viral integration resumed after drug washout, but still remained relatively low at 8 days after washout.In tissue culture, DTG antiretroviral activity lasts longer than that of either RAL or EVG after washout. This observation may help to explain the robustness of DTG-based therapy.

BSP1.10

Biochemical And Cell-Based Characterization Of the DTG-Associated S230R Mutation In HIV-1 Integrase

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HIV integrase (IN) is an important therapeutic target for the treatment of HIV/AIDS. HIV-IN catalyzes the DNA 3'-end processing and strand-transfer activities for the integration of retroviral DNA into the host genome, an essential step in the HIV replication cycle. The latest approved integrase strand-transfer inhibitors (INSTIs), including Raltegravir (RAL), Elvitegravir (EVG) and Dolutegravir (DTG), are among the most potent antiretroviral drugs developed to date. The clinical relevance of cross-resistance associated with RAL and EVG has been reported in infected patients butDTG is a more robust drug with a high genetic barrier to resistance. Although rare, a R263K mutation has been observed in IN in some treatment-experienced individuals.

The DTG monotherapy for HIV trial (DOMONO) is ongoing to investigate the efficacy of DTG monotherapy as a switch option for virologically-suppressed HIV-infected patients previously on NNRTI-containing regimens. A single mutation S230R emerged in the IN gene in one patient who experienced virologic failure (HIV-1 RNA > 200 copies/mL). S230R has been reported as an accessory mutation to T66I and L74M and viruses containing T66I/ L74M/S230R had a significant decrease in susceptibility to the diketo acid L-708,906, an early INSTI. To understand the impact of this mutation on viral fitness and DTG resistance, we studied the effects of S230R in strand-transfer assays and characterized the resistance of the NL4.3 virus containing S230R to different INSTIs. Our results show that, compared to the WT-IN, the S230R-IN had a 2.22-fold increase in Km in the absence of DTG. In the presence of DTG, the S230R-containing IN had a 3- fold decrease in DTG susceptibility. The infectiousness of S230R containing viruses in cell culture was also impaired compared to WT virus.

BSP1.11

Controlling HIV-1 Infection by Small Molecule Alteration of Cellular RNA Processing and Signaling

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Regulation of RNA processing plays a central role in the gene expression of eukaryotic cells and also for HIV-1. By exploiting this dependency, we characterized a small molecule modulator of RNA processing, 191, as a potent inhibitor of HIV-1 replication. 191 dramatically reduces expression of both viral structural [Gag (IC_{50}: 1.8 μM) and Env] and regulatory (Rev and Tat) protein/polyproteins which are associated with alterations in viral RNA accumulation and transport. The effect of 191 on Tat accumulation was reversed upon addition of MG-132 suggesting that this compound enhances proteasomal degradation of HIV-1 regulatory factors such as Tat. 191 is an effective inhibitor across various HIV strains including viruses from clades A and B and ones resistant to each representative class of antiretroviral drugs. This molecule exhibits limited change in total protein synthesis, gene expression (0.46% of 11,406 genes), and RNA splicing (0.69% of 9,806 events) in the host cell. Consistent with affecting RNA processing, the level of phospho-serine/arginine-rich (SR) splicing factors (e.g. SRp20/SRp55/SRp75) are altered upon 191 treatment of cells. Analysis of cellular signaling pathways determined that 191 suppression of HIV-1 gene expression is dependent upon activation of Src, epidermal growth factor receptor, and MEK1/2-ERK1/2 in a similar manner to events initiated by the cardiotonic steroid (CS) class of HIV-1 RNA processing inhibitors. CSs bind to the Na^+/K^+-ATPase to signal Src-EGFR to MEK1/2-ERK1/2 and induce an elevation in intracellular Ca^{2+} concentration $[Ca^{2+}]_i$ which can lead to toxicity/arrythmias in cardiovascular patients. In contrast, 191 inhibits HIV-1 gene expression by activating Src-EGFR to MEK1/2-ERK1/2 signaling without changing $[Ca^{2+}]_i$ through activation of G protein signaling pathways at the cell membrane. This study reveals the potential of a future drug in perturbing RNA processing to modulate HIV-1 replication with limited effects to the host and suggests new cellular targets for controlling this infection.

Biomarkers and Diagnostics

Biomarqueurs et diagnostics

BSP2.01

Residual inflammation and endothelial activation in HIV-1 vertically infected children with fully suppressed viral replication on anti-retroviral therapy

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Background: Chronic inflammation persists in HIV-1 infected adults despite effective combination anti-retroviral therapy (cART), and may predispose to cardiovascular disease. Vertically infected children and youth facing a lifetime of infection may also be at risk of asymptomatic inflammation and endothelial activation.

Methods: Cross-sectional study of 43 HIV-1 infected children with sustained viral suppression (SVS) on cART. Plasma samples were analyzed for selected pro-inflammatory cytokines and biomarkers of endothelial activation using commercially available cytometric bead array and enzyme-linked immunosorbent assays (ELISA).

Results: The median age was 13 years (range 3-19 years), and 19 (54%) were girls. Viral load was <40 RNA copies/mL in all cases. Twenty-six patients (60%) had achieved SVS on their first cART regimen (21 started cART in the first year of life), and 17 (40%) had least one regimen failure before SVS. Levels of 6 inflammatory cytokines (IL-12p70, TNF, IL-10, IL-6, IL-1β, and IL-8) were low (<20pg/mL) in all but one patient with an IL-1β level of 20.1pg/mL. Median (IQR) levels of the biomarkers of endothelial activation angiopoietin-1 (Ang-1), angiopoietin-2 (Ang-2), soluble intercellular adhesion molecule-1 (sICAM-1), soluble vascular endothelial growth factor receptor-1 (sVEGFR-1), and soluble endoglin (sEng) were 16 (12-34), 0.47 (0.31-3.5), 84 (67-97), 0.53 (0.25-2.7), and 17.3 (14.4-24.0) ng/mL, respectively. Levels of biomarkers of endothelial activation were significantly inter-correlated: Ang-2 with sVEGFR-1, Ang-2 with sEng, and sVEGFR-1 with sEng ($\rho>0.5$, $p<0.01$ for all comparisons). Using principal component analysis to partition the cohort into quartiles based on biomarkers of endothelial activation, patients in the highest quartile had higher levels of TNF (p=0.005), IL-12p70 (p=0.001), and IL-10 (p=0.008).

Conclusions: Despite excellent virologic control with cART, persistent systemic endothelial activation can be detected in a subset of vertically HIV-1 infected children and youth, and is associated with low-level inflammation. The implication of these findings will be further investigated.

BSP2.02

Smoking Exerts a Greater Effect on Leukocyte Telomere Length than HIV Infection: A Longitudinal Prospective CARMA Cohort Study of Pregnant Women

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Background: Combination antiretroviral therapy (cART), HIV-mediated inflammation, chronic immune activation, and oxidative stress can affect telomerase and/or leukocyte telomere length (LTL), a marker of biological aging. We investigated the longitudinal dynamics of LTL during pregnancy in HIV+ women treated with cART, and HIV- control women.

Methods: A total of 105 (64 HIV+ and 41 HIV-) pregnant women were enrolled in CARMA cohort. Blood was collected at three visits during pregnancy (13-23, >23-30, and >30-40 weeks of gestation) and LTL measured by monochromatic multiplex qPCR. Multivariate ANOVA modeling was used to examine possible demographic, clinical and environmental predictors of LTL among participants.

Results: HIV+ and HIV- women were similar in age (p=0.45), but there were no Black/African Canadians, fewer Indigenous/First Nations, and fewer HCV+ in the HIV- group (p<0.001). HIV+ women were more likely to have low income and smoke throughout pregnancy (p<0.01). All HIV+ women were on cART by their third visit and 87% of them achieved an undetectable HIV pVL at delivery. Among all women, HIV+ status was univariately associated with shorter LTL (P=0.04); however, smoking (p=0.06) was the strongest predictor of shorter LTL multivariately apart from a significant interaction noted between maternal age and weeks of gestation (p=0.01), whereby LTL increased during gestation among younger (<35y) women. Among HIV+ participants, predictors of shorter LTL were the same as those reported in all women, with the stronger association for smoking (p=0.04). In addition, HIV+ women who received a cART regimen with a ritonavir-boosted PI during pregnancy had shorter LTL compared to women who received other regimens (p=0.03).

Conclusion: These results suggest that smoking in pregnancy may affect LTL more than HIV infection itself. This effect appears greater among HIV+ pregnant women; a group whose LTL are also influenced by the type of cART regimen they receive.

BSP2.03

Concordance between Plasma Cotinine Concentration and Smoking Self-reporting by Pregnant Women in the CARMA cohort study

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Introduction: Most studies use self-reported smoking data. However, stigma associated with smoking during pregnancy may lead to underreporting of this behavior and possible study bias. Cotinine, a nicotine metabolite with a ~16h half-life in plasma, urine, or saliva, is often used as a biomarker of smoking. We examined the concordance between self-reported smoking and plasma cotinine concentration among pregnant women in the CARMA-PREG cohort study

Methods: Cotinine was measured by ELISA in plasma collected between 31 and 38 weeks of gestation. Measures were initially done on a sample of 47 HIV+ and HIV- women. In a subsequent analysis, cotinine plasma levels were measured for an additional 31 women to assess the reproducibility of the initial result. We compared the proportion of cotinine-negative and cotinine-positive with self-reported smoking data collected on the same day as blood collection and reported the concordance%.

Results: The self-reported smokers and non-smokers were of similar age, however the self-reported smokers were more likely to be Indigenous/First Nations or White/Caucasian, have low income, and deliver preterm ($p \leq 0.03$). Among the first subset (n=47), 55% reported being non-smokers, 26% reported smoking daily and 4% weekly; 15% reported smoking with unknown frequency. Defining smoking as plasma cotinine ≥5 ng/ml, we observed 90% and 88% concordance between plasma cotinine and self-reported smoking and non-smoking, respectively. Among the second subset (n=31), 58% reported being non-smokers, 35% reported smoking daily, 3% weekly, and 3% who smoked had no frequency data. This time, we observed 92% and 94% concordance between plasma cotinine and self-reported smoking and non-smoking, respectively. Taken together, we observed an overall 91% concordance between plasma cotinine and self-reported data.

Conclusions: These findings suggest that self-reported smoking is a valid measure for smoking during pregnancy in the CARMA cohort, and do not support underreporting as an important source of bias.

Eradication Strategies Towards an HIV Cure

Stratégies d'éradication, vers un remède contre le VIH

BSP3.01

The Role of SMAC-mimetics in Selective Induction of Programmed-cell death of HIV-infected Human Macrophages

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The suppression of HIV-1 replication to undetectable level is achieved using combinatorial highly-active antiretroviral therapy (HAART). However, upon interruption of the treatment, HIV viral load shows a strong rebound due to the persistence of latently-infected cells. During HIV infection, macrophages account for the majority of viral reservoirs because these cells are long-lived and show decreased sensitivity to cytopathic effects of the virus. SMAC-mimetic is a synthetic antagonist of inhibitor of apoptosis proteins (IAPs) and has been implicated as a potential pharmacological candidate for "shock-and-kill" approach towards the development of sterilizing cure for the virus. Our results show that LCL161, a monomer of SMAC-mimetic, induces cell-death in HIV cell line model U1 in increasing concentrations, but not in non-infected counterpart U937. Upon differentiation into macrophage-like phenotype, differentiated U1 cells show an increased cell death in response to SMAC-mimetic treatment. Similarly, LCL161 induces cell death in monocyte-derived macrophages infected with clinical isolate HIV_{CS204}, but not in mock-infected control. The induction of cell death in the cell line model is in part due to the synergy that exists between pro-inflammatory TNF-a and SMAC-mimetic which leads to the cleavage and activation of caspase-3. In contrast, TNF-a does not play a role in inducing cell death in healthy macrophages treated with LCL161 which suggests that there may be other factors involved in SM-induced cell death in these cells. Notably, there was no significant differences in the levels of TNF-a secreted by mock- and HIV-infected macrophages after SMAC-mimetic treatment. Interestingly, we show that degradation of IAPs by LCL161 and inhibition of RIPK activity by Necrostain-1 lead to cell death of healthy human macrophages and that RIP protein is cleaved in HIV-infected human macrophages. These results suggest that SM-mimetic LCL161 may be a good therapeutic candidate for the eradication of macrophage reservoirs.

BSP3.02

Optimal HIV-1 broadly neutralizing antibodies and their combinations to test towards the eradication of the HIV-1 reservoir

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An HIV-1/AIDS cure can only be achieved by eliminating the HIV-1 reservoir. Potent broadly neutralizing antibodies (bnAb) against the HIV-1 envelope are being clinically tested as a means to eradicate this reservoir. However, to date, administration of these bnAbs into HIV-1 infected individuals have mostly been met with modest benefit and more importantly, negligible reductions in the size of the HIV-1 reservoir indicating a failure towards the elimination of HIV-1 infected cells. A fundamental question that remains is that it is still unknown which antibodies, alone or in combination, can best recognize the envelope on the surface of infected CD4 T cells and hence initiate their lysis via complement mediated lysis or ADCC. In this study, we tested the ability of a panel of eleven HIV-1 envelope-specific antibodies to bind surface envelope on primary CD4 T cells infected with diverse HIV-1 primary isolates belonging to clades A, B, C and D. Additionally, we also examined the abilities of these antibodies to, individually or in combination, induce antibody-dependent complement mediated cell lysis (ADCML) of infected CD4 T cells. Surprisingly, we observed the CD4 binding site antibodies such as VRC01 and 3BNC117 to exhibit minimal binding of infected CD4 T cells in contrast to their neutralization potency and breadth. V1/V2 loop targeting antibodies such as PG9 and PG16 were strong binders and facilitated the elimination of infected cells. Overall, we observed a varied response of each bnAb tested, suggesting that binding and/or neutralization do not necessarily correlate with killing. Therefore, to establish a comprehensive understanding of which antibodies to use for future trials directed towards a cure, a series of parameters in addition to neutralization efficiency needs to be tested, such as antibody-mediated elimination of infected primary CD4 T cells.

BSP3.03

Development of a latency reversing activator vector (ACT-VEC) platform as a curative approach for SIV

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Introduction: The advent of new curative therapeutics designed to eradicate HIV-1 is hindered by the virus' ability to establish latent pools of replication-competent provirus in resting CD4+ T lymphocytes. While the 'shock-and-kill' strategy is a promising area of investigation, current latency reversal agents (LRAs) have been largely unable to induce viral gene transcription or impact the latent reservoir's size. Hence, there is a dire need for the development of novel strategies that induce HIV-1 proviral gene expression and eradication.

Methods: Using a non-human primate model, we have developed immunogenic virus like particles for use as a novel latency reversal activator vector (ACT-VEC). As most latently infected cells are thought to be HIV-1 specific, ACT-VEC formulations were designed to be highly heterogeneous and represent the entire viral quasi-species present in SIV infected macaques. This, we hypothesized, would stimulate the largest diversity of HIV-specific TCR for maximal latency reversal. SIV infected and cART treated macaques either received four monthly vaccinations (90ug intra-muscular, 10ug intra-lymph) of ACT-VEC (n=4) or served as virally infected, untreated controls (n=4). cART was removed one month post-fourth vaccination in all groups. Viral rebound was determined by qRT-PCR and blood collected to determine anti-gp120 antibody titres and antiviral T cell immune responses.

Results and Conclusions: Our results show that all macaques experienced viral rebound post-cART cessation, although a 10-20-fold reduction was seen in ACT-VEC groups, compared to a 3-8-fold reduction in untreated, infected controls. Furthermore, ACT-VEC treatment was shown to reduce the size of the viral reservoir, as determined by the TILDA assay. To better understand the impact of ACT-VEC on SIV infection, we now evaluate vaccine elicited humoral and cellular responses. We present evidence that ACT-VEC is both a safe and highly efficacious LRA that may be able to facilitate cure.

BSP3.04

Co-Receptor Binding Site Antibodies Enable CD4-Mimetics to Expose Conserved Anti-Cluster A ADCC Epitopes on HIV-1 Envelope Glycoproteins

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Background: HIV-1 has evolved a sophisticated strategy to conceal conserved epitopes of its envelope glycoproteins (Env) recognized by antibody-dependent cellular cytotoxicity (ADCC)-mediating antibodies. These antibodies, which are present in the sera of most HIV-1-infected individuals, preferentially recognize Env in its CD4-bound conformation. Accordingly, we recently demonstrated that small CD4-mimetics (CD4mc) able to "push" Env into this conformation sensitize HIV-1-infected cells to ADCC mediated by HIV-positive sera. Here we tested whether CD4mc also expose epitopes recognized by anti-cluster A monoclonal antibodies such as A32, thought to be responsible for the majority of ADCC activity present in HIV-positive sera and linked to decreased HIV-1 transmission in the RV144 trial

Results: We made the surprising observation that CD4mc are unable to enhance recognition of HIV-1-infected cells by anti-cluster A antibodies in the absence of antibodies such as 17b, which binds a highly conserved CD4-induced epitope overlapping the co-receptor binding site (CoRBS). Our results indicate that CD4mc initially open the trimeric Env enough to allow the binding of CoRBS antibodies but not anti-cluster A antibodies. CoRBS antibody binding further opens the trimeric Env, allowing anti-cluster A antibody interaction and sensitization of infected cells to ADCC.

Conclusion: Our results suggest that ADCC responses mediated by cluster A antibodies in HIV-positive sera involve a sequential opening of the Env trimer on the surface of HIV-1-infected cells. The understanding of the conformational changes required to expose these vulnerable Env epitopes might be important in the design of new strategies aimed at fighting HIV-1. Moreover, this combination of Abs could represent a broad and potent approach to unlock HIV-1 Env and sensitize HIV-1-infected cells to ADCC.

HIV Latency and Viral Reservoirs

Latence du VIH et réservoirs viraux

BSP4.01

An HIV-infected individual on suppressive ART with uncommonly high levels of integrated viral DNA

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Introduction: HIV DNA persists as an integrated genome in memory $CD4^+$ T-cells during ART. The homeostasis of the CD4 compartment is associated with HIV persistence in virally suppressed individuals. Here we report the unique case of an HIV-infected individual on suppressive ART with uncommonly high levels of integrated HIV DNA.

Methods: The participant (57 years old black man) was under suppressive ART for more than 3 years at the time of leukapheresis. HIV-CMV-EBV-HBV and HCV serologies are positive. Circulating $CD4^+$ T-cell subsets (Naïve, Central, Transitional and Effector memory (N, CM, TM and EM, respectively)) were sorted by flow cytometry. The frequencies of cells with total and integrated HIV DNA and inducible multiply-spliced HIV RNA were measured by qPCRs and TILDA, respectively, in the sorted subsets. PBMCs were stimulated with peptide-pools (HIV, HCV, HBV, CMV, EBV, Flu) and frequencies of cells expressing IFN-γ, TNF-α and IL-2 were measured by flow cytometry.

Results: The frequency of $CD4^+$ T-cells harbouring integrated HIV DNA was 31070 cells per million. Strikingly, 26% of EM-cells harboured integrated HIV DNA, representing 99% of all integrated HIV genomes. In contrast, the frequency of cells carrying inducible HIV was not particularly enriched in EM-cells when compared to CM- and TM-cells (9, 89 and 32 cells with inducible HIV per million, respectively). In an attempt to amplify the *gag* and *pol* genes by PCR, we identified deletions in both genes in the proviruses harboured by EM cells, thereby confirming the poor inducibility of proviruses (0.01% of proviruses in EM were inducible when compared to 1.5% and 2.6% in CM- and TM-cells, respectively). Frequencies of antigen-specific $CD4^+$ T-cells were low to undetectable.

Conclusions: All together, our results suggest a massive clonal expansion, with an unknown origin, of a defective provirus in cells displaying an EM phenotype.

BSP4.02

An Effective New Combination Treatment to Disrupt HIV-1 Latency

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Introduction: Since the beginning of the HIV epidemic, intensive research has paved the way for advanced antiretroviral treatment. Although this treatment has tremendously improved the quality of life for HIV-infected patients, developing a cure is essential. The main obstacle to HIV eradication is the presence of latent HIV reservoirs, which reside mainly in the CD4+ T lymphocytes. These latently infected cells are not recognized by the immune system and the current treatment, leading to the re-emergence of viral particles upon treatment cessation.

Methods: Our efforts to devise ways to wipe out latent reservoirs have focused on the strategy referred to as "shock and kill." This strategy uses latency reversing agents (LRAs) to reawaken latent reservoirs (the "shock"), which are then recognized and purged by a boosted immune system (the "kill"). For our initial attempt, we conducted a high-throughput screening of small molecules to identify potent LRAs. The capability of these compounds were evaluated on both reporter cell lines harboring mini-dual florescent HIV-1 LTR reporters and CD4+ T cells purified from aviremic HIV-1 infected patients on antiretroviral therapy.

Results: Through intensive assessment of the latency reversing activity of potential small molecules, we have discovered a novel compound, referred to as P.H.02, which in combination with a previously discovered LRA, "Ingenol-3-Angelae," shows very promising latency reversal activity. This new combination treatment causes neither global T cell activation nor significant cell toxicity at clinically relevant tested concentrations. Quantitative viral outgrowth assay (qVOA) further confirmed the ability of this combination treatment to disrupt latency on CD4+ T cells isolated from HIV-infected patients on aintiretroviral therapy.

Conclusion: We have identified an effective new combination treatment to reverse HIV-1 latency. The treatment is an ideal candidate to abrogate persistent viral infection when used in advanced antiretroviral therapies.

BSP4.03

Evaluation of the MOLT-4 Viral Outgrowth Assay for the Quantification of the HIV Viral Reservoir

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New strategies to eradicate HIV-1 and its reservoir from HIV-infected individuals have emerged and are currently evaluated. However, the success and development of these strategies are impaired by the availability of reliable and accurate assays to monitor and measure the size of the HIV reservoir in a quick and efficient manner, suitable for large scale studies. Currently, the gold standard assay to measure HIV reservoir is the limited dilution Quantitative Viral Outgrowth Assay (QVOA) which quantified replication-competent viruses. This assay presents many limitations, one of which, it is time consuming and requires a large amount of blood supplies. Recently, a new assay we refer here as the MOLT-4 VOA, has been developed in efforts to shortening the time and cost of the standard QVOA. The goal of this project was to further validate the MOLT-4 QVOA. Using the latently HIV-infected CD4+ T cell ACH2 cell line as a reference material, we compared the results from the MOLT-4 QVOA to the Standard QVOA for their efficiency to quantify replication-competent viruses in HIV-latently infectious cells. We introduced a defined number of infectious ACH2, each containing one proviral copy, to uninfected CD4+ T cells isolated from PBMCs from healthy donors. P24 ELISA and PCR were used for quantification of replication-competent viruses and results were reported as Infectious Units Per Million (IUPM) using the infection Frequency Calculator IUPMStats v1.0.

Based on the amount of ACH2 added to the assay, we found that the MOLT-4 QVOA assay was not as efficient to quantify replication-competent viruses, giving a much lower IUPM.In close, we recommend further validation of the MOLT-4 QVOA assay before its use. As of now, the standard QVOA remains the current culture-based assay to measure latent replication competent viruses.

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BSP4.04

Altered stability of HIV-infected memory cells following very early ART

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Background: Initiation of ART during primary HIV infection restricts the size of the HIV reservoir. However, less is known about the cell subsets in which HIV integrates and persists during the earliest phase of HIV infection.

Methods: Integrated HIV DNA was quantified by Alu-PCR in sorted naïve (T_{NA}), central (T_{CM}), transitional (T_{TM}) and ef-

fector (T_{EM}) memory cells from Thai HIV-infected individuals who started ART within the first weeks of infection (Fiebig stages I-V based on HIV RNA, p24 and HIV antibodies). Participants who initiated ART during chronic infection were used as controls.

Results: During acute infection 57% of Fiebig I individuals were devoid of integrated HIV DNA in all subsets, whereas integrated genomes were detected in at least one memory subset in 21/22 Fiebig II-V individuals (95%) and in all subsets from chronically infected controls. The frequency of infected cells in each subset was strongly correlated to plasma viral load (p<0.0001).After 24-96 weeks of ART, the frequency of cells with integrated HIV DNA decreased in all subsets from all acutely treated individuals, whereas it remained stable in individuals treated during chronic infection. Importantly, the earlier ART was initiated, the steeper was the decay in integrated HIV DNA in T_{CM} (505, 25, 8, and 2-fold decrease (FD) in Fiebig II, III, IV-V and chronic), T_{TM} (279, 25, 5 and 2-FD) and T_{EM} cells (50, 35, 3 and 1-FD).

Conclusion: Memory cells harboring integrated HIV DNA rapidly accumulate as plasma viral load increases. Whereas ART initiated in chronic infection had no impact on the amount of integrated HIV DNA in memory subsets, initiation of ART in acute infection decreased the frequency of infected T_{CM}, T_{TM} and T_{EM} cells. These results suggest that the majority of memory cells infected during acute infection are short-lived.

BSP4.05

Development and validation of a simplified quantitative viral outgrowth assay

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Background: The quantitative viral outgrowth assay (QVOA) is recognized as the "gold standard" assay for measuring the frequency of CD4+ T cells harboring replication competent proviruses, despite its limitations (labor-intensive, cost, large blood volume requirement, and lack of precision). We developed a novel assay (modified QVOA, mQVOA) to reduce the time of culture and to enhance sensitivity and precision in individuals with the smallest reported HIV reservoirs.

Methods: mQVOA relies on CD3/CD28 stimulation and HIV amplification using MOLT-4/CCR5 as feeder cells, which reduce the variability due to donor-dependent efficiency. Up to 9 million CD4+ T cells from 14 ART-suppressed participants treated during chronic infection were activated with anti-CD3/CD28 antibodies in limiting dilution. After 2 days of culture, MOLT-4/CCR5 cells were added to the culture and p24 production was assessed by ELISA at days 7, 14 and 21. In addition, the frequencies of CD4+ T cells harboring total/integrated HIV DNA and inducible tat/rev RNA were measured by real time PCR and TILDA, respectively.

Results: The median frequency of latently infected CD4+ T cells as estimated by mQVOA was 1.3 [0.5-1.5] cells/million, which is 34 times less than the frequency measured by TILDA (23.4 [12.3-53.7] cells/million), and 439 and 780 times less than the frequencies of cells harboring proviral and total HIV DNA, respectively. The intra-assay coefficient of variation of mQVOA was 0.28 (compared to 0.95 for classical QVOA), which confirms the robustness of the modified assay. mQVOA correlated with proviral DNA (r=0.58, p=0.033) and tended to correlate with TILDA (r=0.53, p=0.057) and total HIV DNA (r=0.57, p=0.059).

Conclusions: mQVOA is a simpler method than standard QVOA to quantify the frequency of CD4+ T cells harbouring replication competent HIV, and may show better reproducibility than the classical QVOA. This novel assay could prove to be a useful tool for HIV eradication studies.

BSP4.06

Studying the Role of MicroRNAs in HIV-1 Replication and Latency in Macrophages

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Micro(mi)RNAs regulate gene expression by associating with proteins of the RNA-Induced Silencing Complex, leading to silencing or degradation of their target mRNA. miRNAs are important in many cell functions and their deregulation is associated with many diseases.

During HIV-1 infection, miRNAs play a role in viral replication and in the establishment of viral reservoirs. Evidence suggests that macrophages contribute to HIV-1 persistence, but the precise mechanism regulating virus production in macrophages is poorly understood.

Our hypothesis is that miRNAs play a vital role in HIV-1 replication and latency in macrophages by the regulation of mRNA expression.

A list of miRNAs that are differentially expressed in HIV-1-infected macrophages has been generated and we have selected the most variable in HIV-1-infected cells. We have cloned the miRNAs on an expression plasmid and their target sequence downstream of a reporter gene. We are currently evaluating the extent of the miRNA knockdown in different cells. Next, the miRNA will be overexpressed and expression of predicted targets mRNAs will be measured by RT-qPCR and their corresponding proteins will be measured by western blot. Finally, these miRNAs will be coexpressed with an HIV-1 molecular clone in a monocytic cell line, and viral production will be monitored through

the reverse transcriptase assay to determine if these miRNAs are susceptibility or resistance host factors.

An inducible model of HIV-1 latency has been set up in the lab. The RNAs from the reactivated and non-reactivated cells will be isolated and sequenced. Bioinformatics analysis will identify miRNAs that are differentially expressed. Selected miRNAs will be validated as above and analyzed for involvement in HIV-1 latency in macrophages.

Identification of targeted mRNAs in HIV-replicating and latently infected macrophages will help understand the role of miRNAs in the establishment of latency in macrophages and other reservoir cells.

BSP4.07

Characterization of suppressive myeloid cells of the human testis: implication for HIV-1 persistence

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Introduction: Despite viral control in antiretroviral therapy (ART)-treated individuals, HIV persists in anatomic reservoirs. We demonstrated the presence of HIV DNA in the testes of individuals receiving ART. In animal models, the testis is described as a site of immune privilege where immune responses are suppressed, notably through the expression of indoleamine 2,3-dioxygenase (IDO) in macrophages and dendritic cells (DCs). Herein, we characterized human testicular myeloid cells to evaluate their immunosuppressive properties that may contribute to HIV persistence.

Methods: Matched testis and blood samples were collected from 9 uninfected individuals undergoing sex reassignment surgery. Peripheral blood mononuclear cells (PBMCs) were isolated by ficoll gradient density centrifugation and testicular cell suspensions were obtained by enzymatic digestion. Myeloid (mDCs), plasmacytoid (pDCs) dendritic cells and myeloid-derived suppressor cell (MDSCs) were assessed using multicolor flow cytometry. *In situ* localization of testicular immune cells was evaluated by immunostaining of frozen sections. IDO mRNA expression was quantified by qPCR.

Results: Testicular cell suspensions contained 9% of leukocytes, of which 30% were myeloid cells. Testicular myeloid cells harbored a higher expression of MHC class II molecules than their peripheral counterparts (p=0.004). Immunosuppressive macrophages (lin^- $HLA\text{-}DR^+$ $CD14^+$ $CD163^+$) represented 20% of the testicular leukocytes. The majority of testicular DCs (lin^- $CD14^-$ $HLA\text{-}DR^+$) were mDCs ($CD11c^+$), contrasting with rare pDCs ($CD123^+$). MDSCs were not detected in the testis while representing 0.5% of PBMCs. Macrophages and mDCs as well as T cells were detected in the testicular interstitium but not pDCs. Importantly, IDO mRNA levels were remarkably higher in the testis than in PBMCs ($p< 0.001$).

Conclusion: Our results show for the first time the existence of an immune privilege mediated by immunosuppressive myeloid cells in the human testis, which could potentially favor HIV persistence. Such findings will contribute to orient tissue-specific viral eradication strategies.

BSP4.08

HIV-1 Latency-Reversing Agents and the Central Nervous System

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Soon after HIV -1 primary infection, the virus crosses the blood-brain barrier (BBB) and is maintained in the brain, which is a shrine protecting HIV-1 from the immune system and some antiretroviral drugs. To eliminate latently infected cells persisting despite long term effective antiretroviral therapy, an approach to treat patients with compounds that reactivate the virus was proposed. However, effect of these latency-reversing agents (LRA) on brain cells is poorly known. In this study, we aimed to analyze the impact of LRA and viral infection on astrocytes, the most frequent cell type in the brain.

Primary astrocytes were infected with VSV-G pseudotyped HIV-1 before treatment with various LRA for 24h. Cells and supernatants were then used to evaluate effects of infection and LRA on (i) astrocytes viability and metabolic activity, (ii) chemoattractant and pro-inflammatory cytokines secretion and gene expression, (iii) modulation of neutrophils transmigration across the BBB by astrocyte-conditioned medium using a three-dimensional *in vitro* model of the BBB.

We demonstrated that latency-reversing agents only slightly decrease astrocytes metabolic activity, indicating that LRA tend to be well tolerated by astrocytes and cause a minimal toxicity if used at therapeutic concentration. We also observed an increase in the secretion of the chemoattractant cytokine CCL2 and pro-inflammatory cytokines IL-6 and IL-8 upon HIV-1 infection and/or Bryostatin treatment. On the contrary, JQ1 treatment induced an inhibition in the secretion and expression of these cytokines by astrocytes. Using a BBB model, we showed that JQ1 and Bryostatin treatment of astrocytes respectively decrease and increase neutrophils transmigration across the BBB, possibly via an increased IL-8 secretion.

Modulations of chemoattractant and pro-inflammatory cytokines secretion and gene expression by astrocytes as

well as neutrophils transmigration across the BBB in response to HIV-1 infection and HIV-1 LRA suggest a possible risk of inflammatory syndrome upon HIV-1 reactivation.

BSP4.09

Identification of novel microRNAs involved in HIV-1 latency in reservoir cells.

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Despite antiretroviral treatments, HIV-1 remains integrated in reservoir cells. Latent infections have low or no transcriptional activity and fail to generate virus. Non-productive expression after viral integration may result from insufficient levels of transcriptional activators, chromatin silencing, and specific microRNA activity. Indeed, some data show that microRNAs could contribute to the establishment of latency. Several therapeutics approaches are investigated to achieve HIV-1 eradication, involving the elimination or inactivation of viruses that persist in multiple reservoirs. In these strategies some drugs, called LRAs (latency-reversing agents) are used to disrupt the latency. The use of LRAs, targeting multiple pathways combined with anti-retroviral therapy may accelerate viral reservoirs exhaustion.

Results: To find markers and new targets of HIV-1 latency, we have analyzed microRNA/mRNA expression patterns during HIV-1 reactivation. In our experiments we use a HIV-1 latent model in lymphocytic, monocytic and macrophage cell lines. In this model, we can distinguish reactivated cell by the expression of the Green Fluorescence Protein (GFP) because the HIV-1 Gag protein is fused with the GFP. By using different techniques including Western-blot, immunofluorescence and cell sorting, we have set up and characterized the best conditions for HIV-1 reactivation for several LRAs including Histone deacetylase inhibitors, Histone Methyltransferase inhibitors, Bromodomain inhibitors, and Akt/PKC agonists. We found that in this model, the combination of two LRAs, Prostratin and SAHA, was a better reactivator than Prostratin or SAHA alone. We also showed that other drugs with different mechanisms reactivate this model (JQ1, HMBA, Chaetocin, and Disulfiram). We then isolated the reactivated and the non-reactivated cells from different reactivation treatments and purified RNA. We are analyzing the microRNA/mRNA expression profiles of the reactivated and non-reactivated cells by RNA sequencing. We expect to identify novel microRNA-based latency mechanisms that will help to identify strategies to eliminate the virus from the reservoirs.

BSP4.10

The Role of Host RNA Surveillance Proteins on HIV-1 Latency

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HIV-1 establishes latent infection in CD4+ T lymphocytes and myeloid cells and post-transcriptional regulatory events can contribute to its persistence. RNA stability and metabolism are affected by RNA surveillance proteins such as UPF1, UPF2 and SMG6. In our previous work, we demonstrated that UPF1 stabilizes and promotes nucleocytoplasmic export of the HIV-1 genomic RNA (vRNA) and enhances its translatability in the cytoplasm. Thus, we hypothesize that the RNA surveillance proteins can interact with the residual vRNA present in latently infected cells and influence the HIV-1 persistence at a post-transcriptional level. In this study, we used overexpression/siRNA-mediated knockdown studies to elucidate the roles of RNA surveillance proteins on HIV-1 latency reactivation and replication in model T-cell lines (J-Lat 10.6) and primary monocyte-derived macrophages (MDMs). In the J-Lat cells, an overexpression of UPF1 did not lead to a transcriptional activation of the provirus, but a reactivation was observed in in 26.8 (±9.4)% of cells indicating that UPF1 contributes to the reactivation at a post-transcriptional level. UPF1 knockdown led to a 57.6 (±4.4)% reduction in reactivation and reduced RNA levels. Overexpression of UPF2 and SMG6 led to a 55.2 (±12.5)% and 63.2 (±5.0)% decrease in the HIV-1 gene expression, respectively, indicating that they are negative regulators of proviral reactivation. In primary MDMs, the silencing of UPF2 and SMG6 increased the percentage of infected cells by 2.13 (±0.25)- and 1.76 (± 0.25)-fold, respectively, corresponding to an increase in Gag expression. Overall, these data suggest that RNA surveillance affects HIV-1 gene expression in viral reservoirs. Since the maintenance of latency is a major obstacle to an HIV-1 cure, understanding the post-transcriptional control of viral RNA metabolism can lead to the development of novel curative strategies.

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BSP4.11

A New Highly Sensitive Retinoic Acid-Based Viral Outgrowth Assay to Detect Replication-Competent HIV Reservoir

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Background: Current antiviral therapies (ART) successfully control viral replication in HIV-infected subjects; however, the persistence of viral reservoir represents a major barrier for the cure. The development of HIV eradication strategies represents a major research priority. Sensitive assays are needed to assess the efficiency of such strategies. Here we describe a modified viral outgrowth assay (VOA) that measures replication-competent viral reservoirs in low numbers of CD4+ T-cells.

Methods: CD4+ T-cells were isolated from PBMCs of HIV-infected individuals with undetectable plasma viral load under ART (HIV+ART). Quantification of integrated HIV-DNA was performed by ultrasensitive PCR. For the VOA, T-cells were stimulated with CD3/CD28 Abs for three days. To ensure optimal cell viability and viral cell-to-cell transmission, cells were split every three days. All-trans retinoic acid (ATRA) was added to facilitate viral reactivation and/or transmission. HIV reactivation was quantified by HIV-p24 ELISA in cell culture supernatants collected every three days and by flow cytometry analysis of intracellular HIV-p24 expression at day 12 post-culture.

Results: In the absence of ATRA, HIV reactivation was detected in CD4+ T-cells isolated from 8 out of 10 HIV+ART individuals. Levels of viral replication varied in different donors and did not correlate with integrated HIV-DNA levels *ex vivo*. This assay was highly reproducible and results from independent experiments were significantly correlated ($r=0.96$, $p<0.0001$). Of particular importance, ATRA greatly increased and accelerated HIV reactivation efficacy in all donors tested, including those with undetectable HIV reactivation upon TCR triggering alone. The cost of this assay is estimated at 200$ per donor.

Conclusions: We described an easy, sensitive, and highly reproducible VOA that measures replication-competent HIV reservoirs in CD4+ T-cells of ART-treated individuals. This assay may be used to assess the efficiency of HIV eradication strategies and evaluate the risk of viral rebound upon treatment interruption.

HIV Virology (Viral and Host Factors)

Virologie du VIH (Facteurs liés au virus et à l'hôte)

BSP5.01

HIV-1 Gag -Dicer interaction effects in the RNAi pathway and in the viral cycle

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RNA interference (RNAi) is a post-transcriptional gene process in eukaryotes that controls host cell physiology such as differentiation, development and cell differentiation. RNAi occurs via the activity of small interfering RNAs (siRNA) or micro RNAs (miRNA), which are ~22 bp small non-coding double-stranded RNAs that hybridize to a target mRNA for further cleavage (siRNA) or translational repression (miRNA). This process requires Dicer, TRBP and Ago2 which form the RNA Induced Silencing Complex (RISC). In plants, insects and nematodes**,** RNAi is the key factor for immune responses against viral infections as well. In mammalian cells, it is still under debate whether RNAi is part of the immune system or not. What is known is that viral proteins can affect the RNAi pathway. HIV-1 is not the exception, whereby HIV-1 encodes Tat and Vpr proteins that affect Dicer function. In this work, we have identified a novel interaction between HIV-1 Gag and Dicer. By immunofluorescence (IF), proximity ligation assay (PLA) and co-immunoprecipitation (co-IP), we show that HIV-1 Gag interacts with Dicer in an RNA-independent fashion. We have mapped this interaction with Dicer to the nucleocapsid (NC) and Matrix (MA) domains. We are currently mapping the interaction domain in Dicer. Using 32P-miRLet7 and 32P-miR29a we show that Gag does not affect Dicer cleavage. This is consistent with our previous data that demonstrated that RNAi is functional during HIV-1 replication. Our results suggest that miRNA incorporation in the RISC may account for different miRNA amounts observed in HIV-1 infected cells. We are currently evaluating this incorporation by Dicer RIP-seq in the presence or absence of Gag. Through this results, we will show subtle modifications to the RNAi pathway mediated by Gag-Dicer interaction. These modifications could explain why the RNAi pathway is functional but modified by HIV-1.

BSP5.02

Impaired downregulation of NKG2D ligands by Nef protein from elite controllers sensitize HIV-1-infected cells to ADCC

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HIV-1 Nef clones isolated from a rare subset of HIV-1-infected elite controllers (EC), with the ability to suppress viral load to undetectable levels in the absence of antiretroviral therapy, are unable to fully downregulate CD4 from the plasma membrane. Residual CD4 left at the plasma membrane allows Env-CD4 interaction, which leads to increased exposure of Env CD4-induced epitopes and increases susceptibility of infected cells to antibody-dependent cellular cytotoxicity (ADCC). ADCC is mediated largely by natural killer (NK) cells, which control their activation status through the cumulative signals received through activating and inhibitory receptors. Recently, the activating NKG2D receptor was demonstrated to positively influence ADCC responses. Since HIV-1 Nef has been reported to reduce the expression of NKG2D ligands, including MICA, ULBP1 and ULBP2, we evaluated the relative abilities of Nef from EC and progressors to downmodulate NKG2D ligands. Furthermore, we assessed the impact of EC and progressor Nef on the ADCC susceptibility of HIV-1-infected cells. We observed a significantly increased expression of NKG2D ligands on cells infected with viruses coding for Nef from EC. Importantly, NKG2D ligand expression levels correlated with enhanced susceptibility of HIV-1-infected cells to ADCC. The biological significance of this correlation was corroborated by the demonstration that antibody-mediated blockade of NKG2D significantly reduced ADCC of cells infected with viruses carrying Nef from EC. These results suggest the involvement of NKG2D/NKG2D ligand interactions in the enhanced susceptibility of EC HIV-1-infected cells to ADCC responses.

BSP5.03

Characterization f Pre-Existing HIV-Specific CD4 T Cells in Uninfected Individuals

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Background: CD4 T cells (Thelper, TH) play a key role in antiviral immunity. Studies in mice and humans suggest that antiviral TH responses can be generated prior to pathogen exposure by cross-reactivity with other micro-organisms, and may shape TH responses upon infection or immunization. However, the functionality of such pre-existing HIV-specific TH in HIV-negative subjects is unknown.

Methods and Results: We investigated HIV-specific TH responses in HIV-uninfected donors (UD, n=18) and compared them to those of HIV-infected subjects (HI, n=53). We measured TH proliferative responses to HIV antigen (Ag) peptide pools using CFSE assays and grew HIV-specific TH cell lines (CL). We determined *ex vivo* responses by ICS and by co-upregulation of activation-induced markers (AIM) after Ag stimulation: i) CD69 and CD40L; or ii) CD25 and Ox40. We identified a high prevalence of HIV-specific proliferative TH responses in UD: 33% had a robust CFSE response to one or more HIV Ags (Gag, Env, Nef or Pol). Gag was less immunodominant in UD than HI. While ICS for Th0/1 cytokines (IFNg, IL2, TNF) and CD40L failed to identify HIV-specific TH in PBMCs directly *ex vivo*, they confirmed functionality of Gag- and gp41-specific CL derived from these UD. In contrast to ICS, AIM assays detected HIV-specific TH from UD directly *ex vivo*. Compared to total TH, HIV-specific $Ox40^{+}CD25^{+}$ TH were enriched in central memory and T follicular helper cells and preferentially expressed CXCR3. There was a direct correlation between the magnitudes of HIV-specific TH measured by the AIM and CFSE assays.

Conclusions: These results demonstrate that HIV-specific TH cells exist in a substantial proportion of UD, can target diverse HIV Ags and are detectable by functional assays including CFSE and AIM. These cross-reactive CD4 T cells could impact the development of virus-specific TH responses upon acute HIV infection and influence vaccine-induced immunity.

BSP5.04

HIV-1 Regulates Autophagy by Controlling mTORC1 and Lysosome Activity

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Eukaryotic autophagy is essential for maintaining cellular energy and metabolic homeostasis as well as for controlling multiple immunological functions. It provides a mechanism for the elimination of intracellular microorganisms, controls inflammation and is suggested to act as both an inducer and effector of innate and adaptive immune responses against intracellular pathogens, including viruses. Mounting evidence indicates that autophagy is targeted by HIV-1 and has led to efforts to understand the role of autophagy in HIV-1-infected cells. We recently demonstrated that HIV-1 induces the mammalian target of rapamycin (mTORC1) activation and promotes lysosome repositioning, two key mechanisms that regulate autophagy. Here we show that HIV-1 has inhibitory effect on autophagy, by lowering the accumulation of LC3-II and blocking p62 degradation (two key markers for autophagy activation), after exposure to the pro-autophagic compound Arsenite. These effects of HIV-1 are comparable to those obtained by co-treating cells with Arsenite and 3-MA, or Wortmanin, two inhibitors of autophagy. Using confocal and super-resolution microscopy, we demonstrate that HIV-1 redistributes LC3-positive mTOR-laden vesicles to the periphery of the cells, that normally cluster at a juxtanuclear region. Thus, HIV-1 likely decreases the number of juxtanuclear lysosome fusion events to impede autophagy. Finally, because lysosome localization influences their luminal pH, we tested if HIV-1 induces changes in the lysosomal pH, thereby impeding trafficking to repress autophagy. A combination of pH-sensitive lysosomal dyes and high-resolution microscopic analyses in live cells revealed that HIV-1 may regulate lysosomal acidification. A thorough understanding of how HIV-1 commandeers lysosome trafficking and autophagy could be translated and applied in novel approaches to eradicate the virus, putatively from its reservoirs. Therefore, targeting host machineries, proteins and signaling pathways on which HIV-1 depends will add to the arsenal to combat HIV-1.

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BSP5.05

Elevated frequencies of regulatory cells in the genital tract of HIV-1 highly exposed seronegative (HESN) women commercial sex workers

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Introduction: The majority of HIV infections affect women, mostly through heterosexual intercourse, particularly in sub-Saharan Africa. There is no current cure for HIV and the development of preventive strategies such as vaccines and microbicides remains the best solution to eradicate the HIV pandemic. We believe that efforts to develop effective devices should aim at mimicking and/or soliciting immune responses observed in the context of natural immunity to HIV. We have established an ongoing cohort of highly HIV-1-exposed female commercial sex workers (CSWs), in Cotonou (Benin), in which we have identified individuals who remain HIV-1-uninfected (HESN) after more than 4 years of active prostitution. We have shown that these women present a low-inflammatory cytokine profile in their genital tract. HIV interacts with many receptors such as Toll-like receptors to induce IFN-α, an important antiviral and immunomodulatory cytokine, which acts with other molecules to initiate a "tolerogenic/regulatory" anti-inflammatory loop. In view of further unravelling elements associated with a low-inflammatory natural immunity to HIV-1, we have characterized genital myeloid cells and regulatory T-cells and their frequencies.

Methods: Endocervical cells were collected by cytobrush in our 3 study groups; HESN and HIV-infected CSWs, as well as controls. Expression profiles of TLR-7, IFN-α, IL-10, HLA-G, and ILT-4 were analyzed on HLA-DR$^+$ myeloid cells and CD4$^+$ T-cells by flow cytometry.

Results: Endocervial myeloid HLA-DR$^+$ cells of HESN CSWs had an increased IFN-α and tolerogenic IL-10$^+$HLA-G$^+$ IL-T4$^+$ profile, moreoverwe found higher frequencies of CD103$^+$CD14$^+$CD11c$^+$ cells expressing IFN-α and IL-10. Furthermore, HESN CSWs had higher frequencies of PD-1 expressing regulatory Foxp3$^+$ CD4$^+$ T-cells than the 2 other groups.

Conclusion: These data suggest that tolerogenic myeloid cells expressing higher levels of IFN-α and regulatory T-cells could have a role in the modulation of mucosal inflammatory responses associated with the protection against HIV.

BSP5.06

LAG-3 inhibition of T cell activation

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Background: Persistent antigen stimulation of lymphocytes can lead to impaired cytokine production and cellular proliferation; this is known as 'exhaustion'. Exhausted cells express proteins that contribute to this dysfunctionality; LAG-3 is one such protein. When antigen is presented to a T cell, LAG-3 binds to MHC class II on the antigen presenting cell and impairs T cell activation; however, the mechanism of LAG-3-mediated impairment is unknown. Additionally, LAG-3 is upregulated on T cells latently infected with HIV. LAG-3 blockade may enhance the ability of latently infected cells to become activated and simultan-

eously, restore functionality of exhausted cells. In this way, LAG-3 blockade could encompass both arms of a "shock and kill" strategy, but a greater understanding of how LAG-3 inhibits cell function is needed.

Objective: To clarify the effects of LAG-3 blockade on human T cells.

Approach and Results: We stimulated human PBMC with the superantigen SEB with or without antibody blockade of LAG-3. We found that LAG-3 blockade enhances T cell proliferation, in support of similar findings by other groups.We also evaluated cross-linking methods for assessing the LAG-3 mechanism of inhibition.

Future Directions: We will use cross-linking and blockade methods to assess the intracellular effects of LAG-3. Specifically, we will assess the impact of LAG-3 on the T cell receptor signaling pathway. This will inform how LAG-3 inhibits T cell activation and its potential to reverse HIV latency.

BSP5.07

Incompatibilities between HIV-1 reference strains NL4.3 and SF2 reveal critical intra-molecular interactions in Nef

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Background: HIV-1 Nef enhances viral pathogenesis in part by downregulating cell surface proteins CD4, HLA-I and SERINC5 and modulating T cell signalling. Nef alleles from NL4.3 and SF2 strains display 86% amino acid similarity and are often used as experimental controls.

Methods: Mutants were generated by overlap extension PCR. Downregulation of CD4, HLA-I and SERINC5 was assessed by flow cytometry following transfection of Nef and SERINC5-(iHA) into CEM cells. Signalling was examined in Jurkat cells transfected with Nef and an NFAT-driven luciferase plasmid. Luminescence was measured at 6 hours following anti-CD3 stimulation. All functions were normalized to wild type Nef SF2.

Results: A Nef chimera encoding residues 1-57 (N-terminal arm) derived from SF2 and residues 58-206 (core) from NL4.3 was significantly impaired for its abilities to inhibit T cell signalling and to downregulate HLA-I and SERINC5 (36%, 27% and 62% activity, respectively), but remained functional for downregulation of CD4 (93%). Reversion of a threonine to arginine at residue 71 (T71R) in the PxxP motif on the NL4.3 core substantially restored activity (104%, 75% and 87%, respectively). Mutagenesis of the N-terminal arm indicated that the impact of T71R was modified by residues R8, S14, D54, and duplication of RAEP (residues 22-25). Linked genotype-phenotype data from 138 patient isolates demonstrated that clones encoding a duplication/insertion after position 25 were modestly more functional for signalling inhibition and HLA-I downregulation (p=0.008 & p=0.02, respectively), but not for CD4 downregulation (p=0.92).

Conclusions: Intra-molecular interactions between Nef's N-terminal arm and its core domains are critical for multiple functions, including modulation of T cell signalling and downregulation of HLA-I and SERINC5. Nef function may be optimized by alteration of binding between the highly variable N-terminal domain and the more conserved core. Our results suggest that this interaction could be explored as a new target for antiviral therapies.

BSP5.08

A highly conserved residue in HIV-1 Nef alpha helix-2 modulates protein expression

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Extensive genetic diversity is a defining characteristic of human immunodeficiency virus type 1 (HIV-1) and poses a significant barrier in the development of an effective vaccine. To better understand the impact of this genetic diversity on the HIV-1 pathogenic factor Nef, we compiled a panel of reference strains from the NIH Los Alamos HIV database. Initial sequence analysis identified point mutations at Nef residues 13, 84 and 92 in a subtype C reference strain C.BR92025 from Brazil. Functional analysis revealed impaired MHC-I and CD4 downregulation of Nef C.BR92025, which corresponded to decreased protein expression. Metabolic labeling demonstrated Nef C.BR92025 has an increased rate of protein turnover compared to the subtype B reference strain B.JRFL, which based on mutational analysis is related to Nef residue A84. An alanine to valine substitution at position 84, located in alpha-helix 2 of Nef was sufficient to alter the rate of protein turnover in an otherwise highly expressed Nef protein. In conclusion these findings highlight HIV-1 Nef residue A84 as a major determinant of protein expression that may offer an additional avenue to disrupt or mediate the effects of this key HIV-1 pathogenic factor.

BSP5.09

Responses of KIR3DS1+ versus KIR3DS1- NK cells to HLA-null cell stimulation

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Background: KIR3DS1 (3DS1) is an activating Natural Killer (NK) cell receptor (NKR) implicated in several viral infection, autoimmunity and cancer outcomes. In the context of HIV, co-carriage of *3DS1* and *HLA-Bw4*80I* alleles is associated with slower time to AIDS while *3DS1* homozygotes (hmz)

have a reduced risk of HIV infection. The ligand for 3DS1 is HLA-F, a non-classical MHC-1b antigen expressed on the HLA-null 721.221 (721) cells and HIV-infected $CD4^+$ T cells (iCD4).

Methods: PBMCs from 9 *3DS1hmz* donors stimulated with 721 cells. The frequency of $3DS1^{\pm}CD3^-CD56^{dim}$ NK cells exhibiting any combination of IFN-g, CD107a, or CCL4 function (total) and total IFN-g, CD107a, and CCL4 was assessed using gating strategies that included and excluded NK cell subsets co-expressing other NKRs that may contribute to $3DS1^+$ NK cell function. For results for inclusive gating on total functional, IFN-γ and CD107a positive cells PBMC from 7 *3DS1*hmz were tested twice (16 observations). For inclusive CCL4 and all exclusive gating experiments PBMC from 8 subjects were tested.

Result: We confirmed that 721 cells expressed HLA-F. Acid pulsing 721 cells, which favors formation of HLA-F open conformers that bind 3DS1, did not improve their ability to stimulate $3DS1^+$ NK cells. A significantly higher frequency of inclusively gated $3DS1^+$ than $3DS1^-$ NK cells responded to 721 stimulation for total, IFN-γ and CCL4 functions ($p \leq 0.05$, Wilcoxon matched-pairs test), A higher frequency of exclusively gated $3DS1^+$ than $3DS1^-$ NK cells responded to 721 stimulation for all functional subsets analyzed though differences did not achieve statistical significance.

Conclusion: We speculate that the interaction of 3DS1 on *ex vivo* NK cells with HLA-F on 721 cells is responsible for activating a higher frequency of $3DS1^+$ than $3DS1^-$ NK cells. *3DS1hmz* may have a reduced risk of HIV infection because HLA-F on iCD4 activates $3DS1^+$ NK cells for anti-viral functions.

BSP5.10

A Selective Role for UAP56 in Mediating HIV-1 Env Expression

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Toward development of novel strategies to inhibit HIV-1 replication, we have been examining the role of host factors in viral RNA processing and utilization. While most host mRNAs use NXF1 for export to the cytoplasm, HIV-1 unspliced (US) and singly-spliced (SS) RNAs require Rev mediated export by CRM1 to synthesize Gag and Env, respectively. To understand what advantage might be gained by using the CRM1 export pathway, we have performed shRNA knockdowns (KDs) of ribonucleoprotein (RNP) components involved in RNA export and translation for their effects on HIV-1 Gag and Env synthesis. Here, we report on our analyses of three factors, SKAR, UAP56 and Aly/REF, implicated in export and translation of host mRNAs. While KD of SKAR had no impact on expression of HIV-1 structural proteins, depletion of UAP56 and Aly/REF had limited effects on Gag expression but resulted in reduced Env synthesis. While KD of Aly/REF resulted in a reduction in SS and MS (multiply-spliced) viral RNA levels consistent with its role in RNA processing, reduced UAP56 levels had no impact on HIV-1 RNA abundance. Subsequent subcellular fractionation showed increased nuclear retention of SS and to a lesser degree, US viral RNAs upon UAP56 KD suggesting a novel role for UAP56 in Rev/ CRM1 trafficking of these RNA. Understanding how individual host factors contribute to HIV-1 gene expression provides insights that facilitate the development of novel therapies to control this infection.

BSP5.11

Identification Of Env As The First HIV-1 Antagonist Of The Interferon-Induced Restriction Factor HERC5: Evidence For Env Isolate Dependency.<CharStyle:>

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HERC5 has been evolving under strong positive selection for >413 million years, placing it at the forefront of the virus-host interface in vertebrates. We showed that HERC5 inhibits HIV-1 particle production by two mechanisms: HERC5 inhibits nuclear export of incompletely-spliced HIV-1 RNA and blocks an early step in the assembly of Gag at the plasma membrane. Despite potent HIV-1 restriction by HERC5 *in vitro*, infected individuals fail to control HIV-1 replication even though HERC5 is highly expressed during acute and chronic infection. This begs the question: does HIV-1 evolve an antagonist of HERC5 *in vivo*?

One of the most variable HIV-1 proteins is envelope (Env). In addition to being essential for binding and entering cells, Env counteracts some host restriction factors. For example, HIV-2 Env antagonizes tetherin, and prolonged passage of HIV-1 in IFITM-expressing cells produces Env mutants that overcome IFITM restriction. To determine if divergent Env proteins antagonize the ability of HERC5 to block Rev-dependent nuclear export, we independently co-expressed two different strains of Env with HERC5 and demonstrated that Env-IIIB, but not Env-BaL, antagonized HERC5 and fully rescued particle production. We also showed HERC5 and Env interact. To determine if biologically-relevant Env sequences antagonize HERC5, we developed a yeast-based cloning strategy to efficiently clone patient-derived Env sequences into an NL4-3 backbone. Env sequences from HIV-1-infected individuals in Uganda and Zimbabwe were individually cloned into the NL4-3 backbone. Co-expression of these constructs with or without HERC5 resulted in differences up to 4-fold in particle production. Interestingly, 2 of 6 patients screened thus far exhibited full rescue of particle production, 3 of 6 exhibited rescue of nuclear export (mechanism 1) but not particle release (mechanism 2), and 1 of 6 exhibited no rescue in particle production. Our data reports for the first time that specific strains of Env antagonize HERC5.

BSP5.12

HIV-1 Antisense Protein (ASP) Induces Autophagy and Is Also Targeted by the Proteasome Pathway

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Antisense transcription has been demonstrated to exist for HIV-1 and has further been proposed to encode a protein termed Antisense Protein (ASP), which was recently supported by *in silico* analyses. We have previously detected ASP in various mammalian cell lines by Western blot (WB), flow cytometry and confocal microscopy analyses and have reported that this protein induces autophagy, potentially through multimer formation, which improved viral production in a monocytic cell line. The aim of the current study was to further examine the mechanism of ASP-induced autophagy and to assess the susceptibility of ASP to degradation by autophagy and the ubiquitin-proteasome system (UPS). We firstly confirmed that expression of ASP from different HIV-1 clades induced autophagy by detecting increased LC3-II levels and decreased p62 (SQSTM1) levels, two well-known autophagy markers. Interestingly, we also found that clade A ASP, which lacks the first 25 amino acids, showed a more stable monomeric form and a lower capacity to induce autophagy. Through confocal microscopy, ASP was noted to co-localize with p62 and LC3-II in autophagosome-like cellular structures. Furthermore, co-immunoprecipitation experiments in COS-7 and HeLa cells confirmed the interaction between LC3-II, p62 and ASP. Interestingly, immunoprecipitation experiments in transfected 293T cells demonstrated that ASP is ubiquitinated. Using expression vectors for ubiquitin mutated at specific lysine residues blocking either autophagy or UPS, we found that ASP is subject to degradation through both pathways, although more intensively by UPS. We are thus suggesting that, although we have shown that ASP induces autophagy, which impacts HIV-1 replication, its abundance is also controlled by degradation mediated by UPS. Understanding the mechanisms underlying the degradation of ASP is essential to better assess its function and eventually determine if it could be a new target for antiretroviral therapy or vaccine development.

BSP5.13

PML/TRIM19 contributes to the antiviral state against HIV-1 in a cellular context-dependent manner.

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The promyelocytic leukemia (PML) protein (also termed TRIM19) belongs to the tripartite motif (TRIM) protein superfamily and is required for the proper assembly of a nuclear sub-structure termed PML nuclear body (PML NB). Since its discovery, PML was found to be involved in a wide variety of cellular activities including antiviral responses. The antiviral activity of PML against several DNA and RNA viruses has been well documented. Yet, the potential role of PML in immunity against lentiviruses is still unclear. To shed light on this possible PML function, we used both mouse and human models of PML-KO cells and infected the cells with pseudotyped lentiviral vectors expressing GFP in place of Nef as a marker for viral infectivity and gene expression. We found that PML is involved in the intrinsic immunity against lentiviruses in mouse embryo fibroblasts (MEFs) at two distinct steps, reverse transcription and post-integration proviral gene expression. The restriction mechanism that acted at early steps of infection was saturable at high doses of the lentiviruses even in the presence of excessive PML, demonstrating that PML is not the direct effector. The role of PML in the IFN-induced antiviral state against HIV-1 was also investigated. Our data showed that PML is involved in innate immunity against HIV-1 mediated by IFN-I in murine cells. The role of PML in the restriction of lentiviruses was analyzed in several human cell lines as well that were knocked out for PML using CRISPR/Cas9. In contrast to the results obtained in MEF cells, PML had no role in both intrinsic and innate immunity against lentiviruses in human cells. Altogether, our results reveal that PML restricts lentivirus infection indirectly in an isoform-specific and cellular context-dependent manner.

BSP5.14

Investigating the Role of Membrane Trafficking Regulator Sorting Nexin Proteins in HIV-1 Nef-mediated Extracellular Vesicle Release

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Despite treatment with anti-retroviral therapies, HIV-1 infected individuals have been found to have increased levels of extracellular vesicles within their plasma. Interestingly, these extracellular vesicles contain the HIV-1 accessory proteins Nef and Vpu, in addition to host cellular proteins implicated in inducing the activation of uninfected cells. Specifically, the secretion of extracellular vesicles from infected cells is mediated by Nef expression. However, the mechanism by which Nef mediates secretion of extracellular vesicles remains unknown. We hypothesized that Nef-mediated secretion of extracellular vesicles exploits membrane trafficking regulator proteins within the sorting nexin family. Using *in vitro* pull-down assays and bimolecular fluorescence complementation (BiFC), we demonstrated that sorting nexin 18 (SNX18) interacts with Nef *in vitro* and within cells. This interaction is dependent on the SH3 domain of SNX18 and a polyproline motif on Nef. Within cells, the Nef:SNX18 complex visualized utilizing BiFC localized to compartments containing CD63, a marker of extravesicular vesicles. Utilizing shRNA knock-down of endogenous SNX18 we are exploring the requirement of SNX18 in Nef-mediated extracellular vesicle release. This

work will shed light on the mechanisms through which extracellular vesicles are released from infected cells and thereby contribute to immune activation.

BSP5.15

PACT and ADAR1 multi-protein complex and its pro-HIV-1 function

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Our field of interest is the evading mechanism of Human Immunodeficiency Virus (HIV) in regards to the interferon-induced Protein Kinase R (PKR). Upon activation with dsRNA from a virus or by PKR Activator (PACT), PKR shuts down protein translation via phosphorylation of eukaryotic translation Initiation Factor 2α, thus, halting the production of new virions. While studying the aforesaid pathway in the context of HIV-infection, we observed that PACT acts as an inhibitor of PKR contrary to its initial function. The Adenosine Deaminase Acting on RNA (ADAR1), which was also thought to have anti-viral properties, has PKR inhibiting and proviral functions. Our aim is to determine the role of ADAR1 and PACT on PKR activation in HIV-replicating cells and in patients. Our hypothesis is that the combined activity of ADAR1, PACT and an HIV-1 component plays an important role in the establishment of HIV-1 infection in the host by acting on PKR and other anti-viral pathways.

We analyzed peripheral blood mononuclear cells (PBMCs) from HIV-1 infected and non-infected donors for interferon pathway and PKR interactome. ADAR1 is overexpressed in HIV-infected, and not in the healthy or treated sample groups. Moreover, an inverse correlation between ADAR1 and the phosphorylation of PKR is observed in some untreated patients. We established a cell model of PBMCs overexpressing ADAR1 using lentivirus and analyzed the proteins of the PKR pathway and viral production. Those cells showed an increased production and higher activity of virions compared to non-transduced cells. We then mapped a direct interaction between ADAR1 and PACT by immunoprecipitation assays. Furthermore, we showed that PACT, ADAR1 and Tat act in a multi-protein complex that stimulates the expression of a reporter gene expressed from a promoter with HIV-1 TAR element. This interaction is a potential target for a therapy aiming at the prevention of viral production.

BSP5.16

HIV-1 Nucleocapsid-induced stress granule assembly is disrupted by dsRNA binding protein Staufen1

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The HIV-1 nucleocapsid (NC) is a 9kDa viral protein that acts at pivotal stages of the viral replication cycle. It is composed of an N-terminal basic region, two zinc fingers and a linker region and has nucleic acid binding and chaperone activity. NC recruits a number of host proteins, including the double-stranded (ds)RNA-binding protein, Staufen1. Staufen1 was shown to regulate several steps in the replication cycle, such as Gag multimerisation and genomic RNA encapsidation, mediated at least in part via its dsRNA-binding domain (dsRBD) and resulting association to NC. We first observed that the overexpression of NC alone leads to the induction of SG assembly in >65% of NC-expressing cells (Yu et. al. Virology, 2016). In addition, NC interacted with key SG components TIAR and G3BP1 as shown by co-Immunoprecipitation assays. Moreover, NC-induced SG assembly was deemed unique because it was largely resistant to the SG blockade imposed by the HIV-1 capsid (CA). We then tested Staufen1's ability to block NC-induced SG assembly. Indeed, in Staufen1/NC coexpressing cells, NC-induced SG assembly was blocked in >85% of cells. Finally, it was found that NC reduces global translation rates, as judged by puromycylation of *de novo* synthesized proteins and polysome profile analyses. This work sheds light on an unexpected function of NC in RNA metabolism. A comprehensive understanding of the molecular mechanisms by which a fine balance of the HIV-1 proteins, NC and CA, act in concert with host proteins such as Staufen1 to modulate the host stress response will aid in the development of next generation anti-retrovirals.

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BSP5.17

Studies on the non-neural cholinergic system in HIV-infected individuals

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The non-neural cholinergic system (NNCS) works independently from neuronal cholinergic system and plays an important role in regulating inflammatory tone in the

body. The main effector molecule of the system, Acetylcholine (ACh), is an evolutionarily conserved neurotransmitter produced by neurons. It is also produced abundantly by non-neural cells. Outside the nervous system, CD4+ T cells and gastro-intestinal tract epithelial cells constitute the main source of this molecule. ACh exerts its effects via ACh receptors (AChR) of nicotinic (n) and muscarinic (m) types, which are expressed abundantly in immune cells in the body. The NNCS modulates differentiation, proliferation and functioning of several types of immune cells in the body. Very little is known about the regulation of the non-neuronal cholinergic system in HIV infections. We measured concentrations of ACh in the circulation of HIV-infected individuals. The concentrations were increased in these individuals. Anti-retroviral therapy (ART) tended to restore them to their physiological levels. Moreover, the concentrations of SLURP-1 (Secreted Ly6/Urokinase type plasminogen activator Receptor-related Peptide-1), an allosteric ligand for the α-7nAChR, were also increased in the circulation of HIV-infected individuals, and ART also tended to normalize them. In contrast to an increase in the concentrations of ACh and SLURP-1, the expression of the α-7nAChR tended to decrease on CD3+CD4+ T cells in the virus-infected individuals. As ACh exerts it anti-inflammatory effects mainly via α-7nAChR, we determined the effects of an agonist as well as of an antagonist of this receptor on HIV replication in human IL-2 and PHA-activated blasts. The agonist decreased whereas the antagonist increased the viral replication. Our results suggest that α-7nAChR agonists that do not cross blood brain barrier may be beneficial in reducing viral replication and attenuating aberrantly activated immune system in HIV-infected individuals.

BSP5.18

Reverse transcriptase inhibitor resistance substitutions can alter the SAMHD1-dependent HIV-1 replication profile in primary human cells

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The enzymatic properties and phenotypes of mutated viruses containing the drug resistance mutations M184I/V and E138K, alone or in combination have been studied. These reverse transcriptase inhibitor (RTI) resistant mutant viruses display different enzymatic processivity and polymerization rates under high and low dNTP levels. SAMHD1 is a recently identified host restriction factor that inhibits viral replication by limiting dNTP stores in myeloid cells and resting CD4+ T-lymphocytes. It is therefore conceivable that cells that possess different dNTP levels might be differentially susceptible to the effects of drug resistance substitutions.

Accordingly, we infected various primary immune cells with RTI resistant viruses and measured viral infection by qRT-PCR. We also used the same viruses to infect THP-1 stable cells lines that express or are down-regulated for SAMHD1. We found that viruses harboring M184V replicated better than wild type in resting CD4+ lymphocytes and monocyte-derived dendritic cells (MDDC) isolated from CD14+ cells. M184I containing viruses replicated better in cells with higher dNTP levels such as activated CD4+ T-lymphocytes and THP-1 lacking SAMHD1.

SAMHD1 restricts HIV replication in myeloid cells and resting CD4+ T-lymphocytes at least in part by limiting dNTP cellular stores to thus inhibit reverse transcription. Several mutations that confer resistance to HIV against reverse transcriptase inhibitors (RTI) also improve RT affinity for dNTP substrates. We show here that some RTI-resistant viruses replicate better than wild-type viruses in resting CD4+ T-lymphocytes and monocyte-derived dendritic cells. Given that resting CD4+ T-lymphocytes and myeloid cells that express high levels of SAMHD1 contribute to the persistent HIV reservoir, our results have potential implications for the development and long-term archiving of RTI-resistant viruses.

BSP5.19

The role of 3'PPT and cPPT in HIV-1 replication

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It has been shown that the reverse transcription is an essential step in HIV-1 life cycle, in which central and 3' Polypurine tracts (cPPT and 3'PPT) function as primers for synthesis of the plus strand DNA. However, why HIV-1 has two PPTs and which one is more important are not yet known.

In the present study, we utilized a yeast recombination technique to introduce extensive synonymous mutations into cPPT and/or 3'PPT, and tried to completely destroy their priming function. The resultant mutated PPT RNA/DNA hybrids were subjected to in vitro priming assay, and the mutant clones were then detected for replication capacity through infecting both U87.CD4.CXCR4 and CEM×174 cell lines.

The results showed that the extensive mutations could significantly reduce the priming function of either cPPT or 3'PPT. However, the viral clone with the mutations in cPPT could still replicate almost as efficiently as the wild-type virus, while the 3'PPT mutant significantly decreased the viral replication efficiency. The clone with mutations in both PPTs further reduced the viral replication efficiency. We also found that the insertion of new PPT sequence in other regions of HIV-1 genome was not able to rescue the viral replication. This study suggests that 3'PPT sequence only is sufficient in supporting HIV-1 replication, and the cPPT might not be essential for virus replication.

BSP5.20

The HIV-1 Antisense Protein (ASP) Demonstrates Post-translational Modifications and Nuclear Localisation with an HIV-1 LTR-Inducing Activity

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Recent *in silico* analyses of different HIV-1 isolates have confirmed the existence of an antisense open reading frame overlapping the HIV-1 *env gene*, termed Antisense Protein (ASP). The detection of this protein has been difficult and although we have previously suggested that ASP could be associated to autophagy, its function remains unclear. Based on its link to autophagy, we hypothesized that ASP is weakly expressed in infected cells and might thus be more stable in this context. Detection of ASP from different HIV-1 clades was thus tested in various cell types using a new lentiviral vector. We first showed that, for all tested ASP-expressing vectors, ASP was stably detected at a higher molecular weight than expected and presented different signals. Further experiments demonstrated that this was not due to ASP dimer formation. Western blot analyses and confocal microscopy revealed that ASP, although predominately located in the cytoplasm, also presented a nuclear distribution. Interestingly, treatment with leptomycin B, a nuclear export inhibitor, resulted in higher nuclear accumulation. By transfection of 293T cells, we further demonstrate that the naturally N-terminal truncated subtype A ASP and a similarly truncated version of subtype G ASP could transactivate the HIV-1 LTR, unlike full length versions of ASP from any non-A subtypes. Intriguingly, the HIV-1 LTR-inducing capacity of N-terminally truncated ASP correlated with a more pronounced nuclear distribution. Moreover, transduction of ACH-2 cells with ASP-expressing lentiviruses resulted in induced HIV-1 expression, as determined by Western blot analyses. Our data suggest that nuclear localisation of ASP might be dependent on amino terminal truncation, which is associated to its capacity to induce HIV-1 LTR activation. Efforts are ongoing to determine the nature of the post translational modification of ASP by mass spectrometry analyses and to further address the ASP-induced modulation of HIV-1 LTR activity.

Host Genetics and Viral Evolution

Génétique de l'hôte et évolution virale

BSP6.01

Substantial intra and inter-individual Nef diversity and immune escape burden in a Canadian early HIV-1 infection cohort

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Introduction: HIV-1 diversity and immune escape represent major challenges to vaccine and eradication strategies. The gene encoding the accessory protein Nef exhibits particularly rapid within-host immune-driven evolution and high between-host diversity. We characterize intra- and inter-individual Nef diversity and immune escape in early HIV-1 infection.

Methods: This was a cross-sectional study of 30 individuals with early (< 6-months) HIV-1 infection recruited in Toronto. A minimum of three Nef clones per participant were isolated from plasma HIV-1 RNA via nested RT-PCR and standard molecular cloning followed by sequence verification. HLA class I types obtained via PCR-SSOP were inferred to subtype-level resolution using a probabilistic imputation method. HIV-1 subtype B clonal Nef sequences were analyzed for the presence of published HLA-associated polymorphisms (defined at the HLA supertype, type and subtype levels).

Results: Analysis of plasma Nef sequences identified 25 (83.3%) subtype B, 3 (10.0%) subtype AE, 1 (3.3%) subtype G, and 1 (3.3%) recombinant BF infections. Within-host Nef clones differed by a mean of 3.5 (standard deviation [SD] 3.0; range 0-10) non-synonymous substitutions. After exclusion of individuals who had likely not yet resolved peak viremia, within-host Nef amino acid diversity correlated positively with plasma viral load (Spearman's R= 0.43, p=0.046). Among HIV-1 subtype B infections, clonal Nef sequences exhibited specific adaptations to the individual's HLA allele(s) at a mean of ~6% of sites known to be under selection by those HLA alleles, and exhibited inferred adaptations at an additional mean of 64% of sites. No correlation between pVL and escape burden was observed.

Conclusion: A substantial minority (>15%) of recent HIV-1 infections in this Toronto cohort are non subtype-B. Within hosts, Nef diversity and immune escape burden are already substantially elevated in early infection. Seeding of the reservoir with diverse, HLA-adapted sequences may represent a barrier to their elimination by host immunity.

BSP6.02

TILRR, a transcript variant of FREM1, is a potential enhancer of inflammation and HIV-1 vaginal infection through interacting with NFκβ signaling pathway

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TILRR is a novel regulatory component, which stimulates host defense against infection through binding to IL-1R1 and TLR complex and enhancing the recruitment of MYD88 in the Ras-dependent NFκβ signal transduction pathway. Our previous study identified FREM1 as a novel candidate gene in correlation with HIV-1 resistance/susceptibility in the Pumwani Sex worker cohort. In this study, we investigated the effect of TILRR on global gene expression profile of NFκβ signaling pathway by over-expressing it into human cell lines.TILRR was overexpressed in HeLa cells using eGFP tagged plasmid construct.

TILRR RNA overexpression was confirmed by qRT-PCR. The effect of TILRR on the expression of 84 genes linked to NFκB pathway was subsequently investigated by qRT-PCR. Conditioned media were also tested for the protein level expression of important cytokine/chemokines using Bioplex cytokine/chemokine bead assay.

Overexpression of TILRR significantly upregulated 32- and 52-genes, along with downregulated 15- and 4-genes in IL-1β treated and non-treated cells, respectively. We observed that most of the pro-inflammatory cytokine/chemokine encoded genes, like IL-1β, IL-6, TNFα, and IL-8 (chemokine) were significantly increased at mRNA level expression. We further noticed that all important cytokine/cheomokines, those assessed for mRNA level expression, were also consistently secreted at the protein level expression in conditioned media. All data obtained from 3-independent experiments using two unique techniques, which suggest a potential link of TILRR in HIV-1 vaginal infection through enhancing the NFκβ and inflammatory responses.

Although how TILRR influence the expression of these genes needs to be further studied, our study is the first to show that TILRR may influence the expression of genes directly involved in HIV-1 infection in addition to its role in enhancing NFκB and inflammatory responses. NFκB and inflammatory response pathways are extremely important in HIV-1 transmission; therefore, further study of the role of TILRR may identify novel intervention targets and strategy against HIV-1 vaginal infection.

BSP6.03

Subtype-specific HIV Adaptation to Host Immunity Revealed Through Statistical and Functional Analyses

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Background: The extent to which viral genetic context constrains HLA-driven immune escape pathways in HIV remains incompletely understood. We combine phylogenetically-informed statistical analyses with *in vitro* functional assessments to investigate HLA-driven adaptation in a host population where multiple HIV-1 subtypes co-circulate (Uganda).

Methods: HLA-associated polymorphisms in HIV-1 Gag, Pol and Nef were identified in 200 antiretroviral-naive individuals infected with subtype A1 and 135 infected with subtype D. Their strengths of selection were then compared across HIV-1 subtypes using a phylogenetically-informed logistic regression approach to identify instances of differential selection between subtypes. Multiple testing was addressed using q-values. Infectious molecular clones expressing consensus and mutant subtype A1 or D gag/protease sequences in an HIV-1 NL4.3 backbone were constructed using Gibson Assembly and used to produce VsVg-pseudotyped virus stocks. *In vitro* replication of these viruses was assessed using a 7-day GFP-reporter-based assay.

Results: A total of 83 Gag, 198 Pol and 105 Nef HLA-associated polymorphisms were identified in subtype A1 and/or D at $q<0.2$ (all $p<9x10^{-4}$). Of these, 34% (Gag), 39% (Pol) and 27% (Nef) exhibited significant differential selection *between* subtypes ($p<0.05$; $q<0.1$). For example, HLA-B*57:03 strongly selected Gag-T242N in subtype D (Odds Ratio [OR]=250; $p=2x10^{-10}$), but not subtype A1 (OR=1.8; p=0.8)(inter-subtype comparison $p=8x10^{-6}$; q=0.001). This raised the hypothesis that the subtype A1 consensus proline at adjacent Gag codon 243, which differs from the consensus leucine observed in subtype D, is incompatible with T242N. Indeed, a subtype A1 virus carrying 242N/P243 exhibited >10-fold poorer *in vitro* replication compared to consensus A1, confirming HIV-1 subtype-specific constraints on immune escape at this position.

Conclusions: Statistical analyses applied to linked HIV-1/HLA datasets can illuminate HIV-1 codons where mutational immune escape pathways may be constrained in

certain HIV-1 subtypes. Functional validation of these incompatible mutation combinations may help identify subtype-specific mutationally-constrained viral regions for vaccine design.

BSP6.04

Genetic overlap between resistance to HIV acquisition and psychiatric and inflammatory traits

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Other than the well described CCR5Δ32 polymorphism, identification of genetic loci that modify host susceptibility to HIV infection has been elusive. This is likely due to the difficulty in defining phenotypes of reduced HIV susceptibility which limit sample sizes (and therefore power) for genome-wide association studies. Polygenic approaches that assess the combined impact of multiple variants have proven successful in identifying missing heritability and understanding genetic architecture for many phenotypes. Recently, polygenic approaches have been developed to directly assess the potential for genetic overlap (i.e. shared genetic aetiology) between traits that account for differential linkage disequilibrium (LD) around associated loci. We applied one such method, LD score regression, to compare the genetic architecture of HIV acquisition to data from publicly available phenotypes. We compared association results from a GWAS of HIV acquisition performed in >11,000 individuals to >200 traits obtained from the NHGRI GWAS catalogue. We observed significant levels of genetic overlap between HIV acquisition and schizophrenia (rG= 0.19, p=0.0007), ulcerative colitis (rG= 0.22, p= 0.0061), and inflammatory bowel disease (IBD; rG=0.19, p=0.01). Refinement of model covariate demonstrated that the overlap between HIV acquisition and schizophrenia is driven in part by their shared overlap with cannabis use and sexual behavior. We further investigated which individual SNPs were most strongly associated across traits and observed three SNPs that exceeded our threshold for statistical significance. Two of these are eQTLs in whole blood for genes coding for proteins suspected to be involved in HIV biology: rs1819333 in *CCR6* (p=0.0002) and rs4932178 in *FURIN* (p=0.00033). These results highlight the ability to use polygenic methods to gain new insights into complex diseases and identify potential biomarkers for HIV acquisition risk.

BSP6.05

Associations Between Host Characteristics and Within-Host HIV Evolution

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Background: Host characteristics may affect within-host evolutionary rates leading to variation in genotypic diversity. Phylogenetics can be used to quantify genotypic diversity relative to different host characteristics. In a phylogenetic framework we quantify within-host genotypic diversity in BC patients to elucidate associations between host characteristics and HIV genotypic variation.

Methods: Retrospective genotype data from BC patients (N=1,341, median sample number = 4, average duration of time covered per patient = 2,404 days) with 2 or more longitudinal samples tested at the BC Centre for Excellence in HIV/AIDS was combined with patient characteristics collected by the BC Drug Treatment Program. Using phylogenetic trees generated from the sequence data and comparing nucleotide and amino acid changes we calculated **within-host diversification-rates** (branch splitting rate relative to time) and **phylogenetic-diversity** (within-host phylogenetic tree branch length sums) for each patient over time. The distribution of these scores were analysed for demographic characteristics such as risk factor [men who have sex with men (MSM), injection drug users (IDU), heterosexuals (HET)], hepatitis C infection (HCV), treatment history and ethnicity using R.

Results: Patients with HCV co-infection were found to have higher diversification rates ($p< 0.001$) compared to patients without HCV. Comparing risk groups, IDU were found to have higher diversification-rates compared to MSM ($p< 0.001$) and HET ($p< 0.001$). Comparing ethnicities, First Nations had higher diversification-rates compared to Asians ($p< 0.001$), Blacks ($p<0.001$), and Caucasians ($p<0.001$). Patients without virological resistance to Non-Nucleoside Reverse-Transcriptase, Nucleotide Reverse-Transcriptase and Protease inhibitors had lower phylogenetic-diversity ($p<0.001$) compared to patients with resistance.

Conclusions: These results imply HCV co-infection, risk factors, ethnicity and drug resistance are associated with variation in within-host viral evolution. This variation likely arises through differences in adherence, viral load and infection duration; further analyses will model their effects. Disentangling factors influencing within-host evolution is crucial for understanding viral adaptation.

Immunology of HIV and Vaccines

Immunologie du VIH et vaccins

BSP7.01

Studies on the regulation of IL-37 and its receptor in HIV-infected individuals: implications for HIV replication and T cell death

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Interleukin 37 (IL-37) is a relatively new member of the IL-1 family. Like other members (IL-1 beta and IL-18) of the family, it is synthesized as a precursor protein, which is cleaved by caspase-1 into its mature form. However, unlike these members of the family, IL-37 is an anti-inflammatory cytokine with intracellular and extracellular functions. Both its precursor and mature forms bind with the IL18 receptor alfa chain (IL-18Ralfa) with very low affinity compared to that with IL18. IL-37 does not antagonize IL-18 but can form a complex with IL-18 Binding Protein (IL-18BP), and increases the ability of IL-18BP to neutralize mature IL-18. IL-37 transgenic mice are relatively protected from the lipopolysaccharide (LPS)-induced septic shock, dextran sulphate-induced colitis and allergen-induced airway hyper-responsiveness. We investigated the regulation of IL-37 and its receptor component SIGIRR in HIV-infected individuals. For this purpose, IL-37 concentrations were determined in serum samples with an ELISA kit. We also determined expression of SIGIRR on different cell types and measured its soluble form in the virus-infected individuals. The impact of the cytokine on HIV replication was also determined in vitro in monocyte-derived macrophages (MDM) as well as in PHA blasts. We also tested the ability of the cytokine to reduce the expression of activation markers on PBMC. In these experiments, no significant difference was observed in the concentrations of IL-37 between HIV-infected and healthy control individuals. However the virus-infected long term non-progressors showed significantly higher levels of this cytokine. The cytokine also increased survival of the cells in freshly thawed PBMC. The cytokine reduces production of the virus in human cells and reduces expression of CXCR4 on T cells. Restoring the functional activities of the cytokine may benefit HIV-infected individuals by attenuating inflammation and immune activation.

BSP7.02

Influenza vaccine responses are limited in HIV positive individuals, and not predicted by altered B cell phenotype

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Introduction: Human Immunodeficiency Virus (HIV) is a chronic disease, and while antiretroviral (ARV) agents allow for disease control, long lasting immune changes persist. Influenza vaccination is recommended for HIV$^+$ patients even though it is known that it is less effective in providing immunity. It is not clear if there are clinical or immune cell markers that are predicative of influenza vaccine response in HIV+ individuals.

Purpose: Identify immune cell exhaustion and clinical markers associated with poor response to influenza vaccination in HIV$^+$ patients.

Methods: Peripheral blood mononuclear cells (PBMC) from 12 HIV$^+$ patients (10 male, 2 female) were collected pre-influenza vaccination and 6 months post vaccination after obtaining informed consent. HAI assays for the 3 components of the 2015-2016 trivalent influenza vaccine were performed. Standard of care clinical and virologic data were obtained through routine blood draws. B cell (CD10, CD19, CD20, CD21, CD27) and T cell (CD3, CD4, CD8, CD27, CD28, Tim-3, PD-1, CTLA-4, and CD57) immunophenotyping was performed. CMV status was determined by clinical and in-house serologic assay, as well as T cell ELISpot.

Results: As previously reported, influenza vaccine titers were low or limited, with only 5 influenza responders regardless of previous vaccination. No individuals had self-reported influenza disease. Influenza response was not predicted by CD4+ T cell count, CD4:CD8 ratio, viral load suppression or the frequency of B cell tissue like memory (TLM) cells. TLM B cells were not elevated in the responders versus non-responders. CMV responses were present in the all individuals, and data on the correlation between influenza titer, and CMV specific T cell responses will be presented.

Conclusion: Poor responsiveness to a potent vaccine such as influenza is not directly related to traditional immune exhaustion markers. A more comprehensive analysis of cumulative immunity will be necessary to accurately predict vaccine response.

BSP7.03

Multiple Inhibitory Immune Checkpoints Modulate HIV-specific CD4 T Cell Exhaustion.

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Chronic viral infections, like HIV, lead to waning of virus-specific T cell function, termed « exhaustion ». This exhaustion weakens CD4 T lymphocyte (TH) function, negatively impacting viral control. Elite controllers (EC) can spontaneously control HIV replication without treatment and have preserved TH function. Here we compare the role of inhibitory receptors (IR) as immune checkpoints in HIV-specific TH exhaustion from EC and chronic progressors (CP).

We collect PBMCs from HIV-infected untreated subjects either with controlled viral load (EC; <40 copies/ml; n=9) or uncontrolled VL (CP; >5000 copies/ml; n=11). We identify HIV-specific TH by the surface co-expression of activation markers (CD69, CD154) following a 9-hour *in vitro* stimulation with a pool of peptides from HIV (Gag or Env) or other pathogens (CMV, Tetanus, HBV), then phenotype them by flow cytometry.

HIV-specific TH preferentially express several IR in CP compared to EC: PD-1 (85,0% vs 65,4%; *P*<0,05), the newly defined TIGIT (63,4% vs 36,0%; *P*<0,01), and CD200 (61,6% vs 28,3%; *P*<0,01). Interestingly, the latter two are markedly upregulated on cells specific to HIV antigens only. Co-express of IRs is also much higher in HIV-specific TH from CP than EC (49,5% express all 3 IR simultaneously, vs 13,6%; *P*>0,001). Furthermore, HIV-specific TH differentiation is skewed towards a T follicular helper (pTfh) phenotype in both groups, with further upregulation in IR on the pTfh compared to non-pTfh.

We validated an innovating technique to characterize HIV-specific TH cells. With this method, we show that dysregulation of HIV-specific TH is driven by an increase in variety and quantity of IR, and that these cells have a skewed differentiation. Our findings could help identify potential therapeutic targets to reverse exhaustion in CPs, paving the way towards a functional cure.

BSP7.04

Pathogenicity of CD16+ Monocyte-Derived Dendritic Cells during HIV-1 Infection

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Background: During HIV-1 infection, $CD16^+$ monocytes represent a major source of pro-inflammatory cytokines and their exacerbated frequency is not normalized with ART. Monocytes are precursors for dendritic cells (DC), key antigen-presenting cells. It remains unknown whether $CD16^+$ and $CD16^-$ monocyte-derived DC (MDDC) are functionally distinct and if the altered $CD16^-/CD16^+$ ratio impacts on the quality of immunological responses during HIV infection. Here we performed a genome-wide transcriptional profiling of CD16+ *versus* CD16- MDDC subsets in relationship with their ability to present antigens and disseminate HIV to CD4+ T-cells.

Methods: Monocyte subsets were isolated by flow cytometry (BD-AriaII). MDDCs were obtained by culture in presence of GM-CSF/IL-4. Genome-wide transcriptional profiling were performed using the Affymetrix technology in matched $CD16^+/CD16^-$ MDDC from n=5 subjects before and after exposure to LPS and HIV. The *trans*-infection ability and immunogenic potential were evaluated by co-culturing MDDC with autologous $CD4^+$ T-cells in the presence or absence of HIV (NL4.3BaL) and antigens (SEB, CMV, *C. albicans, S. aureus*).

Results: Despite a similar ability to express classical DC markers, $CD16^+$ distinguished from $CD16^-$ MDDC by a superior ability to transmit HIV infection to $CD4^+$ T-cells proliferating in response to *S. aureus*. Genome-wide transcriptional profiling revealed unique molecular signatures in $CD16^+$ *versus* $CD16^-$ MDDCs in terms of surface markers, and differences relative to the gene ontology terms transcription factors, cytokines, adhesion, chemotaxis, and cell projection. Gene set variation analysis identified canonical pathways and biological processes enriched in $CD16^+$ and $CD16^-$ MDDCs. A meta-analysis using the *NCBI Interaction database* identified differentially expressed HIV dependency factors.

Conclusion: These results reveal the critical role played by $CD16^+$ MDDC during HIV infection, with relevance for viral reservoir establishment and persistence in $CD4^+$ T-cells during ART. These findings point to the importance of $CD16^+$ MDDC targeting in the development of a successful HIV cure.

BSP7.05

Phenotypic and Functional Maturation of NKG2Cnull Natural Killer Cells in HIV-infected Individuals

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Inactivation of a natural killer cell (NK) activating receptor gene, NKG2C, diminishes resistance to HIV-infection and accelerates disease progression. NK expressing NKG2C and CD57 expand following cytomegalovirus (CMV) infection, downregulate FcRγ, and demonstrate enhanced antibody-dependent cellular cytotoxicity (ADCC). Insufficient differentiation of NK with superior ADCC in HIV/CMV co-infection could diminish immunological control of HIV. Therefore, our objective was to investigate if CMV-driven NK differentiation is impaired in HIV-infected NKG2C^{null} individuals.

Prospective NKG2C^{null} individuals identified by flow cytometry were verified by polymerase chain reaction. Phenotypic (CD57$^+$, FcRγ$^-$) and functional (IFN-γ, TNF-α induction) NK differentiation was compared between matched NKG2C^{null} and NKG2C-expressing individuals by flow cytometry following stimulation through natural cytotoxicity receptors by K562 cells or through CD16 with the monoclonal antibody 3G8. Our data so far indicate similar CMV-driven differentiation of NK in NKG2C^{null} and NKG2C-expressing HIV-infected individuals matched for age and infection history (Table 1).

Our results imply equivalency, but whether comparable functional differentiation occurs in a CMV-specific context remains undetermined. To assess CMV-specific ADCC, CMV-infected MRC-5 fibroblasts will be ^{51}chromium labeled and incubated with peripheral blood mononuclear cells from our matched study groups together with either CMV-seropositive or control plasma. This system enables interaction between NKG2C and its ligand, HLA-E. Diminished ability to control CMV infection might indirectly contribute to the impact of NKG2C deletion on progression of HIV infection.

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Table 1. Differentiation of NK in NKG2Cnull versus NK2GC-expressing individuals

Phenotypic characteristics			
NKG2Cnull n=8 (Median, IQR)		**NKG2C+ n=8 (Median, IQR)**	
% NK CD57$^+$	55.90, 48.20-81.20	56.45, 52.78-68.20	(p = ns)
% NK FcRγ$^-$	27.55, 19.83-43.83	29.05, 17.33-62.45	(p = ns)
Functional characteristics			
% NK IFN-γ$^+$ (K562)	3.25, 1.75-4.15	1.00, 0.50-5.50	(p = ns)
% NK TNF-α$^+$ (K562)	2.00, 1.20-5.48	3.40, 1.33-4.68	(p = ns)
% NK IFN-γ$^+$ (3G8)	11.90, 4.93-17.73	9.10, 5.23-14.55	(p = ns)
% NK TNF-α$^+$ (3G8)	10.15, 1.63-15.05	10.95, 6.43-16.08	(p = ns)

BSP7.06

Impact of sustained virologic suppression on HIV-specific cell-mediated immune responses in children and adolescents

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Background: Cell-mediated immune (CMI) responses play a major role in controlling viral replication in adult and pediatric HIV-1 infection. Gag-specific CMI is strongly associated with levels of viremia and HIV disease progression. We examined the relationship between Gag-specific T-cell responses and the extent and duration of sustained viral suppression (SVS) resulting from treatment with combination antiretroviral therapy (cART) in a group of HIV-infected children.

Methods: Peripheral blood mononuclear cells (PBMC) obtained from HIV-infected children and adolescents (n=51) were used in ELISpot assays to measure IFN-g production in response to stimulation with clade-matched HIV-1 Gag peptide pools. ELISpot positivity was defined according to standard criteria (>50 spot-forming units [SFU] per 10^6 cells and 2 SD over negative controls). The magnitude (cumulative, mean, and median SFU per 10^6 cells) and breadth (proportion of pools inducing IFN-g production) were compared with age and duration of virologic suppression under cART.

Results: Nineteen subjects (37.3%) were infected with clade B HIV-1 and 17 with clade C (33.3%). Median absolute CD4+ T cell counts at baseline were 714 cells per mm^3 (interquartile range=539-952 cells per mm^3). A statistically significant association was observed between age (median=13.7 years, interquartile range=9.99-16.4 years) and magnitude of the IFN-g response (cumulative: p=0.0011; mean: p=0.0013; median: p=0.0015; Spearman correlation test) and between age and breadth of antigenic recognition (p=0.0004). Proportion of life on effective cART leading to SVS (PLEC; median=37.8%, interquartile range=13.2-67.6%) was also negatively correlated with the magnitude (cumulative: p=0.0008; mean: p=0.0009;

median: p=0.0237) and breadth (p=0.0247) of Gag-specific IFN-g responses.

Discussion: The positive correlation between age and HIV-specific T-cell responses suggests progressive evolution in magnitude and breadth of antigenic recognition with age in HIV-infected children. The proportion of life with SVS, likely reflective of reduced exposure to HIV antigens, emerged as a strong, independent negative predictor of HIV-specific CMI.

BSP7.07

CD4-Mimetics Sensitize HIV-1-infected Cells to ADCC Mediated by Antibodies Elicited by Multiple Envelope Glycoprotein Immunogens in Non-Human Primates

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Introduction: Recent studies have linked antibody Fc-mediated effector functions with control of human immunodeficiency virus type 1 (HIV-1) and simian immunodeficiency virus (SIV) infections. Interestingly, the presence of antibodies with potent antibody-dependent cellular cytotoxicity (ADCC) activity in the Thai RV144 vaccine trial correlated inversely with HIV-1 acquisition risk. These antibodies were recently found to recognize HIV envelope (Env) epitopes exposed upon Env-CD4 interaction. Accordingly, small CD4-mimetics (CD4mc) able to force Env to sample the CD4-bound conformation were shown to sensitize HIV-1-infected cells to ADCC mediated by sera from HIV-1-infected individuals. However, whether this strategy also works with antibodies elicited through Env-immunization is not yet known.

Methods: We explored the capacity of CD4mc to sensitize HIV-1-infected cells to ADCC mediated by sera from Env-vaccinated non-human primates (NHP) using a FACS-based ADCC assay. We also evaluated their ability to sensitize HIV-1 viral particles to neutralization by sera from these NHP-immunized animals.

Results: We found that antibodies elicited in immunized NHP were unable to mediate ADCC in the absence of CD4mc. Interestingly, the ability of these antibodies to neutralize viral particles correlated better with recognition of infected cells than with their ability to mediate ADCC.

Conclusion: Our observations indicate that CD4mc are capable of sensitizing HIV-1-infected cells to ADCC mediated by easy-to-elicit non-neutralizing antibodies, suggesting that combining a vaccine with a CD4mc compound might be useful as a prophylactic strategy against HIV-1 transmission. They also indicate that recognition of an infected cell does not fully explain the ability of a given antibody to mediate ADCC, suggesting that other factors such as the angle of approach might be important for this Fc-mediated effector function.

BSP7.08

Sustained antibody (Ab)-dependent functions in the absence of detectable viremia is associated with non-progressive HIV infection

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Background: Understanding the correlates of protection during HIV infection represent an important step toward the development of a potent HIV vaccine. High levels of Ab-dependent (AD) cellular cytotoxicity (ADCC) activity was associated for the first time with a reduced risk of HIV infection in the RV144 vaccine trial. Here, we evaluated levels of anti-gp120 specific Abs and AD functions such as ADCC, AD cellular trogocytosis (ADCT), AD cellular phagocytosis (ADCP) and AD complement deposition (ADCD) in patients who naturally control HIV infection without antiretroviral treatment (i.e. elite controllers, EC), as compared to treated and untreated progressors (TP, UTP).

Methods: The study population included 18 UTP, 24 TP and 37 EC. Plasma concentrations of total IgG and anti-gp120 IgG were measured by ELISA. CEM.NKr.CCR5 (PKH26+) infected with HIV or coated with gp120 were incubated with plasmas and used as targets cells (TC) for ADCC, ADCT and ADCD assays. The joint ADCC/ADCT assay measured the frequency of dead/apoptotic TC and PKH26+ effector cells respectively. The ADCD assay measured deposition of the C3b-complement component on TC. The ADCP assay measured the uptake of gp120-coated beads by THP-1 cells.

Results: Plasma from UTP and EC had significantly higher levels of anti-gp120 Abs than TP, before and after normalization with total IgG (p<0.0003, no differences between UTP and EC). Both UTP and EC showed significantly higher ADCC, ADCT, ADCP and ADCD activities than TP (Kruskall-

Wallis test). Anti-gp120 Ab concentrations in plasmas were positively correlated with AD activities in TP and EC but not in UTP (spearman test).

Conclusions: By contrast with TP, EC are able to maintain high levels of anti-gp120 Abs and AD functions in the absence of detectable viremia. The absence of correlations between anti-gp120 Abs levels and AD functions in UTP suggests that Abs generated during viremic episode have reduced/altered Fc-mediated functions.

BSP7.09

Ectopy-associated enhancement of neutrophil protease and leukocyte recruitment pathways during pregnancy

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Introduction: HIV risk increases two-fold during pregnancy but the mechanisms are not well understood. In non-pregnant women changes to the female genital tract (FGT) mucosa, such as increased inflammation and microbiome alterations, have been linked to increased HIV risk. Here we assessed host and bacterial differences in pregnant and non-pregnant women with varying degrees of cervical ectopy using a systems biology approach.

Methods: Cervicovaginal lavage samples were collected from 23 pregnant and 25 non-pregnant women. The samples were analyzed for host and microbial proteome alterations by tandem mass spectrometry. Differential protein expression between conditions was analyzed using t tests, IPA software and hierarchical clustering.

Results: 550 human proteins and 376 bacterial proteins from 10 genera were identified. 56 human proteins (10%) were differentially abundant between pregnant and non-pregnant women and 31 (5.6%) between those with and without ectopy. Both pregnancy and ectopy associated with proteome alterations involving movement of leukocytes, inflammatory response and inhibition of matrix metalloproteinases. Ectopy was associated with increased IL-8 signaling (p=1.7E-4) and leukocyte migration (p=2.14E-4) while pregnancy had immunosuppressive effects with under-expressed primary immunodeficiency signaling (p=2.1E-4), decreased inhibition of matrix metalloproteinases (p=4.07E-3) and lower leukocyte extravasation signaling (p=1.45E-2). 15 women had non-Lactobacillus (nLD) bacterial communities dominated by *Gardnerella vaginalis* while 32 had *Lactobacillus* (73% *L. iners*, 6% *L. crispatus*). Neither pregnancy nor ectopy associated with microbiome groups. However, the proteome alterations associated with ectopy corresponded with a nLD microbiome (p=0.046).

Conclusions: Although there were overlapping biological functions altered during pregnancy and ectopy, these were divergent, with ectopy associated with increased neutrophil-associated and leukocyte migration inflammation pathways. This may suggest that modulation of specific target cell recruitment pathways via ectopy could be putative underlying mechanisms of increased HIV-acquisition risk in women who are pregnant.

BSP7.10

Stabilizing Env: Residues in the gp41 Ectodomain Regulate HIV-1 Envelope Glycoprotein Conformational Transitions Induced by gp120-directed Inhibitors

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Interactions between the gp120 and gp41 subunits of the human immunodeficiency virus (HIV-1) envelope glycoprotein (Env) trimer maintain the metastable unliganded form of the viral spike. Binding of gp120 to the receptor, CD4, changes the Env conformation to promote gp120 interaction with the second receptor, CCR5 or CXCR4. CD4 binding also induces the transformation of Env into the pre-hairpin intermediate, in which the gp41 heptad repeat (HR1) coiled coil is assembled at the trimer axis. In nature, HIV-1 Envs must balance the requirements to maintain the non-covalent association of gp120 with gp41 and to evade the host antibody response with the need to respond to CD4 binding. Here we show that the gp41 HR1 region contributes to gp120 association with the unliganded Env trimer. Changes in particular amino acid residues in the gp41 HR1 region decreased the efficiency with which Env moved from the unliganded state. Thus, these gp41 changes decreased the sensitivity of HIV-1 to cold inactivation and ligands that require Env conformational changes to bind efficiently. Conversely, these gp41 changes increased HIV-1 sensitivity to small-molecule entry inhibitors that block Env conformational changes induced by CD4. Changes in particular gp41 HR1 amino acid residues can apparently affect the relative stability of the unliganded state and CD4-induced conformations. Thus, the gp41 HR1 region contributes to the association with gp120 and regulates Env transitions from the unliganded state to downstream conformations. This new information might be important in the design of new Env-based immunogens stabilized in the ground state and mimicking the native trimer exposed at the surface of infectious viral particles.

BSP7.11

Comparison of SIV transgene expression by Cynomolgus Macaque Cytomegalovirus (CyCMV) and Varicella-Zoster Virus (VZV)

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Introduction: Although more prominent in circulation with Cytomegalovirus (CMV), both CMV and Varicella Zoster Virus (VZV) generate robust adaptive immune responses in the tissues, characterized in particular by effector memory CD8+ T cells. Nonetheless, CMV and VZV differ in cell tropism, immune modulation and life cycle. Both have been suggested as ideal viral vectors against intracellular pathogens including HIV/SIV. Our group has studied and presented data on a VZV-based SIV vaccine in cynomolgus macaques, which has shown efficacy as a preventative and therapeutic vaccine. To compare these vectors directly we have synthesized a SIV transgene-expressing CMV for use in cynomolgus macaques based on the cynomolgus macaque CMV (CyCMV) Mauritius bacterial artificial chromosome (BAC).

Methods: Two SIVmac239 based viral transgenes: a Gag-Pol fusion, and a Nef-Tat-Rev fusion, were utilized. BAC recombination facilitated the insertion of both transgenes in separate CyCMV Mauritius BAC constructs. CMV BAC DNA was transfected into fibroblast cell culture, then passaged as virus. Infected cells were lysed and expression of transgenes was quantified by western blot and compared to VZV BAC transgene expression.

Results: Local sequencing showed that the SIV transgenes were inserted into CyCMV Mauritius BAC between genes CyUS2 and Cy116 without alteration to their sequences. With the integrated transgenes CyCMV Mauritius BAC was cultured successfully as a virus in fibroblast cell lines. Both SIV constructs were expressed in infected Telo-RF cells. The CMV immediate early 1 (IE1) gene was used as a housekeeping gene to quantitate transgene expression relative to CMV infection. Expression of both GPF and NTR were observed in their respective constructs. Transgene expression was similar to expression levels induced by VZV-SIV constructs.

Future Directions: Our group will compare immunogenicity of these vectors within cynomolgus macaques.

BSP7.12

The Human Immunodeficiency Virus-1 Protein Nef Drives T cell Exhaustion by Upregulating the Cell Surface Levels of Tim-3

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Immune responses are tightly regulated by multiple T cell inhibitory receptors. Chronic viral infections are characterized by the upregulation of inhibitory receptors leading to T cell exhaustion. Recurrent encounter with viral antigens stimulates immune cells impairing the host immune response. Exhausted T cells display diminished cytotoxic potential, reduced poly-functionality and lower proliferative capacity. Here, we examined the role of the HIV-1 proteins Nef and Vpu in mediating T cell exhaustion. We demonstrated that HIV-1 infected blood mononuclear cells elicited higher frequencies of surface PD-1, LAG-3 and Tim-3. Specifically, Nef enhanced surface expression of Tim-3 via Nef's $LL_{164/154}$ motif. Conversely, PD-1 and LAG-3 upregulation were not restricted to Nef or Vpu expression demonstrating that Nef selectively targets Tim-3. Moreover, profiling the phenotype of HIV-1 infected $CD4^+$ T cells demonstrated higher frequencies of Nef-induced Tim-3 levels in the naïve and central memory compartment. Taken together, our data highlights the prospect of reversing T cell anergy in HIV-1 infections using therapeutics targeting Nef.

BSP7.13

In Vitro Examination Of HIV Envelope-Derived Antigens For Their Ability To Engage Germline-Reverted VRC01 And VRC01-Class Precursors

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Background: The elicitation of VRC01-class neutralizing antibodies (nAbs) by vaccination may require immunogens that can prime the appropriate precursor B cells. Here, we present data from in vitro binding assessments of a panel of antigens derived from the envelope glycoprotein (Env) of HIV strain 45_01dG5, an early autologous strain from the donor from whom VRC01 was recovered, ahead of studies to assess their immunogenicity.

Methods: Six variants of the 45_01dG5 Env were constructed and assessed for binding to affinity matured (mat) and germline reverted (gl) VRC01, naïve VRC01-class precursors (B046 and B053), and non-CD4-binding site (CD4bs) Abs (B4e8, 412d, A32). The N and C termini and V1V2 loops were truncated in all antigens to limit non-CD4bs responses upon immunization. A subset also contained extra glycans in V3 for added focus, a Ser375-to-Tyr change to help instill a CD4-bound conformation, and a T-helper (Th) epitope (PADRE) to heighten responses. All

proteins were expressed from stably transfected CHOK1 cells and purified by Ni-NTA and size-exclusion chromatography. Antigen binding was assessed by ELISA and flow cytometry.

Results and Conclusion: All antigens without the S375Y mutation were bound strongly by VRC01mat, albeit that a construct with 3 copies of the PADRE motif was bound with 2-fold lower relative affinity. In contrast, VRC01mat bound constructs with the S375Y change and one PADRE motif equally well. VRC01gl, B046 and B053, expressed as IgM on the surface of cells, bound with reasonable affinity to constructs with the S375Y change but not those without it. Poor or no binding was observed with A32 or 412d while B4e8 binding was observed only to constructs in which the V3 was not covered with glycans. These engineered antigens should permit further assessment of features that may impact priming of desired Th and B cell responses and, ultimately, VRC01-class nAbs.

BSP7.14

Characterization of Fc dependent anti-gp120-specific antibody functionality in Elite Controllers associated with HIV control

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Background: Antibodies (Ab) have antigen specific combining sites and an Fc portions that bind Fc receptors (FcR) on innate immune cells, trigger activation of phagocytosis and complement deposition. These Fc-mediated functions are implicated in HIV control. Here, we compared plasma from HIV^+ untreated progressors (UTP), antiretroviral therapy (ART) treated progressors (TP) and elite controllers (EC) for anti-HIV envelope (gp120)-specific IgG functionality in Ab-dependent (AD) complement deposition (ADCD) and AD cellular phagocytosis (ADCP) assays.

Methods: Plasma samples from 18 UTP, 24 TP and 32 EC was quantified for total IgG and anti-gp120-specific IgG concentrations. The ADCD assay assessed deposition of the C3b complement component on gp120 coated CEM.NKr. CCR5 target cells (T). The ADCP assay measured the uptake of gp120-functionalized fluorescent beads by THP-1 (E) monocyte-like cells. Activity was measured as the area under the curve (AUC) of the ADCD and ADCP score (% fluorescent T/ E x the mean fluorescence intensity (MFI) of T/E, respectively for 2 concentrations of input plasma IgG). For both the assays, positive and negative controls were pool of plasma from HIV^+ and HIV^- individuals, respectively.

Results: Both EC and TP had viral loads (VL) <50 copies/ml plasma while UTP had high VLs. Plasma from EC and UTP had significantly higher levels of ADCD and ADCP activity than those from TP (Kruskall-Wallis test with Dunn's post-tests). Plasma from EC and UTP did not differ from each other in terms of ADCD and ADCP activity (Dunn's).

Conclusions: Plasma from EC contains Abs that are ADCD and ADCP competent despite VL control. This contrast with plasma from TP, which lose these activities in conjunction with VL control. Future work should address how EC maintain these Abs with AD functions and whether their presence play a role in EC VL suppression in the absence of treatment.

BSP7.15

Early Recovery of Antibody-Mediated Neutralization and ADCC Responses in HIV-Positive Individuals under Dolutegravir-based Antiretroviral Therapy

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Background: Dolutegravir (DTG) is the newest and most potent member of the integrase inhibitor drug family. No reports of drug resistance have been reported in patients receiving first-line DTG treatment since its FDA approval in 2013. It has been shown that resistance mutations associated with first-line treatment contribute to functionally impaired viruses without compensatory mutations. The impact of DTG-treatment on viral evolution in patients is not clear, but characterization of host immune responses against HIV-1 will shed light on the status of viral infection during suppression achieved by antiretroviral (ARV) therapy.

Methods: Our study is a longitudinal observational study. Sequential serum samples were obtained from patients suppressed with DTG-based or Elvitegravir (EVG)-based therapy (n=8 and n=5, respectively) at one month (T1), two months (T2), and five to six months (T3) after treatment initiation. The antibody-dependent cellular cytotoxicity (ADCC)-mediating potency and virus neutralization titers of the serum samples were measured.

Results: T2 and T3 sera from four individuals treated with DTG- or EVG-based ART (two in each group) were tested for their ability to mediate ADCC activity. The serum dilutions at which 50% of the infected target cells were killed were 48-fold higher at T2 and 11-fold higher at T3 for DTG-treated individuals when compared to EVG-treated individuals. The 50% neutralization titers of the sera were 1:227 at T1, 1:640 at T2, and 1:647 at T3 for DTG-treated individuals and 1:247 at T1, 1:225 at T2, and 1:633 at T3 for EVG-treated individuals.

Conclusions: Patients treated with DTG compared to EVG had more robust levels ADCC responses ($p < 0.01$) and earlier recovery of neutralization titre overtime. These data are consistent with reports of a reduced likelihood of HIV Env evolution following exposure to DTG compared to other drugs.

BSP7.16

KIR3DL1 alleles and their Epistatic Interactions with HLA Class I Influence Resistance and Susceptibility to HIV-1 acquisition in the Pumwani Sex Worker cohort

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Objective: To determine the associations of KIR3DL1/S1 and its epistatic interactions with HLA class I alleles with resistance and susceptibility to HIV-1.

Design: Despite repeated exposure to HIV-1 a subset of women enrolled in the Pumwani sex worker cohort remain HIV uninfected. Our previous studies have shown that specific HLA class I and II alleles were associated with this natural immunity to HIV-1. In this study we investigated the association of KIR3DL1/S1 and its epistatic interactions, a part of innate immune response, with resistance or susceptibility to HIV-1.

Methods: We used a sequence-based typing method to genotype KIR3DL1/S1 of 641 women in this cohort. The association of KIR3DL1/S1 and its epistatic interactions with HLA class I were analyzed using SPSS statistics software.

Results: 3DL1*041 is significantly associated with resistance to HIV-1 infection(p=0.009, OR:3.359, 95%CI:1.39-8.32). Whereas, 3DL1*020 was associated with susceptibility to HIV infection (p=0.029, OR:0.316, 95%CI:0.10-1.04). Epistatic interactions between 3DL1 alleles and specific HLA class I alleles were observed. Among them the co-existence of 3DL1*041 with BW4 (p=0.00001, OR:13.33, 95%CI:3.43-51.9), or BW6 (p=0.008, OR:3.92, 95%CI:1.51-10.17), increased the odds ratio to remain HIV uninfected. Further, 3DL1*041+/BW4+ women who entered cohort HIV negative remained uninfected (p=0.032). Whereas, co-existence of 3DL1*1501 with C*02:10 (p=0.0000003), B*15:03(p=0.0003), A24 supertype(p=0.0009), or A*23:01 (p=0.0032) increased susceptibility to seroconversion.

Conclusions: The effects of interactions between 3DL1 and HLA class I alleles on resistance/susceptibility to HIV-1 infection suggested that innate immunity plays an important role in HIV-1 infection and should be studied and explored for HIV prevention.

BSP7.17

Identification and Characterization of Antigen-specific Peripheral Follicular Helper T Cells in HIV-infected Subjects on Antiretroviral Therapy

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Follicular helper T cells (Tfh) are a subset of memory CD4 T cells that plays a crucial role in germinal center (GC) formation, where they provide help for B cell maturation and antibody production in the context of natural infections and vaccination. HIV infection leads to a functional and phenotypic impairment of GC Tfh as well as their circulating counterpart (peripheral, pTfh). pTfh exhibit analogous functional properties to GC Tfh and a dysregulation that is not normalized by ART. The mechanisms of these impairments are unknown but may be related to an antigen (Ag)-specific and/or an unspecific, general modulation.

PBMCs from ART-treated subjects were stimulated with HIV proteins (Gag, Env and Nef), CMV (pp65) or HBV for 9h. Ag-specific CD4 T cells were detected by the upregulation of surface activation markers CD40L and CD69 and characterized phenotypically for the expression of markers of: pTfh (CD45RA, CXCR5); differentiation subsets (CCR6, CXCR3); activation (ICOS); and inhibitory markers (CD200, PD-1, TIGIT).

The magnitude of Ag-specific responses varied between donors and phenotypic differences were detected between antigens. In contrast to ICS procedures, the CD69/CD40L assay was able to identify Ag-specific Tfh. We observed a preferential expression of pTfh markers on HIV-specific CD4 T cells compared to CMV and HBV. In addition, Gag-specific CD4 and pTfh expressed higher levels of exhaustion markers compared to CMV-specific T cells despite durable viral suppression on ART. Longitudinal analyses of patients sampled before and after ART-initiation suggest that initiation of therapy results in a decrease of PD-1 and CD200, but not TIGIT, expression on Gag-specific CD4 T cells with therapy.

This approach allows the identification and characterization of Ag-specific pTfh in ART-treated subjects with high sensitivity and specificity. Phenotypic differences between Ag-specific pTfh reveal the contribution of an Ag-dependent mechanism of Tfh impairment, which is not restored by ART.

BSP7.18

Proteomic methods to simultaneously monitor host immunity and its modulation by microbiome composition and function

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Background: Microbiome composition has a significant impact on mucosal barriers and vulnerability to infection, but these host-bacterial interactions are largely uncharacterized. We developed a mass spectrometry (MS)-based workflow to simultaneously evaluate host immune parameters in relation to the microbiome in a large-scale study.

Method: 688 cervicovaginal lavage samples from the CAPRISA-004 trial were analyzed by label-free tandem-MS in 18 separate runs. Women were assigned community state types (CST's) by proportion of bacterial proteins. Unpaired t-tests, hierarchical clustering, and pathways analysis were used to identify host differences between CST's, using the *L. crispatus* CST as the reference.

Results: Batch reproducibility of the 18 MS runs was high ($p<0.00001$, $r_s^2=0.915$), with 5.4% covariance between runs. Of 2,102 host factors detected, 576 (27.4%) were identified in all MS runs for downstream analysis, including pathways important for innate immunity, leukocyte migration, and wound healing. In total, 3,334 bacterial proteins representing 188 species/strains were quantified, resulting in 7 major CST's, dominated by *L. crispatus* (9.3%), *L. iners* (41.4%), *Gardnerella* (23.7%), *Prevotella* (8.1%), *Gardnerella* & *Lactobacillus* (6.7%), *Mobiluncus* (3.2%), and *Pseudomonas* (2.6%). Overall, 184 host pathways were differentially expressed in non-*L. crispatus* CST's. Neutrophil movement pathways were most significantly increased, in CST's with *Gardnerella* (p=8.3E-5), then *Prevotella* (p=1.2E-6), *Mobiluncus* (p=0.0049), and *Pseudomonas* (p=2.4E-5). Cell proliferation pathways decreased most with *Pseudomonas* (p=1.8E-6), then *Gardnerella & Lactobacillus* (p=5.2E-5), *Mobiluncus* (p=1.5E-6), and *Prevotella* (p=1.1E-10) CST's. Of 402 KEGG pathways identified, significant alterations in bacterial metabolism were evident in non-*Lactobacillus* women, including a 36.5 fold increase in detection of pentose phosphate pathway proteins (p=2.0E-80).

Conclusion: Utilizing an integrated proteomics approach, we identified novel pathways altered in non-*L. crispatus* CST's, including increased leukocyte movement, decreased cell proliferation, and changes to bacterial metabolic pathways. These effects may have important implications in reproductive health outcomes, including HIV infection and therapeutics targeting mucosal surfaces.

BSP7.19

The Effects of Oxytocin on the Immune Cytokine Profile of Vaginal, Ectocervical, and Endocervical Epithelial Cells

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Introduction: Oxytocin, a neural hormone, is released during sexual activity to help with the contraction of smooth muscle, and facilitate intimacy. This study examined how oxytocin may impact female reproductive health by modulating immunologic regulation at the female genital tract (FGT). As inflammation can predispose susceptibility to infection, this study tested the hypothesis that oxytocin promotes a less inflammatory environment at the FGT, and, hence, reduces cellular susceptibility to sexually transmitted infections such as HIV.

Methods: Cell lines (Vk2 (Vaginal), Ect1 (Ectocervical), and End1 (Endocervical)) of FGT origin were treated with oxytocin in conjunction with an immune stimulus to analyse inflammation. Cells were grown as monolayers in Keratinocyte Serum Free Medium . Oxytocin (a titration of 1-10 000 pg/mL) was used in conjunction with either LPS (400 ng/mL), Poly(I:C)/LyoVec (1 µg/mL), or alone. Culture supernatants were collected at 1, 3, 8, and 18 hours post-treatment, and cells were lysed for RNA extraction. Supernatants were tested with bead-based cytokine assays (Milliplex), and RNA was tested by qPCR after reverse transcription.

Results and Discussion: Oxytocin alone had no effect on the expression of immunologic genes. Following 3 hours of stimulation cytokines such as IL-6 and IL-1β (among the 30 genes examined) were further up-regulated by high levels of oxytocin. Contrarily, low levels of oxytocin, similar to that found *in vivo*, seemed to down regulate the expression of the pro-inflammatory cytokines IL-6 and IL-1β but only in the context of an immune stimulus.

Significance: These results provide the first evidence that oxytocin may have modulatory effects on the immunologic environment at the FGT and a potential impact on female reproductive health and cellular susceptibility to sexually transmitted infections.

BSP7.20

Blood B Lymphocyte Stimulator (BLyS)/BAFF levels may reflect natural immunity to HIV in highly exposed uninfected Beninese Commercial Sex Workers

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We have previously shown that excess B lymphocyte Stimulator (BLyS)/BAFF in plasma and on surface of blood dendritic cells (DC) of HIV-infected progressors coincides with B-cell dysregulations and increased frequencies of "precursor" innate marginal zone (MZ)-like B-cells. In contrast, both blood BLyS levels and frequencies of this population remained unaltered in HIV elite-controllers. Based on these observations, we hypothesized that control of BLyS and innate B-cell status could be associated with natural immunity against HIV infection. Therefore, we assessed blood BLyS levels and B-cell status in HIV highly-exposed commercial sex workers (CSWs) from Benin. We found blood BLyS levels of HIV-uninfected CSWs were lower than those observed in both HIV-infected CSW and HIV-uninfected non-CSW groups. Furthermore, levels of BLyS expression on blood T-cells and monocytes were lower in HIV-uninfected CSWs when compared to HIV-infected CSWs, but higher than those observed for HIV-uninfected non-CSWs. Concomitantly, HIV-infected CSWs presented a dysregulated blood B-cell compartment, characterized by increased total IgG1, increased frequencies of populations presenting immature and/or innate profiles and a higher ratio of IgG+/IgA+ plasmablasts. In contrast, relatively low levels of BLyS in the blood of HIV-uninfected CSWs coincided with a rather preserved B-cell compartment.

BSP7.21

Characterization of B Cell Subpopulations and Tetanus Vaccine Responses in HIV-Exposed Uninfected (HEU) Children

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Background: HIV-exposed uninfected (HEU) children experience a higher incidence of morbidity/mortality and immunologic abnormalities involving the B cell compartment. Those could be associated with perinatal exposure to HIV and/or combination antiretroviral therapy (cART). Here, we analyzed homeostasis of B cell subsets and vaccine responses in HEU children during their first year of life.

Methods: All HEU children (n=54) were exposed to cART *in utero* and from 12h after birth until 6 weeks of age, and were stratified according to whether or not maternal HIV-1 viral load (VL) throughout pregnancy was detectable (≥40vs.<40 copies/ml). Cord or peripheral blood mononuclear cells were isolated at birth, 6, and 12 months. CD19 B cell subsets (naïve; transitional T1/T2-T3; plasmablasts; classical/activated/atypical memory) were characterized by the expression of CD10, CD20, CD21, CD27 and IgM in flow cytometry. Vaccine responses were analysed with fluorescent tetanus toxoid C fragment (TTCF) oligomers.

Results: Compared to HEU born to mothers with undetectable VL (n=32), HEU infants born to viremic mothers had a lower frequency of B cells (p=0.006) and a higher frequency of plasmablasts (p=0.065) at birth. At 6 months of age, they showed higher frequencies of T1 (p=0.024) and total transitional B cells (p=0.03). At 12 months of age, they showed higher frequencies of non-class switched B cells in classical (p=0.056) and activated (p=0.062) memory subsets. No significant frequency differences were noted in TTCF-specific B cell subsets.

Discussion: These observations suggest an early maturation of the B cell compartment in infants born to mothers with detectable VL in pregnancy, with delayed development of antigen-experienced B cells and disturbance in class switching at 12 months of age. Reassuringly, the presence of equal frequencies of TTCF-specific B cells in both groups argues in support of HEU children being able to develop vaccine responses regardless of exposure to maternal VL.

BSP7.22

Evaluation of Mucosal Inflammatory Cytokine/ Chemokine Response to Novel 12-PCS Vaccine and Traditional Full gag/env Vaccine

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Background: Mucosal inflammatory responses influence susceptibility to HIV infection. We are conducting a nonhuman primate study to compare efficacy of a vaccine targeting the 12 protease cleavage sites with a vaccine targeting full Gag and Env. Evaluation of inflammatory

responses to different vaccine modalities at the site of infection is very important.

Objective: Evaluate mucosal inflammatory responses in macaques vaccinated with rVSVgag/env or rVSVpcs/NANOpcs.

Methods: Mauritian *Cynomolgus macaques* were immunized with rVSVgag/env, rVSVpcs/NANOpcs, or rVSV vector. Weekly cervicovaginal lavage (CVL) and nasal swabs were collected for the multiplex protein assay (Bio-Plex 200 system). Bio-Plex magnetic beads coupled to primary antibodies in combination with biotinylated detection antibodies and PE-labeled streptavidin were used to measure cytokines/chemokines in the CVL samples. The cytokine panel consists of 15 (pro- or anti-) inflammatory cytokines/chemokines to evaluate the inflammatory responses.

Results/Discussion: We observed lower levels of IL-1beta, IL-6, IFNgamma, and RANTES from the rVSVpcs/NANOpcs group at baseline and/or the week after immunization, while IL8, IL-17alpha and IP-10 were lower in comparison only after the first boost. By one week after the first boost, most of the pro-inflammatory cytokines and chemoattractants either had the same or even lower levels for the rVSVpcs/NANOpcs group compared to the rVSVgag/env vaccine group. This result provides insight on the potential of proposed rVSVpcs/NANOpcs vaccine to confer a more site-restricted inflammatory response, avoiding unnecessary and excess immune activation.

Conclusion: Levels of inflammatory cytokines/chemokines play an important role in HIV-1 susceptibility and disease progression. These preliminary data using a custom multiplex protein assay showed a potentially more focused immune response that could avoid excessive inflammatory response and localization of HIV-1 target cells.

Mechanisms of HIV Pathogenesis (including animal models) and Co-Morbidities

Mécanisme de pathogénèse du VIH (dont les modèles animaux) et les comorbidités

BSP8.01

JAK-STAT Signaling Pathways and Inhibitors Affect Reversion of Envelope Mutated HIV-1

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We have reported an HIV Env mutant that was unable to mediate infection as cell-free virus but could initiate cell-cell transmission to some T cell lines following which reversion to wild type occurred. It is well known that HIV can spread efficiently between cells by both cell-free and cell-to-cell routes. Here we show that many amino acid changes in Env that surround the CD4 binding pocket can affect HIV replication. Several of the mutant viruses that we generated were unable to infect T cells as cell-free viruses but were nevertheless able to infect certain T cell lines as cell associated viruses and then to revert to wild type or mutate to increase viral fitness. However, the activation of JAK-STAT signaling pathways caused inhibition of such cell-to-cell infection as well as the reversion/mutation of multiple HIV Env mutants that displayed differences in ability to bind to the CD4 receptor. Specifically, Interleukin-2 (IL2) and phorbol-12-myristate 13-acetate (PMA), both acting to activate JAK-STAT pathway, were able to inhibit cell-to-cell viral transmission. In contrast, a number of JAK-STAT-mTOR inhibitors actually promoted HIV-1 transmission and reversion/mutation. Hence, JAK-STAT signaling pathways may differentially affect the replication of a variety of HIV Env mutants in ways that differ from the role that these pathways play in the replication of wild type viruses.

BSP8.02

Tissue target cell frequency and virus infectious dose are key determinants of intravaginal HIV-1 infection in humanized mice

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Heterosexual transmission is the predominant mode of HIV-1 infection in women. About 40% of HIV-1 infection occurs in the female genital tract (FGT). Factors in the FGT that determine the outcome of HIV-1 exposure are incompletely understood, thereby limiting innovation in prevention strategies. In this study, we examined the kinetics of viral infection, replication and dissemination following intravaginal (IVAG) HIV-1 infection in NOD-Rag2$^{-/-}$ gc$^{-/-}$ mice reconstituted with human CD34+ enriched hematopoietic stem cells (hu-mice). Following IVAG infection, HIV-1 was detected in vaginal washes one week post-infection and decreased significantly from week 3 ($2.8x10^6 \pm 1.0x10^5$ copies/mL) to week 12 ($6.6x10^3 \pm 3.5x10^3$ copies/mL). Conversely, the plasma titre significantly increased from week 1 ($1.6x10^2 \pm 1.0x10^2$) to 5 ($1.7x10^5 \pm 5.0x10^4$) and remained stable up to 12 weeks. Maximum proportion of p24+ CD45+ cells were observed in the vaginal mucosa at week 1, whereas p24+ cells were increased in blood and spleen at 3-5 weeks post-infection. A significant depletion of CD45+CD4+ cells was seen in the blood by 5 weeks post-infection (42.6±9.3% (week 0) vs. 1.6±0.7% (week 5) while uninfected control animals remained unchanged (28.7%±7.9% vs. 13.0±10.6%). Closer examination of vaginal tissues by immunohistochemistry indicated that higher reconstitution of human CD3 cells in tissues was correlated with CD45 reconstitution in blood. Compared to 28% successful infection in Hu-mice with <10% reconstitution in blood, 80% Hu-mice were infected when blood

reconstitution ≥10%. Interestingly, low rate of infection in low reconstituted mice was partially compensated when viral inoculum concentration was increased. Multiple logistic regression analysis showed that CD45% and viral inoculation dose, but not vaginal or serum viral loads correlated with outcome of infection. These results indicate that clinically, number of target cells present in the FGT and semen viral load are likely the key determinants of the outcome of heterosexual HIV-1 exposure.

BSP8.03

HIV-1 exploits the interplay between epithelial and Th17 cells for dissemination

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Background: Epithelial cells(EC) are the first to capture HIV/SIV at portal sites of entry and transmit the virus to subjacent immune cells *via* transcytosis. The interplay between EC and Th17 cells is critical for the maintenance of immune homeostasis at mucosal level as well as viral dissemination. Th17 cells produce cytokines that act on EC to promote the production of CCL20/MIP-3α,a chemoattractant of $CCR6^+$Th17 cells. Herein,we investigated the impact of HIV-1 on the interplay between EC and Th17 cells and studied EC-T cell trans-infection in an environment rich in CCL20.

Methods: Intestinal EC line HT-29 was stimulated with recombinant human TNF-α and/or IL-17A in the presence or absence of transmitted founder virus THRO. Memory $CD4^+$T-cells were isolated by magnetic beads from uninfected individuals and stimulated with CD3/CD28 Abs. EC-T cell trans-infection was studied in co-culture experiments between HIV-exposed EC and activated T-cells. CCL20 and HIV-p24 levels were quantified in cell culture supernatants by ELISA. The expression of IL-17 receptor A and C (IL-17RA/RC) on EC and the intracellular expression of HIV-p24 in T-cells were quantified by FACS.

Results: IL-17A acted only in synergy with TNF-α to promote CCL20 production in EC. This synergy coincided with the TNF-α-mediated up-regulation of IL-17RA expression on EC.HIV exposure further increased CCL20 production by EC in response to IL-17A and TNF-α. HIV trans-infection of T-cells co-cultured with HIV-loaded EC occurred more robustly in the presence of high levels of CCL20 levels produced by EC in response to IL-17A and TNF-α.

Conclusion: We demonstrate that IL-17A acts in synergy with TNF-α to promote CCL20 production in intestinal EC,HIV further amplifies this synergy,and HIV transmission from EC to T-cells is proportional to the magnitude of CCL20 production by EC. Together these results reveal that HIV-1 exploits the interplay between EC and Th17 cells for its own replicative advantage and CCL20 plays an important role in HIV dissemination from the portal entry sites.

Molecular Mechanisms of Co-Infections

Mécanismes moléculaires des coInfections

BSP9.01

Altered Phenotype of M1 and M2a Macrophage Subset May Contribute to CD8+T-cell Dysfunction in Chronic HCV Infection

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Background: Chronic HCV infection causes generalized $CD8^+$T-cell impairment, not limited to HCV-specific $CD8^+$T-cells. In such inflammatory conditions, infiltrating monocyte-derived macrophages (MDM) contribute to a micro-environment that could influence the $CD8^+$T-cells trafficking through the liver. These MDM can differentiate into M1 (classically-activated) and M2a, M2b, M2c (alternatively-activated) subsets. Whether MDM subset generation in chronic HCV infection is altered is not known. Furthermore, how these cells influence $CD8^+$T-cell function has not been described. We hypothesize that MDM subset phenotypes are altered in chronic HCV infection, thereby contributing to $CD8^+$T-cell dysfunction.

Results: MDM subset phenotype analyses in chronic HCV infection suggests a higher proportion of M2a cells expressing $CD206^+$ than M0 undifferentiated subset, whereas in controls, there was no such difference. The percentage of $CD86^+$ cells showed did not vary across subsets in infected individuals, while CD86 expression in M1 and M2a cells was significantly higher than M0 in controls. In infection, the concentration of IL-6 in stimulated M2a subset supernatants was significantly higher than healthy controls. The release of TNF-α by any MDM subset was undetectable in infection, in contrast to high amounts produced by M1 cells in controls. Co-culturing $CD8^+$ T-cells from uninfected individuals with autologous M1 macrophages significantly increased the percentage of $perforin^+$, $CD107a^+$ and IFN-y^+ $CD8^+$T-cells, compared to $CD8^+$T-cells alone. This increase in perforin+ and CD107+ cells was significantly greater that that induced in M2a-CD8T+cells-co-cultures. Co-culturing with M2c cells significantly increased the percentage of $CD107a^+$ cells compared to $CD8^+$ T-cells alone.

Discussion: Phenotypic alterations in MDM subsets in chronic HCV infection are evident both in for surface receptors and secreted cytokines, suggesting impairment of MDM differentiation and potentially function. The importance of the M1 subset in priming $CD8^+$T-cell functions is evident. How the alteration of MDM subsets in chronic HCV infection directly influences $CD8^+$T-cells requires further investigation.

BSP9.02

An in vitro model to mimic selection of replication-competent HIV-1 intersubtype recombination in dual or superinfected patients

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HIV-1 recombination events are common in HIV epidemics, which accelerate viral diversity and posts great challenges to HIV/AIDS treatment and HIV vaccine development. However, the low frequency of recombinant viruses within the entire viral population impedes further studies, and most of the studies to-date have no consideration of functionality of the resultant recombinants. Here we established a Functional Recombinant Production (FRP) system to produce pure and functional HIV-1 intersubtype Env recombinants, and utilize 454 pyrosequencing to investigate the distribution of over 4,000 functional and non-functional recombination breakpoints from either FRP system or dual infection culture. The results revealed that most of the breakpoints converged in gp41 (62%) and C1 (25.3%) domains of gp120, which has strong correlation with the similarity between the two recombining sequences. Yet, the breakpoints also appeared in C2 (5.2%) and C5 (4.6%) domains not correlated with the recombining sequence similarity. Interestingly, none of the intersubtype gp120 recombinants recombined between C1 and gp41 regions either from FRP system or from dual infection culture, and very few from the HIV epidemics, were functional. The new developed FRP technique in this study represents a breakthrough in terms of investigation of functional HIV-1 intersubtype recombinants. The present study suggests that the selection of functional Env recombinants is one of the reasons for the predominance of C1 and gp41 Env recombinants in the HIV epidemics, and provides an *in vitro* model to mimic selection of replication-competent HIV-1 intersubtype recombination in dual or superinfected patients.

BSP9.03

Short Fuse on Inflammation: Cytomegalovirus, T cells and Telomeres in Chronic HIV Infection

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While acute inflammation is an important response to infection, chronic inflammation underlies numerous age-associated pathologies. Many living with long-term human immunodeficiency virus (HIV) infection suffer "premature" age-related illnesses with inflammatory components to their development.

Lifelong cellular turnover equates biological aging with senescent cell accumulation. Exhaustive division and progressive telomere erosion drive replicative senescence characterized by cell-cycle arrest and a pro-inflammatory senescence-associated secretory phenotype(SASP). The contribution of senescent immune cells to the inflammatory landscape remains unknown. Cytomegalovirus (CMV) infection creates an inflated, potentially senescent, $CD8^+$ T lymphocyte population, often magnified in HIV infection. Extensive expansion of CMV-specific lymphocytes could introduce telomere-dependent SASP contributions to unhealthy chronic inflammation.

Plasma and peripheral blood mononuclear cells were collected from 154 HIV^+ individuals and 37 HIV^- controls. CMV-specific $CD8^+$ T cell responses and lymphocyte subset telomere length (TL) were determined by flow cytometry. Plasma levels of interleukin (IL)-1β, IL-6, tumor necrosis factor (TNF)-α, fractalkine (CX3CL1), and C-reactive protein (CRP) were measured by ELISA. HIV+CMV+ individuals showed greater evidence of inflammation (Table 1). In CMV+ individuals tested (*n,* 32), CMV-specific $CD57^+CD8^+$ T cells had shorter telomeres than other $CD57^+CD8^+$ T cells, global $CD8^+$ T cells, and HIV-specific $CD8^+$ T cells, $p<0.0001,<0.0001,0.0036$ respectively.

Our data suggests in chronic HIV infection, immunological effects related to CMV-infection can have a dominant influence on chronic inflammation. Understanding mechanisms behind senescence-associated chronic inflammation, including the role of CMV-immunity, could introduce new strategies to address age-related morbidities.

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Table 1. Comparison of inflammatory markers in HIV+CMV+/- groups

	HIV+CMV+ (n = 110) median, IQM	HIV+CMV- (n = 25) median, IQM	p
Age (years)	48, 44-54	43, 29-61	ns
IL-1β (pg/mL)	10.48, 6.52-21.10	7.70, 5.91-29.11	ns
IL-6 (pg/mL)	8.00, 3.70-24.01	2.43, 2.30-5.39	0.0017
TNF-α (pg/mL)	40.04, 14.41-100.62	23.44, 9.11-196.12	ns
	HIV+CMV+ (n = 110) median, IQM	**HIV+CMV- (n = 25) median, IQM**	**p**
Fractalkine (ng/mL)	0.998, 0.805-1.330	0.816, 0.734-0.987	0.0280
CRP (ug/mL)	0.359, 0.176-0.683	0.165, 0.064-0.419	.0194
Global CD8+ TL (bp)	3627, 2724-4188	-	-
CMV-Specific CD8+ TL (bp)	2349, 1843-3336	-	-
HIV-Specific CD8+ TL (bp)	3471, 2731-3611	-	-

BSP9.04

Association of HPV infection and clearance with cervicovaginal immunology and the vaginal microbiota

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Cervical human papillomavirus (HPV) infection may increase HIV risk. Since other genital infections enhance HIV susceptibility by inducing inflammation, we assessed the impact of HPV infection and clearance on genital immunology and the cervico-vaginal microbiome. Genital samples were collected from 65 women for HPV testing, immune studies and microbiota assessment; repeat HPV testing was performed after 6 months. All participants were HIV-uninfected and free of bacterial STIs. Cytobrush-derived T cell and dendritic cell subsets were assessed by multiparameter flow cytometry. Undiluted cervico-vaginal secretions were used to determine cytokine levels by multiplex ELISA, and to assess bacterial community composition and structure by 16S rRNA gene sequence analysis. Neither HPV infection nor clearance were associated with broad differences in cervical T cell subsets or cytokines, although HPV clearance was associated with increased Langerhans cells and HPV infection with elevated IP-10 and MIG. Individuals with HPV more frequently had a high diversity cervicovaginal microbiome (community state type IV) and were less likely to have an *L. gasseri* predominant microbiome. In summary, HPV infection and/or subsequent clearance was not associated with inflammation or altered cervical T cell subsets, but associations with increased Langerhans cells and the composition of the vaginal microbiome warrant further exploration.

Basic Sciences: Other

Sciences fondamentales : Autre

BSP10.01

Generalized CD8+ T Cell Dysfunction in Chronic Viral Hepatitis in Relation to Liver Damage

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Background: Chronic hepatitis C virus (HCV) infection affects ~170 million people worldwide and can result in fibrosis, hepatocellular carcinoma (HCC), and end stage liver disease (ESLD). Although effective HCV treatments exist, liver fibrosis does not always reverse after cure. Current treatment rates remain too low to reduce ESLD or HCV transmission, partly due to high drug costs and strict patient qualifications. HCV-specific $CD8^+$ T cells, important for HCV clearance, exhibit impaired cytotoxic potential, survival, and proliferation during chronic infection. $CD8^+$ T cells from HCV-infected individuals, regardless of their specificity, have decreased cytokine signaling and their survival is inversely correlated with the degree of liver fibrosis.

Objective: The objective of this study is to delineate the function of circulating $CD8^+$ T cells in HCV-infected individuals with either minimal or advanced fibrosis by measuring indicators of effector function.

Methods: Thawed $CD8^+$ T cells are isolated from untreated, HCV-infected samples and assessed for subset distribution, cytokine expression, and cytolytic activity while correlating with fibrotic scores. In addition, a longitudinal study of 24 patients receiving HCV therapy will determine the reversibility of the observed $CD8^+$ T cell impairment and its potential correlation with fibrosis.

Results: Preliminary data suggests that the proportion of naïve $CD8^+$ T cells in patients with high fibrosis is lower than in uninfected individuals. In addition, HCV^+ individuals with high fibrosis have more naïve and effector memory $CD8^+$ T cells expressing IFN-γ and CD107a following in vitro stimulation, and fewer central memory $CD8^+$ T cells expressing perforin compared to controls.

Conclusion: Our data suggests a functional alteration of immune cells is associated with advancing liver fibrosis in HCV infection. It is not known whether generalized immune impairment persists following successful treatment. Identification of the relationship between immune impairment and liver fibrosis would provide prognostic indicators of liver disease.

BSP10.02

Sex Work Affects Bacterial Diversity and the Abundance of Lactobacilli in the Vaginal Microbiome of Kenyan Women

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Women are at an increased risk of sexually transmitted infections (STIs) than men. One reason for this may be the presence of multiple species of bacteria in the vaginal tract. In general, the vaginal bacteria and immune system work together protecting women from various pathogens, and it has been suggested that a vaginal environment dominated by one type of bacteria called *Lactobacilli* is associated with a "healthy" vaginal microbiome. However ethnic differences in the dominant vaginal bacteria exist where 80-90% of Caucasian and 60% of Black and Hispanic women are *Lactobacillus* dominant. Thus a greater proportion of Black and Hispanic women (40%) have a vaginal microbiome consisting of multiple bacterial species, which can be linked to inflammation, and may enhance the risk of HIV-1 acquisition. The purpose of this retrospective cross-sectional study was to compare the vaginal microbiomes of a cohort of sex workers in Nairobi (N=58) with women from the same community not involved in sex work (Non-Sex Workers; N=19) by sequencing the V3 region of the bacterial 16S rRNA from vaginal lavage. Our results indicate that the New Sex Workers (<3 years of sex work) had significantly greater diversity in their vaginal microbiome than the Highly Exposed Seronegative Sex Workers (>7 years of sex work, HIV-) and the Non-Sex Workers (2.242±0.1606 New Sex Workers vs. 1.957±0.3305 HESN vs. 1.480±0.2496 Non-Sex Workers; P=0.0412; rarefied at 12988 reads). Furthermore, the Non-Sex Workers (11/19; 58%) were more likely than the New Sex Workers (8/48; 17%) to have the "healthy" bacteria, *Lactobacilli*, as the most abundant genus in their vaginal microbiome (P=<0.001). Taken together, our results demonstrate that sex work is associated with increased diversity of the vaginal microbiome, and that women who are new to sex worker are less likely to have the "healthy" vaginal bacteria as compared to Non-Sex Workers.

BSP10.03

Progesterone-based contraception administration influences stress hormone release and lead to a more favourable environment for HIV acquisition

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Introduction: About 35 million women use a progesterone-based injectable contraception such as Depot Medroxyprogesterone Acetate (DMPA). DMPA is the preferred hormonal contraceptive (HC) method used by young women in Sub-Saharan Africa. However, young women are also at higher risk of acquiring HIV and studies have shown association between DMPA and risk of HIV infection. Studies indicated that DMPA possess some glucocorticoid agonist activity. Herein, we investigated how DMPA might impact the endocrinal system and susceptibility to HIV infection.

Methods: Thirty-nine women who had joined sex work within the last 24 months (23 not on HC, 16 using DMPA) were enrolled in this study. Blood (plasma/PBMC) and vaginal (lavage/cytobrush) samples were collected. To avoid impact of natural menstrual cycle phases, women not using HC were enrolled during their luteal phase (confirmed by oestrogen and progesterone measurement). Systemic level of cortisol (stress hormone), thyroid hormone (T3, T4) and insulin were then evaluated. T cell activation was also analysed by flow cytometry on fresh cells.

Results: The systemic level of the stress hormone was 737 fold higher in women using DMPA versus women not using HC ($p<0.0001$). The systemic level of T3 and T4 was 31 and 22 fold times higher in women using DMPA compared to women not using HC ($p=0.02$). There was a positive correlation between the level of cortisol and mucosal T cells immune activation as measured by the proportion of cells expressing CD4+CD69+, CD8+CCR5+, CD8+CD69+ and CD8+CD95+.

Conclusion: Our results indicate that among individuals using DMPA there were significantly higher levels of circulating cortisol. It is interesting to note that DMPA binds to the glucocorticoid receptor with greater affinity than cortisol. It is possible that the increased cortisol leads to a modification of the mucosal immune system, which produces to a more favourable milieu for HIV acquisition.

BSP10.04

Depot Medroxyprogesterone Acetate is Associated with Increased Diversity of the Vaginal Microbiome

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The vaginal microbiome plays a central role in protecting against infections. It has been proposed that a vaginal microbiome rich in *Lactobacillus* helps maintain vaginal health, and bacterial diversity in the vaginal microbiome is consistently linked with an increased risk of STIs. Furthermore, there is evidence that female sex hormones might regulate the vaginal microbiome and clinical studies support a correlation between use of the injectable hormonal contraceptive (DMPA) and a 2-fold greater risk of acquiring and transmitting HIV as compared to women not on hormonal contraceptives. Considering that there are over 100 million women world-wide using hormonal contraceptives, a better understanding of the hormone-microbiome-immunity axis is critical to decreasing HIV risk and designing prevention strategies. The aim of this study was to profile the vaginal microbiome of Kenyan women attending the Sex Worker Outreach Program Clinics in Nairobi who were not on hormonal contraceptives (NH, N=21), or using oral contraceptives (OCP, N=10), or Depot medroxyprogesterone acetate (DMPA, N=24) to determine if hormones alter the vaginal microbiome. Cervico-vaginal lavage was collected and the V3 region of the 16S rRNA was sequenced using Illumina MiSeq. There was no effect on the number of women who had *Lactobacillus* as the most abundant genus in their vaginal microbiomes (14/21 (66%) NH, 8/10 (80%) OCP, 16/24 (66%) DMPA; P=0.397). However, women on DMPA had significantly greater bacterial diversity in their vaginal microbiomes than women who were not on hormonal contraceptives (1.769±.2315 DMPA, 1.103±0.2465 NH; P=0.0150). This suggests that women on DMPA have a more diverse vaginal microbiome which may put them at an increased risk of contracting an STI like HIV. This is the first study to demonstrate the effect of hormonal contraceptives on bacterial diversity in the vaginal tract, and to provide a biological link between DMPA and increased risk of contracting STIs.

Clinical Sciences

Sciences cliniques

Adherence

Respect du traitement

CSP1.01

A clinician-derived HIV patient typology and its influence on ART adherence management

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Background: The effectiveness of antiretroviral therapy (ART) depends on optimal clinical management and patient adherence. Little is known about the patient characteristics that clinicians consider in the management of HIV patients' ART adherence.

Methods: To explore this issue, five focus groups were conducted with 31 HIV clinicians from across France. Transcripts were submitted to a qualitative typological analysis.

Results: Clinician management of patient adherence was based on seven patient profiles. For the 'passive' patient, described as taking ART exactly as prescribed without questioning their doctor's expertise, a directive and simple management style was preferred. The 'misleading' patient, described as concerned with social desirability, reports no adherence difficulties to avoid displeasing their doctor. Given suboptimal clinical outcomes, the clinicians' strategy is to remind them of the importance of open patient-clinician communication. The 'stoic' patient is described as requesting and adequately taking the most potent ART available. Here, clinicians conduct a detailed assessment of side effects, which the patient may minimize. The 'hedonistic' patient's festive lifestyle and sexual risk-taking are seen as compromising adherence; the clinicians' approach is to emphasize the patient's responsibility for his own health and that of his/her sexual partners. The 'obsessive' patient is described as having an irrational fear of ART failure and an inability to distinguish illusory from genuine adherence barriers. Clinicians aim to identify the latter. The 'overburdened' patient is recognized as coping with life priorities that interfere with adherence and a forgiving ART is favoured with them. The 'underprivileged' patient is presented as having limited education, income and housing. Here, clinicians seek to improve the patient's living conditions and access to care.

Discussion: These results highlight the complexity of adherence management from the HIV clinicians' perspective and could be used towards medical education and improving HIV care.

Clinical Trials and Observational Studies of Antiretrovirals and Other HIV Therapies

Essais cliniques et études d'observation des antirétroviraux et autres thérapies anti-VIH

CSP2.01

HIV-Exposed Uninfected (HEU) Newborns Exposed in utero to Ritonavir-boosted PI ART have Lower mtDNA levels compared to ART-Unexposed HEU Newborns

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Background: Zidovudine in pregnancy during the mid-1990's, followed by the introduction of dual/triple antiretroviral therapy (ART) has drastically reduced perinatal HIV transmission. By crossing the placenta antiretrovirals could affect cellular processes in developing fetuses. Antiretrovirals can inhibit mitochondrial polymerase-γ, induce oxidative stress, and affect mitophagy; all these may result in mitochondrial alterations/dysfunction which can be reflected by compensatory changes in mitochondrial DNA (mtDNA) content. Our objective was to investigate the impact of *in utero* ART exposure on infant blood mtDNA content at birth in two cohorts of HEU and HIV-unexposed uninfected (HUU) infants.

Methods: mtDNA content was measured via multiplex-qPCR in dried blood spots collected 0-5 days after birth from 104 HEU infants enrolled in the CMIS Mother–Child Cohort, and 68 HEU and 17 HUU infants in the CARMA Cohort. Factors important ($p<0.1$) univariately were considered in multivariable analyses.

Results: The multivariable linear regression models are shown in Table 1. In sensitivity analyses restricted to infants born at term, gestational age was no longer significantly associated with mtDNA content among all (n=166, p=0.062) or HEU (n=150, p=0.068), respectively.

Conclusions: Our results suggest that infant mtDNA content is related to both *in utero* exposure to HIV and maternal ART burden during pregnancy. Increase in mtDNA among HEUs born to untreated, mono- and dual-NRTI treated mothers compared to HUUs may reflect compensatory mitochondrial proliferation in response to stresses. Addition of ritonavir-boosted PI appears to lower mtDNA content, possibly through failure to compensate, or increased oxidative stress and mitophagy resulting in mitochondria elimination.

Table 1. Multivariable models of mtDNA content at birth among all particpants (n=189) and HEU only (n=172)

	All (N=189, 172 HEU, 17HUU)		*HEU only (n=172)	
Multivariable model explanatory variable	Effect Size (β)	p value	Effect Size (β)	p value
Gestational Age (weeks)	-0.214	0.002	-0.208	0.005
Male	0.085	0.217	0.095	0.195
Ref. Females				
Maternal ART during pregnancy				
AZT (n=46)	0.225	0.047	-0.123	0.224
AZT+3TC (n=21)	0.392	<0.001	0.140	0.117
AZT+3TC+NFV (n=12)	0.190	0.026	-0.008	0.923
AZT+3TC+LPV/r (n=29)	0.081	0.431	-0.214	0.024
Other 2NRTIs+PI/r (n=37)	0.082	0.457	-0.241	0.015
Untreated (n=27)	0.283	0.006	*Ref. Untreated (n=27)	Ref. HUU (n=17)

CSP2.02

Resistance Profile Analysis of Treatment-Experienced Patients Switching to Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Alafenamide plus Darunavir

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Background: Virologically-suppressed, treatment-experienced patients on complex multi-tablet regimens were switched to a simpler antiretroviral regimen. After 48 weeks, viral suppression was maintained in 94.4% of patients who switched to elvitegravir/cobicistat/emtricitabine/tenofovir Alafenamide (E/C/F/TAF) plus darunavir (DRV) compared to 76.1% in the DRV-containing baseline regimen. Detailed ARV regimens and the resistance profile of the study population are described.

Methods: Historical genotypic reports were analyzed for resistance-associated mutations (RAMs). The Stanford

HIVdb algorithm v8.01 was used to calculate genotypic susceptibility scores (GSS). For each drug, a 5-point scale was used: susceptible, potential low-level resistance, low-level resistance, intermediate-level resistance and high-level resistance were scored as 1, 0.75, 0.5, 0.25 and 0, respectively. The total GSS for a given regimen was calculated as the sum of the scores for each individual drug.

Results: A total of 94.8% had documented resistance to >2 classes of ARVs, including protease inhibitors (34.8%), non-nucleoside RT inhibitors (88.1%), and NRTIs (94.8%). The most common NRTI-RAMs were M184V/I (83%) and K65R (23.7%). Thymidine analog mutations (TAMs) were present in 42.2% of patients (40.4% with 3 TAMs). The distribution of GSS at study entry was similar across treatment groups. Patients in the E/C/F/TAF+DRV arm maintained virologic suppression similarly, regardless of the DRV dosage received before switching. In the E/C/F/TAF+DRV arm, 11/89 patients (12.4%) had GSS <2, 51/89 patients (57.3%) had GSS ≥2 and <3, and 27/89 patients (30.3%) had GSS ≥3. Within each treatment group, patients maintained virologic suppression similarly regardless of GSS at study entry.

Conclusion: Despite the high incidence of pre-existing resistance in this population, strategic simplification to E/C/F/TAF+DRV was statistically superior to staying on the baseline regimen. Patients benefited from switching regimen regardless of their prior DRV dose and GSS. Treatment with E/C/F/TAF+DRV offers a simpler and more convenient option for treatment-experienced patients on complex multi-tablet regimens.

CSP2.03

Significant Efficacy and Long Term Safety Difference with Tenofovir Alafenamide-based Single-Tablet Regimen in Naïve Adults

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Background: Two randomized, controlled, double-blind multinational Phase 3 trials compared tenofovir alafenamide (TAF) versus tenofovir disoproxil fumarate (TDF), each in single-tablet regimens coformulated with elvitegravir/cobicistat/emtricitabine (E/C/F). We describe follow up of blinded data through W144, including longer-term safety data.

Methods: ARV-naïve participants were randomized 1:1 to receive E/C/F/TAF (TAF) or E/C/F/TDF (TDF). W144 viral suppression (HIV-1 RNA <50 and <20 c/mL) by FDA snapshot analysis, pre-defined bone and renal safety, and tolerability endpoints are reported.

Results: 1,733 HIV-infected adults were randomized and treated: 15% women, 43% non-white, 23% viral load >100,000 c/mL, median age 34 yrs. At W144, TAF met prespecified criteria for both noninferiority and superiority to TDF by FDA snapshot algorithm (Table 1). Mean [SD] % decrease in BMD was significantly less in the TAF group for both lumbar spine and hip (Table 1). Multiple measures of renal safety were significantly better for participants randomized to TAF (Table 1). There were no cases of renal tubulopathy on TAF versus 2 on TDF. No participants on TAF had renal-related discontinuations versus 12 on TDF (p<0.001). Participants on TAF had greater increases in lipid parameters (Table 1), with no difference in the rate of initiation of lipid-modifying agents.

Efficacy Parameter	E/C/F/TAF (n=866)	E/C/F/TDF (n=867)	Significance
HIV-1 RNA <50 c/mL, n (%)	729 (84.2%)	694 (80.0%)	p=0.021 (diff in percentages [95% CI]: 4.2% [0.6% to 7.8%])
HIV-1 RNA ≥50 c/mL, n (%)	40 (4.6%)	34 (3.9%)	—
Virologic failure or lack of efficacy	17 (2.0%)	17 (2.0%)	—
Other[a]	23 (2.7%)	17 (2.0%)	—
No Virologic Data in W144 Window	97 (11.2%)	139 (16.0%)	—
HIV-1 RNA <20 c/mL, n (%)	702 (81.1%)	657 (75.8%)	p=0.006 (diff in percentages [95% CI]: 5.4% [1.5% to 9.2%])
Safety Parameter[b]			
Renal Safety, change from baseline			
eGFR, mL/min (CG) UPCR β-2M/Cr RBP/Cr	-1.6 (-11.4, 9.4) -10.5% (-43.9%, 38.0%) -25.7% (-58.2%, 13.7%) 34.8% (-4.6%, 83.3%	-7.7 (-18.4, 4.2) 25.2% (-23.8%, 95.2%) 53.8% (-26.0%, 305.1%) 111.0% (38.4%, 264.9%)	All p<0.001
Bone Density, change from baseline			
Lumbar Spine Total Hip	-0.92% (4.12%) -0.75% (4.45%)	-2.95% (4.29%) -3.36% (4.33%)	Both p<0.001
Fasting lipid parameters, change from baseline			
Total Cholesterol (mmol/L) LDL (mmol/L) HDL (mmol/L) Total cholesterol: HDL ratio	0.80 (0.34, 1.27) 0.49 (0.05, 0.93) 0.16 (0, 0.34) 0.2 (-0.3, 0.7)	0.34 (-0.13, 0.78) 0.16 (-0.21, 0.54) 0.05 (-0.08, 0.23) 0.1 (-0.4, 0.6)	All p≤0.006

β-2M/Cr = urine beta-2-microglobulin to creatinine ratio; c/mL = copies/mL; eGFR = estimated glomerular filtration rate; HDL = high-density lipoprotein; LDL = low-density lipoprotein; UPCR = urine protein to creatinine ratio; RBP/Cr = urine retinol binding protein to creatinine ratio

a Other includes discontinued drug due to other reasons and last available HIV RNA ≥50 c/mL or added another ARV.

b For safety parameters, mean (SD) used to summarize BMD; otherwise, median (Q1, Q3) is used

Conclusion: Through W144, participants on E/C/F/TAF had significantly higher rate of virologic suppression (<50 c/mL) than those on E/C/F/TDF, driven by fewer participants on E/C/F/TAF with no W144 data. E/C/F/TAF continued to have a statistically superior bone and renal safety profile compared to E/C/F/TDF through 3 years of treatment.

CSP2.04

Raltegravir (RAL) 1200 mg Once Daily vs RAL 400 mg Twice Daily, given with Tenofovir/Emtricitabine, in Treatment-Naïve HIV-1 Infected Subjects: Subgroup Analyses

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Background: In HIV-1-infected treatment-naive subjects receiving tenofovir/emtricitabine (TDF/FTC), reformulated RAL 1200mg (two 600-mg tablets) once daily (QD) demonstrated potent and non-inferior efficacy at Week 48 compared to RAL 400mg twice daily (BID): 88.9% (472/531) of subjects vs. 88.3% (235/266) achieved HIV RNA <40 copies/mL, respectively (Non-completer=Failure).

Methods: ONCEMRK is a phase 3, multicenter, double-blind, randomized controlled trial comparing reformulated RAL 1200mg QD to RAL 400mg BID, both given with TDF/FTC, for up to 96 weeks in treatment-naive HIV-1-infected subjects. Randomization was stratified by screening HIV-1 RNA (vRNA) and chronic hepatitis B/C status. Results for the primary endpoint (% achieving vRNA <40 copies/mL at Week 48) and secondary endpoint (change from baseline in CD4 count) were summarized within pre-specified subgroups (observed failure approach) to further characterize the effect of RAL 1200mg QD.

Results: Baseline demographics were balanced between treatment groups. Of 797 treated subjects, 85% were male; 59% white, 17% black, 15% Asian; and mean age was 35.9 years. At baseline, mean CD4 count was 415/mm^3; mean plasma vRNA 4.6 $\log_{10}$ copies/mL; 28% had baseline vRNA >100,000 copies/mL, 3% hepatitis B and/or C co-infection, and 34% non-B subtype HIV infection. Primary efficacy results across selected baseline demographic and prognostic factors are shown below (table). Changes in CD4 counts were also similar across subgroups (results not shown).

Conclusions: Reformulated RAL 1200mg QD demonstrated potent and consistent virologic and immunologic efficacy across demographic and baseline prognostic factors, including plasma vRNA >100,000 copies/mL, CD4 ≤200 cells/mm^3, hepatitis co-infection, gender, viral subtype, and geographic region.

CSP2.05

Impact of Niacin on T cell immunity in HIV-Infected Immune Nonresponders on ART

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Background: Tryptophan (Trp) catabolism into immunosuppressive kynurenine (kyn) is involved in dysregulation of immune activation and CD4 lower recovery. Niacin inhibits Trp catabolism loop and represents a potential strategy to improve CD4 recovery. In immune non-responders patients despite successful ART, we assessed whether niacin can improve CD4 counts by decreasing immune activation.

Methods: In this randomized trial, 20 adults receiving ART for at least 12 months with CD4≤350 cells/µl despite undetectable VL for at least 3 months received 2000 mg of extended-release niacin orally once daily for 24 weeks. Side effects, VL, CD4 and CD8 counts, lipid profile, T-cell activation and senescence markers, Tregs and Th17 cells, Kyn/Trp ratio, levels of inflammatory markers IL-6, IP-10, LBP and markers of gut mucosal damage sST2 and I-FABP were assessed at weeks 0, 24 and 48.

Results: 13 patients completed the study as the treatment was disrupted in 5 patients due to adverse events or comorbidity risks and 2 patients were lost of follow-up after week 4. Median [range] CD4 and CD8 at baseline were 230 [196-252] and 530 [330-861] cells/µl respectively and all subjects remained with a VL<40 copies/ml. Significant decreases were observed in plasma levels of triglyceride, total and LDL cholesterol following niacin treatment. During the study, CD4 and CD8 count remained unchanged, however, decreases in CD28-CD57+ senescent CD4 and CD8 cells, and CD4 immune activation (CD38+/HLADR+) were observed. In up to nine patients, improvement on levels of IL-6, IP-10 and LBP were observed. No change in Treg and Th17, plasma levels of sST2, I-FABP and Kyn/Trp ratio, was observed.

Conclusions: Niacin at the dose of 2000 mg/day during 24 weeks showed some adverse events for immune non-

responders despite effective ART. No improvement in CD4 cell recovery was observed during study, while CD4 senescence, activation and differentiation were decreased.

CSP2.06

Long-term Efficacy and Safety after Switching from Tenofovir Disoproxil Fumarate to Tenofovir Alafenamide in Virologically-Suppressed Adults

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Background: Recent HIV treatment guidelines have replaced tenofovir disoproxil fumarate (TDF) with tenofovir alafenamide (TAF) or include both as part of recommended initial regimens. This study assesses long-term efficacy, safety, and tolerability of switching emtricitabine (FTC)/TDF to FTC/TAF, each with various third agents.

Methods: In this double-blind, active-controlled study, virologically-suppressed HIV-infected participants receiving FTC/TDF-containing regimens were randomized (1:1) to switch to FTC/TAF versus continue FTC/TDF while remaining on the same third agent. Virologic suppression (HIV-1 RNA <50 c/mL), markers of bone and renal safety, and safety and tolerability were assessed up to Week (W) 96.

Results: 663 participants were randomized and treated (FTC/TAF n=333, FTC/TDF n=330): median age 49 years, 15% women, median estimated glomerular filtration rate (Cockcroft Gault) 100 mL/min. Third agents included boosted protease inhibitors (46%), integrase inhibitors (28%), and non-nucleoside reverse transcriptase inhibitors (25%). Through W96, virologic suppression was maintained in 89% of participants in both groups (difference -0.5%; 95%CI [-5.3%, 4.4%]). One FTC/TAF participant developed M184V. Drug discontinuation due to AEs was low (FTC/TAF: 2.4% vs FTC/TDF: 1.2%). No cases of Fanconi syndrome or proximal renal tubulopathy occurred with FTC/TAF; one FTC/TDF participant discontinued study drug due to proximal tubulopathy. Biomarkers of renal safety significantly favored FTC/TAF. Lumbar spine and hip bone mineral density (BMD) increased in the FTC/TAF group, while decreased in the FTC/TDF group, with ≥3% improvement at: lumbar spine BMD 40% vs 18%, hip BMD 29% vs 11%, respectively. There were greater increases in lipids with FTC/TAF vs FTC/TDF but no difference in total cholesterol to HDL ratio.

Conclusion: In virologically-suppressed participants switching to FTC/TAF, high rates of virologic suppression were maintained, while renal and bone safety parameters improved. These long-term data support FTC/TAF as a safe and durable backbone, which can be used in combination with various third agents for HIV treatment.

CSP2.07

Primary results from the VALIDATE trial: No impact of valacyclovir on CD4 count decline in HIV-infected adults not receiving antiretroviral therapy (ART)

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Background: Valacyclovir has been shown to decrease plasma HIV viral load (VL) regardless of herpes simplex virus type 2 serostatus, but its impact on HIV disease progression is unknown.

Methods: VALIDATE (CTN-240) was a fully blind, international randomized trial among treatment-naïve HIV-1-infected adults not meeting contemporaneous recommendations for ART. Participants received valacyclovir 500 mg or placebo twice daily and were followed quarterly until having two consecutive CD4 counts ≤350 cells/mm^3 or starting ART for any reason. The primary analysis was a random effects model comparing annual rates of CD4 count decline by study arm, after adjusting for baseline CD4 count. Secondary analyses compared the rate of CD4 count percentage decline, HIV VL, HSV reactivations and drug-related adverse events. The trial was closed after release of the START trial results in August 2015 upon DSMC recommendation.

Results: We randomized 198 participants (72% MSM, 20% women) in Canada, Brazil, Argentina and the United Kingdom. Baseline CD4 count was 592 (491, 694) cells/mm^3 or 28% (23%, 33%), and VL was 4.04 (3.5, 4.5) $\log_{10}$ copies/mL. Over 276 person-years of follow-up, there were no differences in rates of change in absolute CD4 count, CD4 percentage or plasma VL (Table), although valacyclovir decreased HIV VL by -0.22 $\log_{10}$ copies/ml overall (p=.01). Frequencies of microbiologically confirmed HSV reactivations and adverse events were similar between study arms.

Conclusions: In contrast to trials of acyclovir in Sub-Saharan Africa, we found no impact of valacyclovir on ART-untreated HIV disease progression. These results provide further justification for early ART initiation.

CSP2.08

Randomized Trial of Bictegravir or Dolutegravir with Emtricitabine/Tenofovir Alafenamide for Initial HIV Therapy

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Background: Bictegravir (BIC, GS-9883) is a novel, unboosted, once-daily INSTI that demonstrated potent activity in a 10-day monotherapy study and has in vitro activity against most INSTI-resistant viruses.

Methods: Treatment-naïve, HIV-infected adults were randomized 2:1 to receive blinded treatment once daily with BIC 75 mg or dolutegravir (DTG) 50 mg; both were given with open label emtricitabine 200 mg/tenofovir alafenamide 25 mg (FTC/TAF). Treatments were administered without regard for food for 48 weeks. The primary endpoint was the proportion with HIV RNA <50 copies/mL (c/mL) at Week (W) 24 using snapshot analysis. Safety (adverse events [AEs] and laboratory results through Week 48) was a secondary endpoint.

Results: Of 98 patients enrolled, 65 were randomized to BIC+FTC/TAF and 33 to DTG+FTC/TAF. Most subjects were male. Virologic success at W24 was 97% for the BIC arm and 94% for the DTG arm, and at W48 was 97% and 91%, respectively. One subject in the DTG arm had HIV-1 RNA >50 c/mL at W48. No viral resistance was detected in the BIC arm. Mean CD4 count increases at W48 were 258 cells/μL and 192 cells/μL in the BIC and DTG arm, respectively. There were no treatment-related serious AEs or deaths. The most commonly reported AEs were diarrhea (12% in each arm) and nausea (8% BIC, 12% DTG). One subject in the BIC arm discontinued due to urticaria following W24 visit. Median changes in estimated glomerular filtration by Cockcroft-Gault ($eGFR_{CG}$) at W48 were -7.0 mL/min for BIC and -11.3 mL/min for DTG, with no discontinuations due to renal AEs.

Conclusion: BIC+FTC/TAF and DTG+FTC/TAF both demonstrated high virologic response rates at W24 that were maintained at W48. Both treatments were well tolerated, and no significant safety signal was detected in either arm. Further evaluation of BIC for the treatment of HIV infection is warranted.

CSP2.09

The Association of BMI and CD4 counts in among HIV+ individuals initiating antiretroviral therapy

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Background: Some studies demonstrate associations between higher BMI and higher CD4 counts, which may reflect parallel changes in BMI and CD4 counts with disease progression. We investigated whether the strength of the association was maintained with BMI measured 1 year prior to CD4 counts, as a temporal relationship would provide stronger evidence.

Methods: We studied participants in the Canadian Observational Cohort collaboration. We examined the association between BMI and CD4 counts using generalized linear mixed models (GLMM) with random intercept and slope for BMI and using either time-updated values of BMI or time-updated values lagged by 1 year. Women with >10% change in weight within 6 months were excluded as possible pregnancies. The first year of follow-up after cART initiation was excluded and follow-up was truncated at 6 years to ensure that periods of follow-up were consistent between models.

Results: We studied 2033 participants with ≥1 BMI measurement within 6 months of a CD4 count and ≥1 year of follow-up. At cART initiation, the median BMI was 23.7 (21.4-26.5), median age was 40 (33-47), median baseline CD4 was 219 cells/mm^3 (112-320), 87% were men, 19% were IDU. The median year of cART initiation was 2007 (2004-2010). In GLMM adjusting for age, gender, race, a quadratic function of time on cART, regimen class, baseline CD4 and IDU, the association of BMI with CD4 count was diminished in models in which BMI measures were time-updated lagged by 1 year (2.5 (1.2, 6.6), p=0.0002) vs time-updated current values (5.3 (4.0, 6.6), p<0.0001).

Conclusions: The magnitude of the association of BMI with CD4 counts was reduced by approximately one-half when lagged time-updated BMI values were modeled rather than current time-updated values. Further study is needed to improve understanding of the reasons for the correlations.

CSP2.10

Integrase inhibitors and elevated creatinine kinase in HIV+ individuals initiating antiretroviral therapy

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Background: Raltegravir has been associated with marked creatine kinase (CK) elevations and rare muscle toxicity in clinical practice. Whether this occurs with other integrase inhibitors (IIs) is unknown. We conducted a retrospective cohort study comparing changes in CK levels among antiretroviral naïve participants receiving II-based therapy.

Methods: We evaluated participants in the Canadian Observational Cohort collaboration whose first combination antiretroviral (cART) regimen contained an II, and who had ≥1 CK measurement. We defined a Grade 2 CK elevation as ≥272 U/L. We compared time to ≥ Grade 2 levels of CK between participants starting dolutegravir or elvitegravir and participants starting raltegravir with proportional hazards (PH) models. We truncated time at 18 months after cART initiation to ensure similar duration of follow-up between groups.

Results: The initial cART regimen contained raltegravir for 302 participants and dolutegravir or elvitegravir for 154 participants. Patients initiating raltegravir were similar to those initiating dolutegravir or elvitegravir with respect to gender (92% vs 96%, p=0.08), but were older (40 vs 35, p<0.01), had lower baseline CD4 count (320 vs 406, p<0.001), and earlier cART initiation year (2011 vs 2014, p<0.0001). 122 patients had ≥ Grade 2 CK; of these, 22 participants had sustained elevations at >2 consecutive visits. The cumulative probability of ≥ Grade 2 CK at 12 months of follow-up was 0.24 (95% CI (0.20, 0.30)) for those on raltegravir and 0.30 (95% CI (0.22, 0.41)) for patients on DTG or elvitegravir. In PH models, participants on dolutegravir or elvitegravir were similarly likely to develop ≥ Grade 2 CK compared to raltegravir recipients (HR = 1.06, 95% CI (0.66, 1.71) p=0.81), after adjusting for age, gender, baseline CD4 count and viral load, and cART initiation year.

Conclusions: There was no evidence of a difference in development of elevated CK by type of integrase inhibitor.

Co-infections (including HCV, HBV, HPV, Syphilis, TB)

Coinfections (y compris VHC, VHB, papillomavirus, syphilis, tuberculose)

CSP3.01

SOF/VEL In HCV Monoinfected And HIV/HCV Coinfected Patients: Comparison Of Efficacy And Safety Data From Phase 3 Clinical Trials

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Background: 12wks sofosbuvir/velpatasvir (SOF/VEL) has demonstrated high efficacy in HCV genotypes 1-6 patients. Astral-5 completed the phase 3 program-12wks SOF/VEL regimen in HIV/HCV patients. Previous SOF-based combinations showed comparable safety and efficacy in both mono- and co-infected individuals. In order to confirm these data also for SOF/VEL, we compared data obtained in Astral-5 trial with results of mono-infected individuals from Astral 1,2,3.

Methods: Astral-5 enrolled naive and -experienced HCV/HIV co-infected patients of all genotypes, with/without cirrhosis. Patients who were on stable antiretroviral regimens with fully suppressed HIV RNA received SOF/VEL (400 mg/100 mg daily) for 12 weeks. Patients were on a wide range of ARV regimens- emtricitabine/tenofovir disoproxil fumarate or abacavir/lamivudine with backbone raltegravir, cobicistat/elvitegravir, rilpivirine, ritonavir-boosted atazanavir, darunavir or lopinavir . Astral 1,2,3 enrolled treatment-naive and treatment-experienced genotype 1-6 patients, with/without cirrhosis, no limit BMI, no limit age. Patients received SOF/VEL for 12wks.

Results: 106 HIV/HCV coinfected patients were enrolled and treated with SOF/VEL for 12wks. 86% male, 45% black, 77% IL28B non-CC genotypes, 29% had prior treatment failure, and 16% had compensated cirrhosis. The genotype distribution in HIV/HCV patients was 62% GT1a, 11% GT1b, 10% GT2, 11% GT3 and 5% GT4. The median baseline CD4 count was 548 cells/uL with a median eGFR of 97 mL/min. Boosted PI regimens were most commonly used regimen (47%). No patient experienced confirmed HIV virologic rebound. 1035 monoinfected individuals were treated with 12wks SOF/VEL regimen in Astral-1,2,3. Cirrhotics represented 21% (n=220) of the population and 291 (28%) failed

previous treatment. The genotype distribution was 20% GT1a, 12% GT1b, 23% GT2, 27% GT3 11% GT4 3% GT5 and 4% GT6. IL28B non-CC was present in 77% of the patients. Efficacy/safety outcomes of mono- and coinfected patients, including SVR12, HIV parameters and impact of HCV RAVs on outcome will be presented.

CSP3.02

Interdisciplinary Approach to Developing a Hepatitis C Testing Guide – Responding to the Needs of Local Physicians

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Background: A gap in hepatitis C (HCV) testing resources was identified by local family physicians. Requests were received to create a new reference material that concisely describes HCV testing and recommended follow-up care.

Purpose: To describe the process of developing a Quick Reference Guide on the testing and management of HCV, that is locally relevant for family physicians and other public health personnel.

Method: Based upon environmental scans and literature reviews done for the revision of our BCCDC Hepatitis C Guidelines, testing and care management materials were drafted for internal review by the BCCDC Hepatitis program, Public Health Laboratory, and Clinical Prevention Services Surveillance and Education teams. External feedback was received from the HCV Guideline Provincial Working Group (comprised of nurses working in the area of HCV and/or Communicable Disease), physicians working in the areas of Hepatology, Addictions, Inner City Medicine, Public Health and Family Practice, and the provincial STI and Blood Borne Infections working group (comprised of nurse and physician leaders from each health authority). Final approval was received from the BC Communicable Disease Policy Advisory Committee, which is comprised of representatives from each Health Authority and chaired by the Provincial Health Officer.

Result(s): A double-sided 1-page quick reference HCV testing guide has been created that provides information about relevant tests, interpretation, epidemiology, recommended follow-up case management and resources. The rigorous review process ensured that a succinct, provincially relevant document was created that can be widely used by health care practitioners around the province.

Conclusion(s): Using an interdisciplinary collaborative process, a locally relevant provincial testing guide for HCV was created to help support the daily practice of family physicians and public health personnel. Extensive consultation with external partners improved the acceptance and utility of this Quick Reference Hepatitis C Testing Guide.

CSP3.03

High Burden of Oncogenic HPV Infection in High-Risk, HIV-Negative Men Who Have Sex With Men Using a Novel, HPV E6/E7 mRNA Assay

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Introduction: Infection with high-risk human papillomavirus (hrHPV) is a necessary step in anal cancer's pathogenesis. With no universally-accepted guidelines on screening, and given the suboptimal performance of cytology, anal HPV testing is increasingly recognized as an important, adjunctive screening tool for anal cancer precursors. mRNA-based HPV assays targeting the E6/7 oncogenes are emerging as more specific tests for persistent HPV than the traditionally-used DNA-based tests. No data exists on serial monitoring of anal hrHPV in MSM using this novel assay.

Objectives: To describe HPV prevalence/persistence rates in a sample of high-risk, HIV-negative MSM enrolled in a PrEP demonstration project.

Methods: Participants were drawn from PREPARATORY-5, which recruited HIV-negative MSM with high HIV risk as determined by a score of ≥10 on the HIV Incidence Risk Index for MSM (HIRI-MSM) and a history of condomless receptive anal sex in the prior 6 months. Anal samples were tested for hrHPV via the mRNA-based Aptima® HPV Assay at baseline, months 6 and 12. Logistic regression was used to assess characteristics associated with hrHPV infection.

Results: 43 participants were recruited, with median age 33 years (IQR 28-37). 10 (23%) were current smokers, and median HIRI-MSM score was 28 (IQR 19.5-35.5). 24 (56%) participants had hrHPV at any timepoint, and 15 (35%) had persistent hrHPV, defined as hrHPV isolated at two different timepoints. In multivariable logistic regression, current smoking status (OR=9.2, 95%CI=1.16-72.59, p=0.03) and HIRI-MSM score (OR: 1.2 per 1-point increase, 95%CI=1.03-1.33, p=0.01) were associated with hrHPV infection.

Conclusion: Using a novel HPV E6/E7 mRNA assay with higher specificity for persistent infection, this study demonstrated a high burden of overall and persistent hrHPV infection in high-risk, HIV-negative MSM. These findings support the inclusion of MSM at high risk of sexual HIV acquisition when considering interventions related to the prevention and screening of anal cancer precursors.

CSP3.04

Do STI Co-infections and Recreational Drug Use Increase Risk of Virologic Failure among HIV-positive Men on ART? Findings From The OHTN Cohort Study

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Background: Incidence of syphilis, chlamydia and gonorrhea continue to rise among HIV-positive MSM in Ontario. We previously observed an elevated risk of STIs among recreational drug users. Our aim was to determine the effect of a new STI diagnosis and recreational drug use on virologic failure (VF) among MSM successfully treated with ART. Our hypothesis is that any association between STIs and VF would be confounded by drug use.

Methods: The OHTN Cohort Study follows people receiving HIV care in Ontario. STI and viral load data (VL) were retrieved via linkage with the provincial laboratory. We restricted analyses to 2610 MSM who completed >= 1 questionnaire in 2008-2014 and with two consecutive VL<50 within a six-month period on ART. VF was defined as a single VL>=1000 or two consecutive VLs>=200. We modelled STI diagnoses and drug use as time-varying covariates on VF using Cox regression adjusting for confounders. Our model allowed for repeat STI exposures and VFs using the marginal means/rates model.

Results: There were 472 VFs with a 24-month cumulative incidence of 12.1% (95%CI 11.1, 13.1). VFs at time of chlamydia or gonorrhea diagnosis were close to nil. We did not observe an increased risk of VF at the time of a new syphilis diagnosis (HR=1.2 95%CI 0.8, 2.0; aHR=1.1 95%CI 0.7, 1.7). Risk was higher among drug users (non-injection aHR=1.4 95%CI 1.1, 1.8; injection aHR=1.8 95%CI 1.1, 2.6). There was no significant interaction but some evidence of positive confounding between syphilis and VF by drug use.

Conclusions: Regardless of drug use, we did not find an association between a new STI diagnosis and increased risk of VF among men on suppressive ART. Our data are limited by possible misclassification of STI exposures, because not all men were tested, and among those diagnosed, exact dates of acquisition were unknown.

CSP3.05

Predictive Value of AST to Platelet Ratio Index (APRI) for Hepatic Fibrosis Stage by Transient Elastography (TE) in HIV/ HCV Co-infection

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Background: In HCV mono-infected patients, APRI $\leq$0.7 can be used to rule out hepatic fibrosis, and APRI >1.0, >1.5, or >2.0 to indicate cirrhosis. We examined the predictive value of various APRI thresholds in an HIV/HCV co-infected outpatient clinic population.

Methods: TE was performed in sequential HIV/HCV co-infected adults between October 2013 and July 2015. Scores were interpreted as significant fibrosis (F$\geq$2) if $\geq$7.2 kPa and cirrhosis (F4) if $\geq$14.6 kPa. APRI was calculated from lab results within 145 days of TE. Positive predictive value (PPV) and negative predictive value (NPV) were calculated for various APRI cutoffs, assuming that TE scores accurately reflect fibrosis stage.

Results: HIV/HCV co-infected adults (n=163, 87% male, median age 51 years) underwent both TE and APRI (median 23 days apart). Median durations of HIV and HCV infections were 15 and 14 years, respectively. Median current and nadir CD4 counts were 545 and 130 cells/ mm^3, respectively; 98% were receiving ART and 90% had plasma HIV RNA< 40 copies/mL at time of TE. Fibrosis scores by TE were $\geq$F2 in 48% and F4 in 20%. APRI thresholds of 0.7 and 1.0 had PPVs for fibrosis of 72% and 81%, respectively. APRI thresholds of 1.0, 1.5, and 2.0 had NPVs for cirrhosis of 91%, 87%, and 85%, respectively (see Table 1).

Conclusions: In ART-treated HIV/HCV co-infected adults, an APRI threshold of 1.0 adequately predicts fibrosis and rules out cirrhosis. These results support the use of APRI as one aspect of the assessment of fibrosis in this setting.

APRI cutoff	PPV for fibrosis	NPV for fibrosis	PPV for cirrhosis	NPV for cirrhosis
0.7	72%	64%	44%	92%
1.0	81%	62%	58%	91%
1.5	81%	56%	67%	87%
2.0	82%	55%	65%	85%

CSP3.06

Assessment of the Hepatitis C Cascade of care amongst individuals enrolled in an HIV Primary Care Clinic Vancouver, British Columbia

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Introduction: With the advent of direct acting antiviral agents (DAA), HCV therapy is now available to many HIV/HCV co-infected patients not previously candidates for interferon. We reviewed the baseline HCV cascade of care amongst HIV/HCV co-infected individuals engaged in primary care at the St. Paul's Hospital HIV clinic (IDC) in Vancouver.

Methods: A cross-sectional analysis of all adults >=19 years of age with >=2 IDC visits >60 days apart between January 1 2005 and November 25 2015 was performed. Hepatitis C specific markers including HCV antibody, RNA, genotype and evidence of HCV evaluation (liver biopsy or transient elastography) was recorded. A cascade of care was generated for those with positive HCV RNA. Individuals accessing HCV therapy prior to November 2015 were included to allow evaluation of sustained virologic response (SVR).

Results: Overall 1921 individuals were engaged in primary care, and 99.7% underwent at least one HCV antibody test during this time period, with 35% of individuals HCV antibody positive (Table 1). HCV antibody positive individuals were 81% male, 79% reported IDU with median age 44 years (IQR:38-51). Amongst those with detectable HCV RNA (79% of those tested), 23% had undergone HCV therapy by November 2015, with 89% of those with end of treatment response achieving SVR.

Table 1. HCV Cascade of Care in the HIV Primary Care Clinic, St. Paul's Hospital.

	Tested for HCV Antibody	% Antibody positive	%Tested for HCV RNA if antibody positive	% RNA positive if RNA tested	% Genotyped amongst RNA positive	% Assessed with Liver Biopsy or Transient Elastography	% Initiated on HCV Therapy amongst RNA positive
Numerator	1916	663	588	466	385	154	105
Denominator	1921	1916	663	588	466	466	466
% positive	99.7%	35%	89%	79%	83%	33%	23%

Conclusions: In HIV/HCV co-infected patients engaged in interdisciplinary HIV primary care , only 23% had undergone HCV therapy at the start of the DAA era. Efforts to maximize HCV assessment and therapy are required to ensure full benefit of DAAs.

CSP3.07

Can ALT rise serve as a useful marker of hepatitis C (HCV) seroconversion in HIV/HCV co-infected patients?

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Background: Acute HCV infection in HIV-infected individuals is well described. We evaluated detection of ALT elevation as a marker of HCV seroconversion in HIV-infected individuals receiving ART.

Methods: HIV+/HCV –ve individuals initiating ART January 2005 - December 2014 were eligible if they received ART for > 6 months and had available ALT values. Individuals with known HBV and those with baseline ALT> 1.5 ULN were excluded. Subsequent ALT elevations were graded and correlated with documented HCV seroconversion. The association between ALT rise and HCV seroconversion was evaluated using a multivariate confounder Poisson regression model offset by time to seroconversion, adjusted for demographics and risk factors.

Results: Overall 1018 individuals were included, n= 964 (94.7%) male, 11.0% IDU, median age 41 years (Q1- Q3: 33-48 years). Over the study period 36 individuals had documented HCV seroconversion (incidence rate 0.87/100 person-years; 95% CI 0.63– 1.21) (See Table 1). HCV seroconversion was associated with escalating grade of preceding ALT elevation (p-value<0.001). In seroconvertors with elevated ALT, median time from ALT rise to documented HCV positivity was 68 days (Q1- Q3: 2 – 687 days). In multivariate analysis adjusted for ethnicity,MSM and IDU status, grade of ALT elevation (Grade 1 elevation: adjusted risk ratio [aRR] 2.19; 95% CI 0.77 – 6.22, Grade 2: aRR 7.82; 95% CI 2.66 – 23.00, and Grade 3/4: aRR 15.07; 95% CI 5.46 – 41.59) was associated with documented HCV seroconversion.

Table 1. Incidence Rates of HCV Seroconversion, Stratified by Known IDU, MSM Status and Grade of ALT elevation.

Overall N=1018	# of records	# of events	%	Incidence Rate (100 person-years)	95% CI
IDU No	654	18	2.8%	0.67	0.42 1.06
IDU Yes	112	12	10.7%	2.46	1.41 4.30
MSM No	136	9	6.6%	1.56	0.82 2.98
MSM Yes	499	18	3.6%	0.87	0.55 1.37
ALT Grade 0	784	12	1.5%	0.39	0.22 0.69
ALT Grade 1	166	9	5.4%	1.19	0.62 2.28
ALT Grade 2	44	9	20.5%	4.37	2.41 7.94
ALT Grade 3/4	24	6	25.0%	5.17	2.3 0 11.63

Conclusion: Standard of care ALT monitoring readily identifies potential HCV seroconversions in an at-risk population.

CSP3.08

Does the Non-Alcoholic Fatty Liver Disease (NAFLD) Score Predict Liver Fibrosis Progression after HCV treatment in HIV-HCV Co-infected Patients?

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Background: Steatosis secondary to NAFLD is associated with progression of liver fibrosis in chronic HCV. We aimed to determine the role of the NAFLD score in hepatic fibrosis progression following HCV treatment in co-infected patients.

Methods: The Canadian Co-infection Cohort is a prospective multicentre cohort of 1688 co-infected patients. Liver fibrosis progression (regression) was defined as an increase (decrease) of at least one Metavir stage from pre-treatment as determined by FibroScan or aspartate aminotransferase-to-platelet ratio index (APRI). A multivariate logistic model assessed the association of the NAFLD score with the odds of liver fibrosis regression. A linear model estimated the relationship between NAFLD and the percentage change in APRI post-treatment.

Results: Overall, 224 participants with a median age of 49 years; HCV duration 14 years; baseline APRI 1.0 were included; 71% of 238 courses achieved sustained virologic response (SVR). Between 6 and 24 months post-treatment, 4% progressed, 27% regressed and 69% remained stable. In the logistic model, the NAFLD score had no effect on fibrosis regression; however, SVR and pre-treatment APRI were associated with regression (Table 1). In the linear model, the NAFLD score was associated with increases in APRI post-treatment.

Conclusions: SVR was associated with fibrosis regression post-treatment. A high pre-treatment APRI was predictive of recovery, indicating reduction in inflammation or the greater potential for change. After controlling for confounders, a higher NAFLD score appeared to be associated with increases in APRI post-treatment. Management of fatty liver disease following treatment is essential to achieve optimal liver outcomes after cure.

Table 1: Regression models

	Odds of liver fibrosis regression*		Percentage change in APRI post-treatment†	
Variable	**Odds ratio**	**95% C.I.**	**Coefficient**	**95% C.I.**
SVR status indicator post-treatment	5.55	(2.13 ; 16.02)	-0.78	(-0.96 ; -0.60)
Log of pre-treatment NAFLD score	0.63	(0.04 ; 9.33)	0.91	(0.36 ; 1.45)
Log of pre-treatment APRI score	7.39	(3.97 ; 15.16)	-0.56	(-0.67 ; -0.45)
DAA-based treatment indicator	0.92	(0.40 ; 2.11)	-0.13	(-0.30 ; 0.05)
Genotype 3 indicator	0.79	(0.27 ; 2.18)	-0.05	(-0.29 ; 0.18)
HCV duration (per 5 years) at initiation	1.15	(0.91 ; 1.44)	0.04	(-0.00 ; 0.09)
CD4 count (per 100 units) at initiation	1.01	(0.89 ; 1.13)	-0.00	(-0.03 ; 0.02)
* The dependent variable for this model was a binary indicator for fibrosis regression, based on Metavir stage				
† The dependent variable for this model was the natural log of the percentage change in APRI from pre-treatment to post-treatment				
C.I. = Confidence Interval				

CSP3.09

Longitudinal study of HCV diversity and neutralizing antibody responses reveal differential modes of vertical transmission in presence of coinfection with HIV-1

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Background: Coinfection with hepatitis C virus (HCV) and HIV-1 is common and aggravates the prognosis of hepatitis C. HCV exists as quasispecies, and most of its genetic variability is found within hypervariable regions of the E2 envelope glycoprotein. During pregnancy, immune pressures exerted on HCV target solvent-exposed regions of E2, suggesting the involvement of humoral immunity. The objectives of the study were to analyze potential associations between HCV quasispecies evolution and maternal humoral responses, and to characterize the impact of coinfection on these processes.

Methods: Sera from HCV-infected women (n=17) or women coinfected with HCV and HIV-1 (n=20) were collected during all three trimesters of pregnancy and in the post partum period. HCV RNA was extracted, RT-PCR-amplified, and the N-terminal region of E2 was subjected to next generation sequencing (Roche 454 FLX+). Descriptive summary statistics (Shannon entropy; Hamming distance; UniFrac Distance; dN/dS) were computed and HCV-specific maternal neutralizing response was measured using neutralization assays based on autologous HCV-derived pseudoparticles (HCVpp).

Results: High quasispecies diversity was associated with a significantly reduced risk of VT (OR=29.86; p=0.0024) and a lower degree of hepatic inflammation (p=0.0240 and p=0.0088 for ALT and AST respectively) in women infected with HCV only, but not in coinfected women. Neutralization assays performed on samples from 13 patients revealed that quasispecies diversity was positively associated with neutralizing activity (p=0.0085).

Conclusion: These results strongly suggest that maternal humoral immunity is driving HCV diversification during pregnancy and that significant immune pressure exerted on the virus is a protective factor for HCV VT in women infected with HCV alone but not in women coinfected with HIV-1. Taken together, these results highlight the complexity of the mechanisms involved in VT of HCV, and argue in favor of a model whereby these mechanisms are fundamentally different in presence of maternal coinfection with HIV-1.

CSP3.10

Outcomes of influenza infection in HIV positive vs. HIV negative individuals requiring admission to hospital

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Introduction: In the pre-ART era, HIV infection was associated with worse outcomes from influenza. We evaluated differences in outcomes in HIV-positive vs. HIV-negative individuals admitted to hospital with influenza in the ART era.

Methods: Individuals admitted to two acute-care hospitals with laboratory-confirmed influenza August 2009 - May 2013 were reviewed retrospectively. Outcomes were defined as use of influenza antiviral therapy, intensive care admission, duration of admission and in-hospital death. Characteristics of HIV-positive cases were compared to those who were HIV-negative with Fischer's exact test or chi-squared test for categorical variables, and Wilcoxon rank sum test for continuous variables.

Results: Amongst 243 individuals admitted with influenza (88% influenza A), n=55 (22.6%) were HIV-positive. Individuals with HIV were more likely male (63% vs. 47%, p = 0.03), younger (median age 46 vs. 51, p = 0.02), report injection drug use (16% vs. 3%, p = 0.001) and have less comorbid cardiac disease (7% vs. 19%, p=0.037) and diabetes (5% vs. 20%, p = 0.012). ART uptake was high (n=50, 91%) with median CD4 cell count of 290 cells/mm^3 (Q1:Q3 110 – 410 cells/mm^3). Median hospitalization for both groups was 5 days (p= 0.114) with IQR of 4-8 days for HIV-positive and 5-11 days for HIV-negative individuals. ICU admission occurred in 11% of HIV-positive vs. 19% of HIV-negative (p=0.170) individuals. HIV-positive individuals were more likely to receive influenza antiviral therapy (96% vs. 72%, p < 0.001). One death was observed in the HIV-positive group vs. 10 in HIV-negative individuals (2% vs. 5.4%, p=0.464).

Conclusions: For patients admitted to hospital, HIV-positive individuals in the ART era had similar outcomes to HIV-negative individuals, but were more likely to receive influenza antiviral therapy during hospitalization.

CSP3.11

New onset hyperthyroidism following hepatitis C treatment with ledipasvir/sofosbuvir in two individuals living with HIV

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Background: Prior to the era of direct-acting antiviral (DAA) hepatitis C treatment, thyroid function was routinely measured in individuals receiving interferon-based therapies. This was to monitor for the development of interferon-induced thyroid dysfunction. Current hepatitis C treatment guidelines recommend the routine monitoring of thyroid function only for those individuals receiving interferon-based therapies.

Case Descriptions:

Case 1: A 44 year-old female living with HIV and chronic hepatitis C (genotype 1a, treatment-naïve, non-cirrhotic) was treated with a 12-week course of ledipasvir/sofosbuvir. Her other medications included tenofovir/emtricitabine/ritonavir/darunavir. About one month into hepatitis C treatment, she developed increasing fatigue. Routine blood work demonstrated a suppressed TSH of <0.02 mU/L. Her exam was normal apart from a palpable thyroid gland. Subsequent labwork demonstrated an elevated free T4 (24 pmol/L), and a radioiodine uptake and scan was consistent with Graves' disease. She was placed on methimazole, and responded clinically.

Case 2: A 53 year-old male living with HIV and chronic hepatitis C (genotype 1a, treatment-naïve, non-cirrhotic) was treated with a 12-week course of ledipasvir/sofosbu-

vir. His other medications included abacavir/lamivudine/raltegravir, and his other comorbidities included gout, pulmonary hypertension, and proteinuria. Two months after completing hepatitis C treatment, he presented with symptoms of heat intolerance, which on further questioning, had been going on for several months. His exam was normal apart from evidence of hand tremor. Blood work demonstrated a suppressed TSH (0.01 mU/L), and an elevated free T4 (37.7 pmol/L). A radioiodine uptake and scan was consistent with Graves' disease. He was treated with methimazole, and responded clinically.

Discussion: These cases demonstrate a temporal association between DAA hepatitis C treatment, and the new onset of hyperthyroidism. Thyroid function measurements may continue to be a beneficial component of routine hepatitis C treatment monitoring, even in individuals not receiving interferon-based therapies.

CSP3.12

The Effect of Iron Deficiency on Hepatic Fibrosis Progression among HIV-HCV Co-Infected Men and Women

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Background: Chronic iron deposition increases the risk of liver fibrosis/cirrhosis. We aimed to determine if iron deficiency protects against hepatic fibrosis progression in HIV-HCV co-infected men and women.

Methods: The Canadian Co-infection Cohort is a prospective multicentre cohort study of 1635 patients. We analyzed participants with available serum ferritin values and without significant liver fibrosis or end-stage liver disease (ESLD) at baseline. We evaluated the association of iron deficiency (serum ferritin <30 µg/L) with the incidence of significant fibrosis (aspartate aminotransferase-to-platelet ratio index (APRI)>1.5, FIB-4>3.25, or ESLD) by sex, and used Cox models to adjust for potential confounders.

Results: Overall, 668 participants with a median age of 44 years; HCV duration 17 years; baseline APRI 0.5; Aboriginal ethnicity 22% (35% women, 16% men) were included. Of these, 27% of women and 8% of men were iron-deficient. Females and Aboriginals were more likely to be iron-deficient (odds ratio (95% CI): 4.2 (2.6–6.9) and 2.6 (1.6–4.3), respectively). In total, 198 participants (62 women, 136 men) developed significant fibrosis over a median follow-up of 3.5 years. The effect of iron deficiency appeared to differ in women and men so further analyses were stratified by sex. After adjustment, iron deficiency was not associated with liver fibrosis in either men (adjusted hazard ratio (aHR)=1.0, 95% CI, 0.5–1.9) or women (aHR=0.7, 95% CI, 0.3–1.4). However, among women, Aboriginals had a lower risk of liver fibrosis (aHR=0.5, 95% CI, 0.2–0.9). Baseline APRI was significantly associated with liver fibrosis in both sexes.

Conclusions: Iron deficiency does not appear to be associated with a lower risk of liver fibrosis progression in either sex but instead may be acting as a marker of Aboriginal ethnicity. Among women, Aboriginal ethnicity appeared to be protective. Understanding the mechanisms behind this protective effect may yield insights into the pathogenesis of HCV-related liver disease.

CSP3.13

Prevalence and Clinical Presentation of Syphilitic Hepatitis in HIV-Infected Patients

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Background: The reciprocal interaction between syphilis and HIV infections has been well established, but progression to liver inflammation is understudied. Liver enzyme abnormalities are well documented in HIV patients, often attributed to co-infection with viral hepatitis, alcohol use, or direct hepatotoxicity of HAART. However, previous studies have failed to sufficiently examine syphilis as a potential cause of such elevated laboratory values. The aim of this analysis is to determine the prevalence of syphilitic hepatitis among HIV-infected individuals.

Methods: We performed a retrospective analysis of all HIV-infected individuals regularly attending a tertiary clinic in Vancouver, Canada. We identified cases of syphilis resulting in syphilitic hepatitis according to the following criteria: (1) RPR-confirmed Treponema pallidum infection occurring after HIV infection; (2) elevated liver enzyme laboratory tests, including ALP, ALT, and AST that normalized after penicillin treatment; and (3) no clearly identifiable cause of liver inflammation beyond syphilis.

Results: Among 567 HIV-infected patients, 35 were diagnosed with early syphilis based on RPR results. According to our definition, 3 of the 35 cases of early syphilis resulted in syphilitic hepatitis. The characteristics of the cohort demonstrating syphilitic hepatitis are summarized in Table 1. Patients progressing to syphilitic hepatitis tended to have a significantly higher bacterial titer, as shown in Table 2.

Conclusions: Syphilitic hepatitis does occur in HIV-infected populations and should be included on the differential diagnosis for abnormal liver enzyme values. However, its prevalence appears to be minimized through prompt identification and treatment, resulting in far lower rates than previously postulated.

Table 2: Characteristics of Syphilis Patients With and Without Hepatitis (CSP3.13)

Characteristic	Syphilitic Hepatitis (N=3)	Syphilis Without Hepatitis (N=32)
Abdominal Pain	1	1
Pharyngitis	1	0
Rash	2	17
Fever	1	1
Arthralgia	1	6
Skin Lesion	2	7
Median RPR	1:256	1:8
Median CD4 Count (cells/uL)	423	754
Median HIV Viral Load (copies/mL)	<40	<40
Receiving ARVs	3	28
Virologic Suppression (VL <40 copies/mL)	2	24
Male	3	30
Mean Age (Range)	44 (28-63)	46 (25-63)
African-American	1	1
Caucasian	2	27
Hispanic	0	1
Asian	0	3

CSP3.14

Sustained Virologic Response and Renal Function in Hepatitis C and HIV Co-Infected Canadians Receiving Clinical Care

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Background: Hepatitis C virus (HCV) and HIV co-infected patients are at increased risk of chronic kidney disease (CKD) compared to HIV mono-infected patients. We compared kidney function between co-infected patients who developed a sustained virologic response (SVR) to HCV treatment and those who failed treatment.

Methods: HIV patients treated for chronic HCV between January 2003 and July 2016 in the Canadian Co-Infection Cohort were analyzed. Patients were followed from SVR, which was defined as undetectable HCV RNA ≥ 12 weeks after end of treatment, and remained in follow-up with subsequent bi-annual study visits. Estimated glomerular filtration rates (eGFR) were calculated with the CKD-EPI equation at each visit. Linear regression with generalized estimating equations were used to model annual rates of change in eGFR separately for patients with and without SVR. Models were adjusted for demographic, substance abuse, chronic comorbidities, interferon use, and HIV disease and treatment covariates.

Results: We followed 420 patients over a total of 909 person-years. The overall SVR rate was 71% (299/420) and was 61% (171/281) and 92% (128/139) among those treated with and without interferon, respectively. SVR patients were more likely to be female (21% vs. 12%) and have a higher $CD4^+$ count (510 vs. 440 cells/μL), and less likely to have reported recent IDU (16% vs. 25%) and have a detectable HIV viral load (12% vs. 21%). After HCV treatment, eGFR declined at a rate of 1.3 mL/min/1.73m^2/year (95% confidence interval [CI]: 0.8, 1.9) among those who failed therapy. Among those who achieved SVR, eGFR declined at a rate of 0.9 mL/min/1.73m^2/year (95% CI: 0.4, 1.3).

Table 1: Characteristics of Patients Demonstrating Syphilitic Hepatitis (CSP3.13)

Case Number	Age	Race	Duration of HIV (years)	HIV Viral Load	ARV Regimen	Syphilis Stage	RPR Titer	Symptoms	ALT (IU/L)	AST (IU/L)	ALP (IU/L)	Treatment
1	28	AA	5	<40	EVG/c/TDF/FTC	Secondary	1:128	Abdominal pain, pharyngitis, lesion	605	427	541	Benzathine penicillin G (2.4 MU) IM x 1
2	40	C	0	176995	TVD/DRV	Secondary	1:256	Fever, arthralgia, rash	64	ND	307	Benzathine penicillin G (2.4 MU) IM x 3
3	63	C	26	<40	TVD/RGV	Secondary	1:256	Lesion, rash	76	50	382	Benzathine penicillin G (2.4 MU) IM x 1

Conclusion: In our HCV-HIV co-infected population, we found that SVR lead to a modest reduction in the annual rate of eGFR decline. The increased risk of CKD in this population may not be related to persistent HCV replication.

Complications of Antiretroviral Therapy

Complications des thérapies antirétrovirales

CSP4.01

Association between lipodystrophy and length of exposure to antiretroviral therapy in adult HIV-1 infected patients in Montreal

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Introduction: Lipodystrophy is a frequent complication of antiretroviral therapy, and may lead to low adherence to antiretroviral medications. The aim of this study was to establish the prevalence of lipodystrophy and its association to cumulative exposure to the most prevalent antiretroviral drugs in our population.

Method: We conducted a cross sectional study in all HIV-infected patients attending the HIV clinic in the *Centre hospitalier universitaire de Montréal* (CHUM) with an available DEXA scan. For the purpose of descriptive statistics, lipodystrophy was defined as a trunk/limb fat ratio ≥1.5. Association between cumulative exposure to antiretrovirals (measured in years of use) with trunk/limb fat ratio (coded as a continuous variable) was assessed using univariate linear regression for each antiretroviral drug with at least 45 exposed patients.

Results: One-hundred and sixty-six patients were included. Seventy-five percent were male, median age was 56 years, 60% were Caucasian, and all were exposed to antiretroviral drugs. Overall, prevalence of lipodystrophy was 47 %, with a mean trunk/limb fat ratio of 1.87, SD=1.03, min=0.6 and max= 5.87. Patients classified as lipodystrophic were more likely to be diabetic (50 vs. 28%, Fisher's exact p= 0.07) and to have dyslipidemia (47 vs. 19%, p=0.01). Among 9 drugs tested, there was an association between years of use of d4T, ritonavir and raltegravir and higher trunk/limb fat ratio (indicating more lipodystrophy) ($p<0.05$), and no association with AZT, abacavir, tenofovir, lopinavir, atazanavir and darunavir.

Conclusion: Lipodystrophy is very common in HIV infected patients and is correlated with duration of some antiretroviral drugs. Lack of adjustment for potential confounders and other antiretrovirals, as well as lack of power are limitations of this work.

CSP4.02

Transient neonatal electrolyte disorder from in utero exposure to ritonavir and betamethasone: Role for routine electrolyte monitoring

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Background: Transient adrenal dysfunction has been described in HIV infected individuals receiving concurrent treatment with ritonavir and corticosteroids, however, there are no specific recommendations for the monitoring of newborns exposed to these drugs *in utero*. Here we present a case of symptomatic neonatal adrenal dysfunction from *in utero* exposure to these drugs.

Results: A newborn male was born to a 41 year-old HIV infected mother, who had been on a stable antiretroviral (ART) regimen (Truvada, Atazanavir/Ritonavir), with an undetectable viral load throughout pregnancy. At 37+3 weeks gestational age (GA), she received 2 doses of Betamethasone (12mg intra-muscular), and delivered at 37+5 (GA) via c/section without complications. Birthweight was 3610g, and newborn was started on ART prophylaxis (Zidovudine/Lamivudine). At 9 hours of age the baby was found to be jittery, and capillary glucose was low (2.6mmol/L), but later normalized with feeds. On day 2 of life, prior to planned discharge, serum electrolytes were inadvertently measured and the baby was found to be severely hyponatremic (sodium 123 mEq/L) and hyperkalemic, (potassium 7.0 mEq/L). Due to persistent hyponatremia and hyperkalemia, he required saline infusions until sodium and potassium levels normalized by day 6 of life. Testing done on day 2 of life showed low normal DHEAS level (20.4 uumol/L), with low normal 17OH(6.9 nmol/L). Serum cortisol tested on day of life 6 was normal (238.9 nmol/L), as were urine electrolytes, and remain so to 2 months of follow-up . A diagnosis of transient adrenal dysfunction, due to in utero exposure to the combination of betamethasone and ritonavir, was suspected.

Conclusion: Given the high risk of preterm delivery among HIV infected women on ritonavir containing regimens, and the recommended use of bethamethsone in these cases to promote fetal lung maturity, electrolytes should routinely be in the first 48 hours of life in exposed newborn.

CSP4.03

Regulatory T-cells (Tregs) in ART-treated adults with atherosclerosis diagnosed by computed tomography angiography

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Background: Chronic HIV infection results in accelerated aging and cardiovascular diseases due to persistent immune activation. Furthermore, HIV infection is associated with elevated frequency of regulatory T-cells (Tregs) which contrasts with their protective role against cardiovascular diseases. We therefore assessed the frequency of Treg subsets in association with immune activation and senescence in ART-treated HIV-infected adults with or without atherosclerosis.

Methods: PBMC and plasma were obtained from ART-treated HIV-infected adults (VL <40 copies/ml for at least 12 months) with or without atherosclerosis (n=20/group) in the absence of statin treatment. Atherosclerosis was determined by the presence of atherosclerotic features evaluated by computed tomography angiography of the coronary arteries with stenosis of 50% or greater. Patients in each group were matched for sex, age and smoking status. The frequency of Treg subsets, Th17 cells, expression of immunosuppressive purinergic ecto-enzyme CD39, immunosenescence (CD28-CD57+) and activation (CD38/HLA-DR co-expression) on CD8 and CD4 T-cells, were assessed by flow cytometry. Plasma levels of IL-6, marker of microbial translocation LBP and lipid profile were also assessed.

Results: Atherosclerotic patients had higher plasma IL-6 and lower CD4 nadir. Higher frequency of Tregs was observed in patients with atherosclerosis vs. non- atherosclerosis in association with CD4 nadir. Importantly, higher frequency of CD39+ CD4 memory T-cells which produce IL-17A and INFγ as well as CD39+Tregs were detected in atherosclerotic patients in association with elevated d-Dimer and HDL levels. No difference in the frequency of recently migrant thymic CD31+ Tregs, Th17 cells, Th17/Tregs ratio and levels of immune activation, senescence and microbial translocation were observed between the study groups.

Conclusion: These results suggest a potential functional metabolic link between the expansion of both total and CD39+ Tregs and purinergic and lipid metabolism in ART-treated patients with atherosclerosis not receiving statins, which is a known inducer of Tregs.

CSP4.04

The effect of starting anti-retroviral therapy during HIV primary infection on plasma anti-HIV envelope gp120 specific IgG antibody concentrations

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Background: The first detectable anti-HIV gp120 Envelope specific immunoglobulin G (IgG) antibodies (Abs) appear around week 6 of HIV primary infection. The current standard of care for HIV infection is starting antiretroviral therapy (ART) as early as possible after diagnosing HIV infection. Such non-neutralizing Abs with specificity for gp120 may play a role in HIV control through antibody-dependent (AD) innate immune functions. We investigated the effect of starting ART within 90 days of compared to later in infection on changes in the concentration of anti-gp120 specific Abs after a year or more on ART.

Hypothesis: ART that suppresses HIV viral load will lead to decreased levels of anti-gp120 specific IgG.

Methods: The study population included 21 subjects enrolled in the Montreal Primary Infection cohort. Ten started ART at a median (interquartile range [IQR]) of 51.5 (40.75, 66.5) days post-infection. Eleven started ART at a median 127 (118, 148) days post-infection. An ELISA assay was used to determine the anti-gp120 specific IgG concentrations in longitudinally collected samples from before (or soon after) ART and after a median 592 (396, 702) days.

Results: Anti-gp120 IgG levels were stable in subjects starting ART within 90 days of infection (pre/early ART timepoint of 0.45 [0.26, 0.63] mg/mL versus late ART timepoint of 0.66 [0.38, 0.95]mg/mL, p>0.05, Wilcoxon matched pairs test), but fell significantly in those starting ART after 90 days (pre/early timepoint of 2.0 [0.49,0.61] mg/mL versus late ART timepoint of 0.61 [0.38,0.74]mg/mL, p=0.013, Wilcoxon).

Conclusions: Starting ART within three months of HIV infection preserves the concentration of anti-HIV gp120 specific Abs for at least 1 year. If these anti-gp120 specific Abs play a role in HIV control through their action on AD innate immune functions, the timing of ART initiation may determine whether these responses develop and can be maintained on ART.

CSP4.05

Changes in Liver Transaminases are Related to Changes in Glucose Parameters and Adiponectin in HIV-Infected Patients Treated with Tesamorelin, a GHRH Analogue

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Background: Tesamorelin reduces visceral adipose tissue (VAT) in HIV+ patients with lipodystrophy. VAT reduction in responders (27-30%) is associated with improvements in ALT and AST in patients with baseline elevations (>30U/L) in these enzymes. This analysis tested the hypothesis that changes in transaminases in responders would be associated with changes in glucose parameters and adiponectin.

Methods: Combined data from two Phase 3 studies in HIV+ patients with excess abdominal fat. Tesamorelin "Responders" were defined as individuals with ≥8% VAT reduction.

Results: At 26 weeks, change in ALT was -8.9±22.6 (mean±SD) U/L in Responders vs. 1.4±34.7 U/L in non-Responders (p=0.002). Change in AST was -3.8±12.9 vs.0.4±22.4 U/L in Responders vs. non-Responders (p=0.045). Change in ALT was correlated with changes in fasting blood glucose (FBG) (r=0.15, p<0.025) and HbA_{1c} (r=0.14, p=0.036). Among responders without hepatitis B or C, change in ALT was correlated with change in FBG (r=0.17, p=0.018) and trended toward association with changes in fasting insulin (r=0.14, p=0.061) and HbA_{1c} (r=0.13, p=0.076). At 52 weeks, change in ALT was -11.0±24.7 vs.-7.5±18.1 U/L in Responders vs. non-Responders (p=0.02). Change in AST was -3.8±16.8 vs.-5.4±13.4 U/L in Responders vs. non-Responders (p=0.71). Change in ALT trended toward positive association with changes in FBG (r=0.21, p=0.09), fasting insulin (r=0.21, p=0.085), and HOMA-IR (r=0.22. p=0.084), and toward negative association with change in adiponectin (-0.22, p=0.094) in responders. Among responders without hepatitis B or C, change in ALT was positively correlated with changes in fasting insulin (r=0.36, p=0.0008) and HOMA-IR (r=0.33, p=0.016) and negatively correlated with change in adiponectin (r=-0.29, p=0.041). Change in AST was correlated with changes in FBG (r=0.27, p=0.048) and adiponectin (r=-0.28, p=0.049).

Conclusion: Changes in transaminases were associated with changes in glucose parameters and adiponectin in tesamorelin responders. This finding may account for the preservation of glucose homeostasis seen in these patients.

Early Treatment, Reservoirs, and Cure

Traitement anticipé, réservoirs et remède

CSP5.01

CCR5delta32 homozygous stem cell transplant for hematologic malignancy in an HIV positive person

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Background: Functional HIV cure by stem cell transplant has been attempted multiple times but only durably achieved once in the so-called 'Berlin patient'. This HIV positive person received a stem cell transplant from a CCR-5delta32 homozygous stem cell donor as treatment for a hematologic malignancy with discontinuation of antiretroviral therapy without subsequent HIV viral rebound.

Purpose: Describe the clinical course and HIV antiretroviral management of a person undergoing CCR5delta32 stem cell transplant for chronic myelogenous leukemia.

Methods: The 58 year old HIV+CMV+ individual provided written informed consent to participate in the protocol, and is enrolled as part of the ICISTEM (International Collaboration to guide and investigate the potential for HIV cure by Stem Cell Transplantation). Peripheral blood cells were collected by leukapheresis, in addition to ileal biopsies and cerebrospinal fluid prior to transplant. Lamivudine, abacavir and dolutegrevir were maintained pre- and post-transplant. HIV viral load was measured daily for the first 14 days post transplant, in addition to standard of care clinical blood work. Conditioning treatment included irradiation and anti-thymocyte globulin as well as methotrexate, cyclosporine and prednisone.

Results: At submission, the individual is 121 days post transplant with full engraftment, complete donor molecular chimerism, and CML remission. Lamivudine was renally dosed throughout the post-transplant period. Two episodes of mild graft versus host disease were treated successfully with low dose steroid and/or cyclosporine. No HIV virologic rebound was noted, CD4+ T cell counts are near pre-treatment levels, and 2 episodes of CMV viremia were treated.

Conclusions: This HIV+ person has been, to date, successfully treated from a hematologic perspective, and his antiretrovirals (as well as antivirals) were managed well during transplant with moderate renal insufficiency. HIV status in the context of a potentially curative stem cell genotype is unknown, and antiretroviral discontinuation is planned at the one year mark.

CSP5.02

Impact of Timing and Duration of Virologic Suppression on HIV Serologic and ELISpot responses in the EPIC4 cohort

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Background: Early treatment of perinatal HIV infection and sustained virologic suppression (SVS) can limit HIV reservoirs. Loss or limited development of HIV-specific immune responses have been identified as potential correlates of reservoir size and virologic control. We assessed serologic and T cell responses in relation to timing and duration of SVS in cART-treated children.

Methods: HIV serologic responses (expressed as signal-to-cutoff value [S/CO]) and T cell responses (*magnitude* expressed as cumulative frequencies of cells producing interferon-gamma [IFN-g] and *breadth* expressed as proportion of peptide pools inducing IFN-g production) were analyzed according to timing of cART initiation. Subjects' age at effective cART initiation (AETI) and proportion of life on effective cART (PLEC) at baseline were determined.

Results: Thirty-six subjects (age 3.4–21.2 years at baseline) who initiated cART between birth–12.9 years had serologic results. Five had negative serology (S/CO<1), while 3, 8 and 20 had low (S/CO=1-10), moderate (10-100), and high (>100) reactive serology, respectively. One-way ANOVA demonstrated differences in mean AETI and PLEC between serologic response groups ($p<0.01$ for both), with lower responses associated with younger AETI and greater PLEC. Regression analysis showed an association between AETI and S/CO ($p<0.01$, adjusted $R^2=0.37$), and PLEC and S/CO ($p<0.01$, adjusted $R^2=0.45$). ELISpot was performed in 12 subjects. Magnitude of response was associated with AETI (adjusted $R^2=0.67$, $p=0.0002$) and PLEC (adjusted $R^2=0.57$, $p=0.001$). A trend association was observed between AETI, PLEC, and ELISpot breadth (AETI and breadth adjusted $R^2=0.23$, $p=0.06$; PLEC and breadth adjusted $R^2=0.20$, $p=0.08$). There was a significant relationship between S/CO and magnitude (adjusted $R^2=0.30$, $p=0.02$) but not between S/CO and breadth ($R^2=0.05$, $p=0.24$).

Conclusions: Earlier treatment and greater PLEC predicted HIV-specific serologic and T cell responses, with loss of antibody responses and weaker ELISpots amongst those treated from the neonatal period and with a majority of life on effective treatment.

HIV and Aging and Comorbidities (including CVD, Osteoporosis, Neurocognitive Effects)

Le VIH, le vieillissement et les comorbidités

CSP6.01

Executive Dysfunction in HIV Reflects Impaired Control, not Impulsive Responding: Behavioral and EEG Evidence from the Positive Brain Health Now study

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Executive dysfunction can occur in people with HIV, even with well-controlled infection. The brain basis of this impairment, and its relationship with other aspects of cognition, remain unclear. Here, we assessed executive function with the Simon task, a classic test of response control, collecting behavioral and EEG data. We asked whether poor performance reflected impulsive responding, or impaired control. We also tested whether these measures relate to overall cognitive ability, measured by a brief neuropsychological battery, and to clinical variables. 68 participants (8 female; mean age 54.1 (SD 6.8) y) were drawn from two sub-studies of the Positive Brain Health Now study, an ongoing longitudinal study of brain health in older people living with HIV in Canada. They completed the Simon task, a speeded two-choice task which requires control over automatic motor responses, while high-density EEG was collected. Overall cognitive ability was assessed using a brief battery of cognitive tests (B-CAM) and via self-report, and a range of biological and psychosocial variables were collected. Poor performers on the Simon task showed a behavioral pattern consistent with weak executive control, rather than excessively impulsive responding. The two main measures of executive control, incongruent reaction time and the Simon effect, were both correlated with overall cognitive ability as measured by the B-CAM ($r = 0.42$, $P < 0.01$ and $r=0.28$, $P < 0.05$). Evoked potential EEG analysis showed that the amplitude of the P3 component, believed to reflect executive control, was also significantly correlated with overall cognitive ability. Significant associations remained when age was included as a covariate. Thus, executive control measured with the Simon task relates to overall cognitive ability in older people with HIV. EEG results provide preliminary insight into the brain basis of this capacity. On-going work will address whether cognitive training or exercise can improve executive control.

CSP6.02

Blood Mitochondrial DNA Mutations are Associated with Higher Peak HIV Viral Load and Older Age Among Female CARMA Cohort Participants

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Background: People living with HIV experience accelerated aging. The accumulation of somatic mutations is believed to be a marker of biological aging, and has been implicated in age-associated diseases such as those occurring prematurely in HIV+ individuals. We hypothesized that mitochondrial DNA (mtDNA) somatic substitutions would increase with older age and HIV infection.

Methods: Participants in this cross-sectional study were HIV+ (n=92, 12<19y) and HIV- (n=72, 13<19y) females enrolled in the CARMA cohort, who were never infected with hepatitis C or B virus, and were either current or never (but not past) smokers. Blood somatic mtDNA substitution rates/10,000bp were quantified via next generation sequencing with primer IDs. Variables univariately associated with mtDNA substitution rates were included in an ANCOVA of log-transformed values.

Results: MtDNA substitution rates met quality control for 138 individuals (n=75 HIV+, 63 HIV-) aged 1-75 years and their median [IQR] (range) rate was 0.5 [0.3-0.6] (0.0-1.64). Both groups were of similar age (p=0.18) and all HIV+ children had undetectable pVL while this was true for 59% of adults, 32% of whom were current smokers. A significant correlation was seen between mtDNA substitution rates and age (rho=0.36, p<0.001) but not HIV+ status (p=0.49) within the entire sample, nor smoking (current *vs.* never, p=0.76) among adults. Among HIV+ adults, higher mtDNA substitution rates were associated with peak HIV pVL on record (> vs. ≤100,000 copies/mL, p=0.018) but not current HIV pVL (detectable vs non-detectable, p=0.69), CD4+ count (rho=-0.14, p=0.28), or CD4 nadir (rho=-0.21, p=0.10). In a multivariable model of HIV+ adult participants (R^2=0.16) that included age (p=0.05) and peak pVL (p=0.03), both remained independently associated with mtDNA substitutions rates.

Conclusion: Our data suggests that blood somatic mtDNA substitutions increase with age and are more prevalent among individuals showing a high HIV set point but not among smokers.

CSP6.03

Baseline Characteristics of patients enrolled in the Canadian HIV and Aging cohort (CTN 272)

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Objective: To describe the baseline characteristics of patients included in the Canadian HIV and Aging Cohort Study (CTN 272).

Methods: The Canadian HIV and Aging Cohort Study is a prospective study recruiting people living with HIV aged 40 or older, or having lived with HIV for 15 years or more, and HIV-negative controls, with a five-year follow-up. The primary outcome is incidence of overt cardiovascular disease. We present the baseline characteristics of patients included into the cohort to date, and compare them using ranksum and fisher's exact tests.

Results: From September 2011 to October 2016, a total of 797 patients were recruited. 675 (85%) are patients living with HIV, with a mean age of 54, and 592 (88%) are males. 122 (15%) are HIV-negative controls, with a mean age of 55 years old and 98 (80%) are males. Mean duration of infection in the HIV-positives is 18 years, mean nadir CD4 217, and actual CD4 546. 96 patients (12%) had detectable viral loads at enrollment. Framingham risk scores was not significantly different between HIV positive and HIV negative patients. Alcohol consumption was similar (p=0.40), as well as exposure to tobacco (measured in pack-years, p=0.35) and use of intravenous drugs (p=0.52). HIV negative patients exercised less frequently (p=0.01). There were no significant differences in proportions of high blood pressure (26 vs 31% p=0.35), diabetes (10 vs. 13%, p= 0.55) or family history of premature cardiovascular disease (25 vs. 26% p=0.97) in the HIV positive vs negative, respectively.

Conclusion: HIV positive and negative patients recruited in the Canadian HIV and Aging Cohort Study are similar in terms of lifestyle and traditional cardiovascular risk factors. This will allow us to compare the effect of HIV on accelerated aging without too much concern about potential confounding.

CSP6.04

Rosuvastatin does not reduce expression of inflammatory markers on CD14+ monocytes in HIV+ patients on antiretroviral therapy

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People with HIV infection are living longer and more than half of all HIV+ individuals on antiretroviral therapy (ART) are now ≥50 years of age. With increased life expectancy, co-morbidities associated with aging are becoming evident in this patient population and chief among these is cardiovascular disease (CVD). There is compelling evidence that atherosclerosis is an inflammatory condition involving monocytes and the endothelium, and the inflammatory state associated with HIV infection has been linked to CVD progression in HIV+ patients. Notably, when given to HIV negative people with elevated hs-CRP but normal levels of LDL, HMG-CoA reductase inhibitors (statins) reduced the risk of cardiovascular events and all cause mortality.

Patients enrolled in the present study were HIV+, ≥40 years of age, on ART with VL<40 for at least one year, and had CD4 counts ≥350. Patients were randomized to receive rosuvastatin or placebo. Markers of inflammation (CD127 and CD16) were measured on CD14+ monocytes in the blood of study participants at baseline and after 6 months. At baseline, a greater proportion of CD14+ monocytes from HIV+ patients on suppressive ART expressed CD16 and CD127 compared to HIV negative controls (36%±3 vs 15%±2, and 33%±2 vs 11%±5 respectively). Although CD16 expression did not change, treatment with rosuvastatin for 6 months was associated with a 29% increase in CD127 expression on CD14+ monocytes from study participants. Treatment with rosuvastatin for 6 months did not reduce markers of inflammation on monocytes isolated from HIV+ individuals on suppressive ART, and was associated with an increase in CD217 expression. These findings will be correlated with aortic inflammation detected by FDG-PET/CT and coronary flow reserve measured by myocardial contrast echocardiography. These data may provide an indication as to whether statin therapy alters the inflammatory state and CVD risk in HIV+ individuals on effective ART.

CSP6.05

Do Functional Magnetic Resonance Imaging Resting State Networks Reflect Brain Health in HIV?

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A range of cognitive abilities, including executive function, attention, and processing speed can be mildly impaired in a subset of persons living with HIV (PLHIV). The brain basis of these impairments remains unclear. One possibility is that HIV-related brain injury disrupts the efficient functioning of brain networks. As networks degrade, cognitive ability would be lost along a continuum from higher order abilities to simpler brain functions. Resting-state functional MRI (rs-fMRI) is a recently developed method to assess brain networks. This method identifies brain regions in which BOLD signal (and the underlying neural activity) temporally covaries. Disrupted rs-fMRI patterns have been reported in neurological and psychiatric disorders, and there is preliminary evidence of changes in rs-networks in small samples of PLHIV when compared with healthy controls. The present study asked if brain networks identified with rs-fMRI relate to cognitive ability in older PLHIV, drawn from the Positive Brain Health Now study. 34 HIV+ men treated with HAART (mean age 54 (SD 7.2); mean current CD4 668 (362)) underwent rs-fMRI at baseline, prior to a cognitive training intervention. Cognitive ability was assessed with a set of computerized tests that measure cognitive ability as a single latent variable (Brief Cognitive Ability Measure (B-CAM)). The Default Mode, Dorsal Attention, Visual and Executive Control resting-state networks were extracted using Independent Component Analysis as implemented in the FMRIB-Software-Library. After, the relationships between B-CAM scores, CD4 count, age and each of the networks were studied using dual-regression. At the conventional significance level of 0.05, no significant relationships were identified. These preliminary data do not support a simple "network failure" account of cognitive impairment in HAART-treated PLHIV, at least in relation to resting-state networks extracted using Independent Component Analysis of rs-fMRI. On-going longitudinal work will address whether these network measures are sensitive to the effects of cognitive training.

CSP6.06

Incidental Findings of Colonoscopic Examination in HIV-Infected Individuals Participating in a Mucosal Immunology Sub-study (CIHR/CTN257)

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Introduction: Immune dysfunction and gut damage persist in antiretroviral therapy (ART)-treated individuals. To get insight into the gut mucosal immune dysfunction, we performed gut biopsies in participants undergoing primary and chronic HIV infection. Herein, we present incidental colonoscopic findings in HIV-infected and uninfected individuals participating in the Montreal Primary HIV infection study.

Methods: Aviremic ART-treated HIV-infected and uninfected participants were recruited to undergo colonoscopic examination along with rectosigmoid biopsies. In order to increase participant benefits, we selected patients over 50 years of age who would also benefit from colon cancer screening. Socio-demographic data including age, sex, ethnicity and past medical history were recorded and analyzed using graphpad 7.0.

Results: A total of 31 participants including 22 HIV+ and 9 uninfected individuals underwent colonoscopy. While all HIV+ participants were male, 22.2% (n=2) of the uninfected participants were female. All except two participants in the HIV+ group were Caucasians. Average (±SD) age of the participants was 59.0±6.4 years, which was comparable in the two groups. Similarly, mean CD4 T cell count was 606±194 and did not differ among the groups. However, the HIV+ group had a significantly higher mean CD8 T cell count (817±354 vs 274±68.0; p<0.001) and a lower CD4/CD8 ratio (0.8±0.4 vs 2.5±0.7; p<0.001). Abnormal colonoscopic findings, including benign adenoma and hyperplastic polyps with one non-specific colitis, were observed in approximately half (51.6%) of the study participants. A total of 34 polyps were removed, ranging from 1 to 6. Importantly, older age was associated with abnormal colonoscopic findings (p=0.045) irrespective of HIV status.

Conclusion: Incidental abnormal colonoscopic findings were observed in half of the participants and were associated with older age. Therefore, participating in a study involving rectosigmoid biopsies may provide health benefits by the removal of polyps at the risk of developing into colon cancer.

CSP6.07

Cell-free Mitochondrial DNA Levels are Related to HIV Infection, Plasma Interleukin-6 and Leukocyte Count

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Background: Chronic inflammation has been implicated in HIV-mediated age-related comorbidities, and cell-free DNA (cf-DNA) levels have been associated with pro-inflammatory markers such as interleukin-6 (IL-6) in non-HIV studies. Unmethylated mitochondrial cf-DNA (cf-mtDNA) resembles bacterial DNA and, unlike nDNA, induces pro-inflammatory responses in animal and *in vitro* studies. Although few studies report elevated plasma cf-mtDNA in persons living with HIV, we sought to confirm this in a larger sample, in filtered plasma, to investigate whether cf-mtDNA remains associated with IL-6.

Methods: CARMA participants with blood collected between July 2014 and September 2015 were included in this study. Plasma was prepared by 14000g centrifugation followed by 0.45 µm filtration, and cf-DNA was extracted. MtDNA and nuclear DNA (nDNA) were quantified using multiplex qPCR in both filtered plasma and whole blood (WB). WB nDNA copy number (a surrogate for leukocyte count), IL-6 ELISA measurements (>2 *vs.* ≤2pg/ml), age, ethnicity, HIV status, CD4 count, and HIV viral load were considered for inclusion in a multivariable model of cf-mtDNA if important (p<0.15).

Results: MtDNA and nDNA data were obtained for 99 HIV+ and 103 HIV- participants aged 2.5-78 years old. Among all participants, cf-mtDNA levels were univariately associated with cf-nDNA (R^2=0.53, p<0.0001) and WB nDNA (R^2=0.04, p=0.008) levels, along with age, IL-6, and HIV infection, but not HIV viremia. IL-6 itself was not associated with age (p=0.71). In the multivariable model, higher cf-mtDNA levels remained independently associated with younger age (b=-0.34, p<0.0001), higher nDNA copies (b=0.23, p=0.002), high IL-6 (b=0.17, p=0.015), and HIV+ status (b=0.24, p=0.001).

Conclusions: Higher cf-mtDNA in younger participants was not accompanied by high IL-6, and may reflect their higher lymphocyte count. Given the close relationship between cf-mtDNA and WB nDNA, our results suggest that leukocyte cell death is behind the relationship between cf-mtDNA and inflammation, which may be intensified in HIV.

CSP6.08

Lower extremity neuropathy symptoms, depression, and duration of HIV infection are associated with self-reported disability in people living with HIV

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Background: As people living with HIV (PLWH) age, they may experience increased health-related challenges (disability) attributed to comorbidity. Distal sensory polyneuropathy (DSP) is a common comorbidity; its effects on disability are unclear.

Purpose: To compare self-reported disability in PLWH with or without DSP, and to determine the extent to which symptoms of neuropathy in the lower extremities (LE) or other relevant factors predict disability.

Methods: We conducted a cross-sectional survey and retrospective chart review with PLWH. We administered the World Health Organization Disability Assessment Schedule (WHO-DAS 2.0), the Beck Depression Inventory II, the Subjective Peripheral Neuropathy Screen (SPNS), the Brief Pain Inventory, and a demographic questionnaire. LE neuropathy was identified by a weighted score of $\geq$2 on the SPNS LE items. A general linear model was used to assess group differences on self-reported disability after controlling for other possible sources of disability.

Results: Of the 126 participants, 67% were male. The mean age was 49.6 (±10.5) years and mean duration of HIV infection was 15.1 (±8.4) years. In the multivariate model (n=113), participants reporting symptoms of neuropathy in the LE had 6.8% higher WHO-DAS scores (indicating greater disability) (p=.015) compared to those without, after controlling for depression (p<0.001), duration of HIV infection (p=.002), age (ns), and CD4+ count (ns). The strongest predictor of disability was depression (partial η^2=.55) followed by duration of HIV infection (partial η^2=.09) and neuropathy symptoms (partial η^2=.06). Overall, the model explained 60.0% (p<0.001) of the variance in WHO-DAS scores.

Conclusions: Self-reported disability is higher in PLWH with symptoms of LE DSP compared to those without symptoms of LE DSP. Depression and longer duration of HIV infection was associated with self-reported disability. Variance in disability not explained by our model may be due factors not included in the model, such as other comorbidities, employment status, and gender.

CSP6.09

Hepatic Steatosis and Fibrosis Diagnosed by Transient Elastography in Canadians living with HIV: Results of a Large-Scale Screening Program

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Background: Liver disease is a major health concern in HIV-infected patients. However prospective, large-scale data on hepatic steatosis and fibrosis are lacking.

Methods: We prospectively screened an unselected cohort of HIV-infected adults by transient elastography (TE) and controlled attenuation parameter (CAP). Fatty liver (steatosis involving >10% of hepatocytes) was defined as CAP ≥238. Significant liver fibrosis was defined as TE ≥7.1. Predictors of hepatic steatosis and fibrosis were determined using logistic regression analysis.

Results: 1033 consecutive HIV-infected patients (50.5$\pm$9.9 years, 77.6% men, mean CD4 590$\pm$298, 90% on antiretrovirals) were included in 2013-2016. HCV and HBV coinfection was found in 35% and 6% of cases, respectively. Hazardous alcohol use was found in 8% of patients. Prevalence of hepatic steatosis and significant liver fibrosis was 51% and 31%, respectively. The multivariable analysis is reported in the Table. After adjustment, hepatic steatosis was associated with diabetes, being overweight, lower HDL and higher triglycerides, while HCV coinfection was protective. Significant liver fibrosis was associated with duration of HIV infection, being overweight, HCV coinfection, elevated ALT and CD4<200, while black ethnicity was protective.

Table 1. Multivariable analysis of factors associated with Hepatic steatosis and significant liver fibrosis.

	Hepatic steatosis	Significant liver fibrosis
Variable	aOR (95% CI)	aOR (95% CI)
Black ethnicity	0.99 (0.54-1.83) p=0.99	0.26 (0.11-0.62) p=0.002
Duration HIV infection		
(per year)	1.01 (0.98-1.05) p=0.37	1.06 (1.02-1.10) p=0.006
Diabetes	4.16 (1.41-12.33) p=0.01	1.52 (0.50-4.62) p=0.46
BMI>25Kg/m^2	2.59 (1.64-4.09) p<0.001	2.97 (1.62-5.45) p<0.001
HCV	0.50 (0.32-0.80) p=0.003	4.01 (2.22-7.24) p<0.001
HBV	0.85 (0.33-2.17) p=0.73	0.66 (0.20-2.17) p=0.47
Didanosine	1.01 (0.51-2.01) p=0.98	1.14 (0.56-2.31) p=0.71
ALT>ULN	1.26 (0.77-2.05) p=0.36	1.00 (0.99-1.01) p=0.39
CD4>200	1.99 (0.81-4.88) p=0.23	0.40 (0.16-0.96) p=0.04
HDL cholesterol (per unit)	0.34 (0.17-0.69) p=0.003	0.79 (0.41-1.55) p=0.5
Triglycerides (per unit)	1.39 (1.10-1.63) p=0.004	0.99 (0.80-1.22) p=0.91

Conclusion: Hepatic steatosis and fibrosis are major health comorbidities in Canadians living with HIV. Hepatic steato-

sis is particularly frequent in HIV mono-infected patients, likely due to high prevalence of metabolic dysfunction. Liver fibrosis is associated with HCV coinfection, while steatosis is less prevalent, possibly due to the higher prevalence of advanced liver fibrosis, resulting in burned out fatty liver. Non-invasive screening strategies can help early diagnosis and initiation of interventions.

CSP6.10

Comorbidity Risk Scores in Women Aged 45 and Older Living with HIV in British Columbia

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Background: People living with HIV have higher rates of comorbidities at younger ages. Data on validated risk prediction scores in aging women living with HIV (WLWH) is scarce. We applied various risk scores to WLWH 45 years.

Methods: WLWH 45 years enrolled in the CARMA (Children and Women: AntiRetrovirals and Markers of Aging) cohort study with visits in 2008-2016 (N=93) were retrospectively reviewed. Demographic, clinical and biological data were extracted from the CARMA database and medical charts. Participants' risks of developing various comorbidities were calculated using validated risk prediction scores whenever the required data was available, including **Framingham Score**, Aspartate aminotransferase-to-Platelet Ration Index **(APRI)** for liver fibrosis, Veterans Aging Cohort Study **(VACS)** Index to predict 5-year all-cause mortality, and risk score for chronic kidney disease **(CKD)**.

Results: We were able to calculate risk score in 90/93 WLWH. Median age was 52 (IQR 45-69) years, 52% Caucasian, 26% Indigenous. HCV antibody positivity was found in 37% of women, 61% of whom were RNA positive. Prevalence of osteoporosis was 14%. Mean ± SD **Framingham Score was 10.3** ± 4.3 (n=62), corresponding to a 6% risk of cardiovascular disease within 10 years. Mean **CKD risk score** was 10.2 ± 5.3 (n=78), with 17% at high risk for CKD within five years.The median **VACS Index score** was 27 (IQR 12-40) (n=89), predicting a 5-year mortality risk of 10.2% (high). Of those, 33/89 (37%) had APRI **scores** ≥0.5 indicating liver fibrosis stage ≥F2. Only 17/33 (52%) of those were HCV RNA+, suggesting that other causes than HCV contribute to liver fibrosis in this population.

Conclusions: Our results in this relatively young sample suggest that WLWH are at high risk of various comorbidities. Health care providers should assess and treat HCV early, before fibrosis develops, and maximise control of risk factors for other comorbidities.

CSP6.11

Exercise and Cognitive Function in people living with HIV: a Scoping Review

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Since the advent of combination antiretroviral therapy, people with HIV have an increased life expectancy and quality of life. Despite these improvements, 30-60% of people with HIV (PHAs) have some form of cognitive impairment. These cognitive concerns can have significant real-world consequences for employment, medication adherence, driving, and social support. Fortunately, exercise has emerged as a management strategy for cognitive impairment. We conducted a scoping review to determine what is known about exercise and cognitive function in PHAs. We used the Arksey and O'Malley Framework involving the following steps: 1) We searched 5 databases using terms related to 'exercise' and 'HIV'. 2) Two authors independently reviewed titles and abstracts for studies that addressed exercise and cognitive outcomes in PHAs; 3) One author reviewed full texts to identify articles that met our inclusion criteria of studies conducted in the past 20 years, HIV+ participants, reference to some form of physical activity or exercise, and cognitive function outcomes. 4) One author extracted data from included studies onto a standard data extraction form; and 5) We collated the results and summarized the characteristics of included studies. Of the 6458 abstracts screened, 13 studies met our inclusion criteria. Four of the studies were randomized controlled trials, seven were cross-sectional studies, and two were pre-post single group observational studies. The interventional studies included aerobic, resistive, and Tai Chi exercise interventions for 8 to 24 weeks in total duration. Two of the six interventional studies found exercise to benefit self-reported cognitive function in PHAs. Of the seven cross-sectional studies that assessed the relationship between physical activity and cognitive function, all showed a positive relationship between physical activity and cognitive function in PHAs. Results of this scoping review suggest that physical activity is safe and could be associated with preserved or improved cognitive function in HIV.

CSP6.12

Epicardial fat quantitative assessment and its relationship to computed tomography markers of coronary artery plaque vulnerability in HIV patients

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Introduction: HIV patients live longer and are increasingly subject to age-related diseases, more specifically to coronary artery disease. Recently, epicardial fat has emerged as an adipose depot of interest due to its key localization, its metabolic properties and clinical measurability. Only few studies have investigated the relationship between HIV, epicardial fat and coronary artery disease. There is evidence that epicardial fat is increased in HIV patients, and independently associated with calcified and non calcified coronary plaque. We hypothesize that epicardial fat volume is correlated with total coronary plaque volume, and especially with low attenuation plaque volume, which is a marker of plaque vulnerability.

Methods: Our study is cross sectional, nested in the large prospective cohort "Canadian HIV and Aging Cohort Study", a multicenter trial involving >700 HIV patients. We selected 125 consecutive HIV individuals with low to intermediate cardiovascular risk without past or symptoms of coronary artery disease. Participants underwent cardiac computed tomography (CT) including plaque imaging with coronary CT angiography. Association between epicardial fat volume, total plaque volume and low attenuation plaque volume was assessed with multivariate linear regression.

Results: The 125 HIV patients included had a mean age of 55.3 yr (40–74 yr), and 96% were males. The median epicardial fat volume was 93.8 cm^3 (IQR 74.8– 133 cm^3), median total plaque volume 83 mm^3 (IQR 0 – 415.7 mm^3), and median low attenuation plaque volume 22.2 mm^3 (IQR 0–120.2 mm^3). Epicardial fat volume was significantly associated with total plaque volume (p=0.037) and low attenuation plaque volume (p=0.009), after adjustment for age and gender.

Conclusion: Epicardial fat shows an association with total coronary plaque volume and low attenuation plaque volume. This further supports the use of epicardial fat CT quantification as a cardiovascular risk marker in the HIV population.

CSP6.13

No Baseline? No Problem! Strategies to include patients without a baseline value in an analysis of time to kidney disease

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Background: Individuals without baseline values are often excluded from analyses of time to achieving a threshold laboratory marker which may result in lower efficiency and bias if baseline measurement depends on patient characteristics.

Methods: Time to chronic kidney disease (CKD) for participants in the Canadian Observational Cohort was defined as time from cART initiation to one eGFR <60 mL/min/1.73m^2. We classified patients by eGFR measurement: (A) baseline available, (B) no baseline, first follow-up >60 mL/min/1.73m^2, (C) no baseline, first follow-up <60 mL/min/1.73m^2. The following models estimated adjusted hazard ratios (HR) associated with CKD (1) PH including A, (2) PH including A, and B left truncated, (3) Weibull including A, B ignoring left truncation, and C left censored, (4) Weibull as (3) + interval censoring (IC) for A and B, (5) inverse probability weighting (IPW) of eGFR measurement in each 3-month period.

Results: There were 5489, 2215 and 60 participants in A, B and C. Participants in C were older (47 vs 39, 39), had lower CD4 counts (170 vs 249, 208) and were more likely to be women (35% vs 16%, 16%) and IDUs (42% vs 18%, 24%) than in A and B respectively. 489, 187 and 60 participants in A, B and C progressed to CKD. HR estimates are shown for each model (Table).

Conclusions: If disease progresses monotonically, including participants without a baseline as left-truncated or left-censored may be appropriate. If measurement of the outcome depends on disease outcome, IPW according to measurement may reduce bias.

Table. Estimated HRs of CKD from models* with different inclusion criteria

	PH model: A	PH model: A, B	Weibull: A,B,C	Weibull (IC): A,B,C	IPW: A,B,C
Covariate	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
Age (per 10y)	1.89 (1.73,2.07)	1.85 (1.71,2.00)	1.86 (1.71,2.02)	1.87 (1.71,2.04)	1.71 (1.58,1.85)
Female gender	2.27 (1.73,2.97)	2.19 (1.74,2.75)	2.24 (1.79,2.80)	2.23 (1.76,2.81)	2.05 (1.67,2.50)
IDU	2.40 (1.90,3.02)	2.39 (1.96,2.91)	2.10 (1.73,2.56)	2.11 (1.72,2.58)	2.74 (2.29,3.29)
Baseline VL (per log10 c/mL)	1.42 (1.21,1.67)	1.46 (1.27,1.67)	1.39 (1.22,1.59)	1.41 (1.23,1.62)	1.35 (1.19,1.54)
*All models also adjusted for MSM, province, cART initiation year and regimen, and baseline CD4 count					

HIV in Children and Adolescents

Le VIH chez les enfants et les adolescents

CSP7.01

Pediatric Survivors of the HIV Epidemic in Montreal: Children of the CMIS Cohort Study

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Background: In the early 1980's, a localised HIV epidemic among women and children in Montreal led to the creation of the Centre Maternel et infantile sur le SIDA (CMIS) cohort, to prevent further mother-to-child transmission (PTMCT), and optimize care among infected children. The objective of this study was to describe the epidemiology and outcomes among HIV-infected children in Montreal, 30 years after the start of the epidemic.

Methods: Clinical records and the database of the CMIS cohort were reviewed to identify outcomes among HIV infected children followed between 1988 and 2015, who were engaged in care for at least one year at the CMIS.

Results: 184 HIV infected children were enrolled in the cohort; among them, 160 were confirmed perinatal infections. Since 1988, there have been 49 deaths among children followed at CMIS; all of the deceased were diagnosed between 1981 and 1999, with the last death occurring in 1997. Ethnicity among the deceased was predominantly Haitian (60.4%) followed by Canadian (14.6%) and African (12.5%). Among survivors, 75 children were transferred to adult care at the age of 18, 18 transferred to other centers, 4 lost to follow-up, and 38 remain in care. Mean age of children currently in care is 11.6 years (range 4-17), and ethnic distribution is now predominantly African (51.4%), followed by Haitian (20%) and Canadian (14.2%). Nearly one third (32%) of the current cohort was born in Quebec. Reasons for infection included post-partum diagnosis of HIV (5), maternal non-adherence to treatment or refusal of care (5), intra-familial transmission (1), and unknown (1).

Conclusions: The epidemiology of HIV infection among children in Montreal has changed dramatically over time, due to shifting immigration patterns, the survival of infected children, and improved PMTCT strategies. Nonetheless, these results highlight some of the current missed opportunities for prevention among Quebec-born children

CSP7.02

Breastfeeding in the HIV context in Canada – better out in the open

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Background: The risk of vertical HIV transmission (VT) via breastmilk from mothers on combination antiretroviral therapy (cART) with undetectable viral load (VL) is approximately 1-2%. The current Canadian recommendation is for exclusive formula feeding of infants born to HIV-positive mothers. However, for a variety of reasons, some Canadian women elect to breastfeed. We describe two such cases and explore issues related to infant feeding in the Canadian HIV context.

Case Description: Two primigravida women living with HIV who were compliant with HIV care chose to breastfeed their infants despite counseling by Obstetrical and HIV care providers regarding VT risk. Both had sustained undetectable VL throughout pregnancy. Stated reasons for choosing to breastfeed included better bonding with baby (n=2) and fear of inadvertent HIV disclosure to relatives (n=1). Both mothers agreed to close monitoring and adherence to treatment for themselves and the infants (cART with zidovudine, lamivudine and nevirapine) for the duration of breastfeeding.

Case 1: Infant born at 41 week's gestation to mother of African-origin. VL in breastmilk was target not detected; proviral DNA was positive. She breastfed from day 5 to 6 weeks of life. Infant HIV PCR was negative at 3, 19, and 30 days, 7 weeks and 3.3 months of age.

Case 2: Caucasian Canadian mother delivered 31-week gestation twins. Both required a 5 week neonatal care unit stay, during which they received donated breastmilk followed by formula. Mother initiated breastfeeding at home supplemented by formula (insufficient breast milk). HIV

PCR was negative at birth, 1 and 2 months of age in both twins who continue to be mixed fed and receive cART.

Conclusions: For a variety of reasons some HIV-positive Canadian mothers may choose to breastfeed despite the risk of VT. Discussion on infant feeding with prospective mothers is imperative to optimize family and infant care.

CSP7.03

Predictors of Loss to Follow-up in HIV-Exposed Uninfected (HEU) Children

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Background: HIV-exposed uninfected (HEU) children exposed *in utero* to antiretroviral medications may be at increased risk of adverse outcomes, including neurodevelopmental delay (NDD). Despite recommendations for long-term follow-up of HEU's, many parents are reluctant to do so once HIV infection is excluded. The purpose of this study was to assess the rate of loss to follow-up (LTFU) and identify predictors of LTFU.

Methods: Retrospective chart review of HEU children born between January 1, 2008 and December 31, 2012 followed at SickKids. Those born after December 31, 2012 were excluded, as they would not have reached the age of last scheduled visit (5.5 years).

Results: 280 Canadian-born HEU's were reviewed; 17 were excluded (moved out of jurisdiction). 49% were male and 63.6% were of African-Canadian origin. Median maternal age at delivery was 33 years (IQR 30, 36); 94.3% received combination antiretroviral therapy antenatally. Median gestational age (GA) was 38.6 weeks (IQR 37.4, 39.7). 96 (36.5%) children were LTFU prior to 5.5 years of age (17 [6.5%] prior to 18 months, 44 [16.7%] after 18 months, but prior to 3.5 years). At 18 months of age, 92 (35%) had evidence of NDD. 37.9% of patients were referred for NDD interventions, mainly for speech delay. Variables associated with LTFU on univariate analysis included NDD at 18 months (p=0.007) and having sibling(s) (p=0.033); maternal age, maternal ethnicity, GA, caregiver type/number, and distance of residence from hospital were not associated. Multivariable analysis showed that LTFU was less likely with NDD at 18 months (p=0.053), but more likely if the child had siblings (p= 0.034).

Conclusions: The rate of LTFU among HEU children after 18 months of age is substantial, despite high rates of NDD. Our findings suggest that interventions aimed at enhancing parental knowledge of potential adverse health outcomes in HEU children are needed.

CSP7.04

Shorter Leukocyte Telomere Length among HIV+ cART-treated Children is Strongly Associated with Lower Leukocyte Mitochondrial DNA (mtDNA) Content

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Background: We recently reported a high prevalence of chronic lung disease (CLD) among Zimbabwe children living with HIV compared to HIV- peers, despite cART. Shorter leukocyte telomere length (LTL) and mitochondrial DNA (mtDNA) alterations have been reported in association with both chronic lung and HIV disease in adults. Some antiretrovirals can shorten telomeres *in vitro* and induce mitochondrial dysfunction. Our objective was to measure and compare LTL in cART-treated HIV-infected children with and without CLD, and uninfected peers.

Methods: HIV-infected children aged 6-16 were enrolled at the Harare Children's Hospital HIV clinic in Zimbabwe. Age-matched HIV-uninfected controls were from Harare clinics. PBMC LTL and mtDNA content were measured by qPCR. Univariate associations were investigated through Mann-Whitney and Spearman's correlation tests. Important factors ($p<0.1$) were taken forward in multivariable regression models.

Results: Complete demographic, LTL and mtDNA content data was obtained for 257 HIV+ (median age at diagnosis >4y), including 32 (12%) with CLD, and 89 HIV- children. Log-LTL was positively correlated with log-mtDNA content among HIV+ ($p<0.001$) but not HIV- children ($p=0.695$). In a multivariable analysis of log-LTL that included age, sex, DNA extract concentration, log-mtDNA and HIV/CLD status (HIV- *vs.* HIV+/CLD+ *vs.* HIV+/CLD-), shorter LTL was independently associated with being male, HIV+/CLD+ (*vs.* HIV-), as well as with lower mtDNA content and DNA concentration . Among HIV+ children, CLD was not associated with LTL after controlling for CD4 count and the aforementioned variables.

Conclusions: Our results suggest accelerated telomere attrition among HIV+ children, irrespective of CLD. This LTL effect was associated with decreased mtDNA, an observation previously reported in non-HIV contexts, usually in the presence of health stresses. It is unknown whether the LTL association with low DNA is related to neutropenia or is an artefact of DNA extraction. These findings merit further investigation in a larger independent sample.

HIV in Vulnerable Populations and Global Health Issues

Le VIH dans les populations vulnérables et les enjeux sanitaires mondiaux

CSP8.01

Solid organ transplantation in Canadian HIV-infected patient: first results of the TransHIV cohort

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Background: Terminal organ failure has become more prevalent in HIV-infected patient since the improved survival related to antiretroviral therapy (ART). Large cohort studies demonstrated favorable outcomes in solid organ transplantation (SOT). Management of drug interactions between ART and immunosuppression is a challenge in SOT and could lead to an increased rate of rejection. The aim of this study is to describe a Canadian single center experience with SOT in HIV-infected patients.

Materials and Methods: This is an observational cohort study of HIV-infected transplant candidates or recipients at the Centre Hospitalier de l'Université de Montréal (CHUM). Recruitment period began in March 2016 and retrospective data collection was performed in patients who were evaluated or transplanted before this date. Patient outcomes and complications post-SOT were assessed through clinical chart reviews.

Results: Thirteen HIV-infected patients were recruited, including eight transplant recipients (six kidneys, one liver, one lung). Mean delay from the day of referral to SOT is 1735 days (258-2683). Four patients were temporarily removed from waiting list, delaying SOT. Median follow-up is 11 months post-SOT (4-54). No death, graft failure, virological failure or HIV-associated opportunistic infections were recorded throughout the post-SOT period. ART modification was made in five patients, mostly to prevent drug interaction (n=3). Five patients were on ART free of drug interaction post-SOT. Complications post-SOT included one chronic rejection and one BK virus nephropathy. One patient underwent a HIV+/HIV+ kidney transplantation with excellent virological control at eleven months follow-up.

Conclusion: SOT is a viable option for HIV-infected patients with organ failure. ART free of drug interaction should be promoted when possible to prevent rejection. The short-term outcome in our HIV+/HIV+ transplant recipient is encouraging however, more cases and longer follow-up may be required before a conclusive decision is provided toward HIV-infected patients requiring SOT.

CSP8.02

Novel Models of Engagement in Care for HIV-Infected Vulnerable Inner City Populations: the Community Pop-Up Clinic

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Background: There is a high prevalence of HIV infection on Vancouver's Downtown East Side (DTES), mainly attributed to injection drug use. A number of these HIV-infected individuals remain disengaged from care through conventional health care structures. We have developed Community Pop-up Clinics (CPCs) as a tool to address this issue and to favor long-term engagement in multidisciplinary care.

Methods: Participants were recruited at CPCs held at several DTES community centres. OraQuick® HCV Rapid Antibody and HIV Rapid Antibody point-of-care testing was offered. Participants identified as HIV positive were immediately offered a plan to address medical (including HIV care and antiretroviral therapy), psychiatric, social and addiction-related needs at the Vancouver Infectious Diseases Centre, a 20 minute walk from the CPC sites. A questionnaire was administered to collect demographic information, HIV disease knowledge, and data regarding barriers to receiving healthcare. The was a $10 incentive for participation.

Results: A total of 2179 participants (mean age 49.1 years, 75.9% male) were evaluated, with 72 (3.3%) infected with HIV: 65% male, 35% First Nations, 33% homeless, 69% HCV co-infected, 50/72 (69%) co-infected with HCV. Of these 72 individuals, 23 (32%) were successfully linked to ongoing care over the subsequent 6 months, with 15 on successful antiretroviral therapy, and ongoing plans to achieve this goal in the majority of the 72 individuals we have identified.

Conclusion: A significant number of HIV-infected individuals on Vancouver's DTES remain undiagnosed or at least unengaged in care. Our CPC model has successfully identified many of them, and has served as a first step to long-term engagement in care, including implementation of treatment as prevention. An approach such as ours must be an integral part of the provincial strategy to meet the World Health Organization "90-90-90" goal among vulnerable inner city populations.

CSP8.03

HIV Support Groups as a Means of Educating Inner City Patients and Facilitating Viral Load Suppression

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Purpose: Over 20% of the population living in Vancouver's Downtown East Side (DTES) is HIV-positive, consisting

mainly of vulnerable inner city people who inject drugs (PWID). Implementing a strategy to link these individuals to care in a sustainable way is necessary to meet the goals of the "90-90-90" treatment target endorsed by the World Health Organization. We hypothesize that education and support provided in a group setting may be an important tool in achieving this goal in this specific population.

Methods: The group intervention is scheduled 4hours/week, and is led by medical professionals and community-based workers. Attendees are offered breakfast and lunch and receive HIV/AIDS education and the opportunity to voice their health-related concerns. A retrospective analysis to assess the characteristics of patients attending the group regularly (at least once per month) was performed, with HIV plasma viral load measures taken as a surrogate for successful engagement in care.

Results: A total of 74 HIV-positive patients (mean age 52 years, 12% females, 14% First Nations) regularly attended group. Among them, 55 (74.3%) are active PWID, 36 (48.6%) self-identify as homeless/unstably housed, and 25 (33.8%) have a psychiatric eco-morbidity. All 74 were prescribed antiretroviral therapy, 58 (78.4%) with HIV plasma viral load <40 copies/mL. The remaining 16 (21.6%) are on treatment with good adherence and none have experienced a documented virologic breakthrough. Follow-up to document achievement of maximal virologic suppression is ongoing.

Conclusion: In vulnerable inner city patients infected with HIV, a weekly support group such as ours is a successful intervention to maximize engagement in antiretroviral therapy and successful antiretroviral therapy. In our setting, it will be an important component of a strategy to achieve the World Health Organization goals for the long-term control of the HIV pandemic.

CSP8.04

Addressing barriers to cervical cancer screening for women with HIV in low and middle income settings: Demonstration project of an innovative screening approach

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Introduction: Women living with HIV (WHIV) are at greater risk for acquiring human papillomavirus (HPV) and progressing to cervical cancer. In low income settings with poor screening penetration for WHIV and the highest rates of cervical cancer, it is essential to examine options to increase uptake in screening.

Methods: WHIV aged 30-69 years in Uganda engaged in HIV care completed a validated survey on knowledge and intentions toward cervical cancer screening. Demographic and HIV related data was abstracted from chart review. Self-collection based HPV testing was then offered to WHIV. Specimens were tested for high risk HPV genotypes, and women were contacted with results and referred to care.

Results: Of 87 WHIV who completed the survey, 96.4% had never heard of HPV and 98.9% did not think it was necessary to be screened for cervical cancer. WHIV were then contacted by mobile phone, and 40 women agreed to attend the HIV clinic to provide a self-collected sample. Among women tested 45% were oncogenic HPV positive, where HPV 16 or 18 positivity was 15% overall. In logistic regression, time since last HIV blood work (>6months) was associated with attendance for HPV screening (AOR= 3.55 p=0.01). HIV positive women who reported use of oral contraceptives and having blood work >6months were more likely to be HPV positive (OR=6.65 p=0.03) and (OR=0.16 p=0.02). Among WHIV who did not screen, key reasons were lack of time or money to travel.

Conclusions: Among WHIV engaged in HIV care in a low income setting, there was a high prevalence of oncogenic HPV, particularly HPV genotypes 16/18. Cervical cancer screening for WHIV is needed, which could be achieved through integration of reproductive health and HIV services. Despite high acceptability, uptake was low suggesting that integrating cervical cancer screening into existing HIV care visits may yield higher uptake.

CSP8.05

Younger Age and Indigenous Heritage are Associated With High Risk of Poor HIV Cascade Outcomes in Southern Saskatchewan

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Background: Saskatchewan continues to experience an HIV epidemic driven by high rates of injection drug use with disproportionate representation of Indigenous peoples. To best target and optimize the use of limited clinical resources, we determined the characteristics most predictive of success and failure within our HIV treatment cascade.

Methods: All living individuals active in our clinic with a first confirmed positive HIV test in Regina Qu'Appelle Health Region before September 1, 2015 were included. Cases were reviewed to determine demographic and clinical characteristics, as well as HIV cascade outcomes between September 1, 2015 and August 31, 2016. Multivariate regression analysis was utilized to examine factors associated with success and failure within the HIV treatment cascade.

Results: 384 individuals were included in the analysis. Individuals between ages 30 and 50 were less likely to be engaged in care compared to those over age 50 (OR 0.35, 95% CI [0.14-0.88], p=0.03). Individuals of Indigenous

heritage were less likely to be engaged in care compared to those of Caucasian descent (OR 0.46, 95% CI [0.22-0.96], p=0.04). Individuals under age 30 were less likely to be retained in care compared to those over age 50 (OR 0.30, 95% CI [0.13-0.69], p=0.005). Initial engagement in care was a positive predictor for viral suppression (OR 1.96, 95% CI [1.00-3.80], p=0.05). Several factors were negative predictors for viral suppression: being between ages 30 and 50 (OR 0.33, 95% CI [0.14-0.77], p=0.01), a baseline CD4 count < 200 (OR 0.40, 95% CI [0.19-0.84], p=0.02), and being a current smoker (OR 0.22, 95% CI [0.08-0.59], p=0.003).

Conclusions: Younger age and Indigenous heritage, along with heavy baseline immunosuppression, are associated with higher risk of poor HIV cascade outcomes in southern Saskatchewan. Case management and community outreach strategies must be utilized aggressively early after HIV diagnosis in these high-risk populations.

HIV in Women and in Pregnancy

Le VIH chez les femmes et pendant la grossesse

CSP9.01

Causes of Preterm Delivery Among HIV-Positive Women in Canada and Association with Antiretroviral Exposure

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Background: Maternal HIV infection has been associated with an increased risk of several adverse perinatal outcomes, including preterm delivery (PTD). HIV-infected women on protease inhibitor based antiretroviral (ARV) therapy have a higher rate of PTD than women on other regimens.The lack of comprehensive studies on causes of PTD in HIV-positive women is a major limitation in understanding the pathophysiology of the impact of ARV on perinatal complications. The objective of this study is to describe the association between causes of PTD and ARV exposure in pregnancy.

Methods: A total of 1461 HIV positive women were followed in two Canadian Perinatal HIV clinics from 1989 to 2015. Of these, there were 222 cases of PTD, defined as delivery between 22 and 37 weeks completed gestational age.

Results: The overall rate of PTD was 15%. Of these, 57% were spontaneous (preterm labor, preterm pre-labor membrane rupture) and 43% iatrogenic (preeclampsia, gestational hypertension, intra-uterine growth restriction, placenta abruptio, other). There was no significant difference between the groups by type of PTD in their ethnicity, body mass index, or parity. There were no significant differences in timing of ARV initiation, rate of virologic suppression or ARV exposure in pregnancy. Boosted protease inhibitor based regimens were used in 52% of spontaneous PTD and 50% of iatrogenic PTD (p=0.934).

Conclusion: Boosted protease inhibitor exposure was not associated with a specific cause for PTD, suggesting that the association between HIV infection, antiretroviral exposure and PTD involves multiple pathways.

CSP9.02

TAVIE-Woman™: A web-based virtual nursing intervention to meet the specific needs of women living with HIV taking antiretroviral treatment

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Background: The web-based virtual nursing intervention VIH-TAVIE™ was designed to help people living with HIV (PLWH) adhere to their antiretroviral treatment (ART). The content of the intervention is generic and gender neutral. However, it is recognized that women living with HIV (WLWH) experience their condition in a unique way and face gender-specific challenges regarding ART intake. Consequently, it seemed appropriate to adapt VIH-TAVIE™ specifically for women.

Objective: To present the adaptation and the development of gender-specific content from VIH-TAVIE™ to TAVIE-Woman™, to make a demonstration of TAVIE-Woman™ and to present the implementation plan.

Methods: The development of VIH-TAVIE™ and therefore, TAVIE-Woman™, were based on Intervention Mapping framework. In order to create case stories of WLWH who take ART, discussions were held with a healthcare professionals (HCP) team in a mother-child university hospital center composed of obstetrician-gynecologist, nurses and pharmacists. The implementation plan is grounded in a qualitative collaborative approach with HCP, community-based stakeholders and WLWH to target the barriers and facilitators of implementing and adopting TAVIE-Woman™ in clinical settings.

Results: TAVIE-Woman™ intervention consists of four sessions (accessible from laptop, computer, tablet) which contain short video clips (n=125), narratives (n=25) and consolidation tools (e.g., logbook of adverse effects, 70 PDF files). The gender-specific content includes: digital storytelling of three HIV-positive women having different profiles and ethnic background; various case stories about changing ART during pregnancy, neonatal ART prophylax-

is, disclosure to children, adapting to life with HIV, selecting a birth-control method, and social support.

Conclusion: Implementing the TAVIE-Woman™ intervention in two care settings in the Montreal area is planned, in the aim to offer to WLWH tailored education and reliable quality information in French and in English.

CSP9.03

Lopinavir (an HIV Protease Inhibitor) Impairs Uterine Decidualization and Spiral Artery Remodelling

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Background: Protease Inhibitor (PI)-based combination antiretroviral therapy (cART) has been associated with adverse pregnancy outcomes, such as pre-term delivery and small for gestational age births in HIV-positive women. Our group has previously demonstrated that PIs contribute to these adverse events by lowering progesterone (P4) levels and by altering placental angiogenesis. P4 plays a central role in uterine preparation for pregnancy, and a critical P4-dependent process in early pregnancy is formation of the decidua - the maternal component of the placenta. As part of this process, decidual spiral arteries are remodelled into highly dilated vessels to adequately supply maternal blood to the placenta and fetus. The decidua is highly dependent on P4 to remodel or "decidualize" so we hypothesised that the decidualization process would be affected by PI-based cART. Hence we investigated the effects of PIs on the decidua.

Methods: Human HIV-negative decidua and placenta tissue was collected from elective first trimester terminations. The first trimester placental-decidual co-culture model was used to examine the effects of PIs on spiral artery remodelling by immunohistochemistry. A primary decidual cell culture system was used to assess PI-induced changes in the expression of biomarkers of decidualization using multiplex approaches.

Results: Treatment with lopinavir impaired the remodelling of decidual spiral arteries and was associated with changes in the expression of hormones, growth-factors, and cytokines/chemokines known to be the regulators of the decidual transformation. Macrophage derived factors were particularly affected by lopinavir treatment.

Conclusion: Overall, our data reveal the impairment of uterine remodelling during pregnancy as a potential new mechanism by which lopinavir might cause poor placentation, and thus contribute to adverse birth outcomes.

CSP9.04

Demographic differences with impact: Understanding how mothers living with HIV differ from their HIV-negative peers

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Introduction: There is a lack of knowledge about how mothers living with HIV (MLHIV) differ from other mothers, particularly those who are demographically similar. Understanding these differences may have important implications for care and optimizing pregnancy outcomes. The purpose of this study was to identify demographic differences between MLHIV living in Ontario and their HIV-negative peers.

Methods: An observational, mixed-methods design was used in two cohorts of demographically matched women. 30 HIV-negative women were matched to HIV Mothering Study participants from Ontario based on enrolment site and self-reported age, race, and country of origin. This analysis focuses on how the cohorts differed by demographic features that were not used in the matching process.

Results: The sample (n=60) ranged in age from 19-42 (median=30, SD=7.713), with the majority identifying as Black/African (50%) or White (40%). Chi-square tests for association were conducted between HIV status and key demographics. There was a statistically significant association between HIV status and level of education, $\chi^2(2)=10.986$, $p<.01$. As per Fisher's Exact test, there was a statistically significant association between HIV status and income source such that MLHIV were more likely to be on government assistance ($p<0001$), and between HIV status and contact with child protection services ($p<.05$), such that MLHIV were more likely to have had contact.

Conclusions: MLHIV differ from their HIV-negative peers on important and significant determinants of health including income and education. Although HIV and its treatment are being implicated for the high rates of adverse pregnancy outcomes observed among MLHIV, it is critical to consider how demographic variations may also be contributing to these outcomes and what opportunities exist to ameliorate the social and economic circumstances for mothers and their families.

CSP9.05

Comparing cohorts: Demographic differences by pediatric HIV care engagement among young women living with HIV

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Background: Young adults living with HIV who have engaged in pediatric HIV care may differ from their HIV-positive peers who have not. We assessed demographic differences between young women living with HIV in the Canadian HIV Women's Sexual and Reproductive Health Cohort Study (CHIWOS) who had previously engaged in pediatric HIV care to those who had not. The aim of this analysis was to confirm if the two groups did in fact differ to better inform research, care, and support for both groups.

Methods: Baseline data were used for the analysis. We included participants between 18 and 29 years old who responded to a question regarding having ever received pediatric HIV care. Participants were included if they had previous pediatric care experience or none at all. We conducted bivariable analyses to compare demographic variables between young women who reported previous pediatric care with those who did not.

Results: 132 of the 1425 participants met the inclusion criteria; 39 (29%) had previously engaged in pediatric HIV care and 94 (71%) had not. The majority of participants in both groups were recruited in Ontario (61% respectively); there was no statistically significant difference in enrolment by province between the groups. Women who had been in pediatric care were younger (median = 22.5 years, IQR 21-25) than those who had not (median = 26 years, IQR 23-28, p = 0.0001) and were less likely to identify as Indigenous (13%) when compared to young women with only adult care experience (37%, p = 0.034). No other statistically significant differences were found, including gender, sexual orientation, marital status, and education.

Conclusions: We found differences in the demographic of these groups of young women. Understanding how demographic differences impact experiences of adult HIV care will be important to optimize outcomes for all young women with HIV.

CSP9.06

Exploring the Live Birth Rates of Women Living with HIV (WLWH) in British Columbia and the CARMA Cohort

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Background: Prior research has shown that women living with HIV (WLWH) have reduced fertility. However, most studies originated before combination antiretroviral therapy (cART), and few studies examine the impact of universally available cART on birth rates. Using population and cohort level data we examined impact of HIV infection on birth rates for women in British Columbia (BC).

Methods: Live birth rates among WLWH aged 15-49 were compared to BC population data for 2008–2015 using logistic regression, and are expressed as birth rates/1000 women, and odds ratios (OR). In the CARMA cohort from 2008-2015, lifetime live birth rates for 269 WLWH and 215 HIV negative women were compared, adjusting for confounding variables (age, ethnicity, education, substance use) using negative binomial regression to calculate incident rate ratios (IRR).

Results: WLWH had a lower birth rate versus all BC women [27.82, (95%CI=21.74-35.54) *vs.* 41.03 (95%CI=40.79-41.26), OR=0.67, 95%CI=0.53-0.84, p=0.003]. When examined by age, WLWH aged 15-24 had a higher birth rate (OR=2.97, 95%CI=1.35-5.64, p=0.03). WLWH and all BC women aged 25-34 had similar birthrates (OR=0.76, 95%CI=0.54-1.02, p=0.09). In women aged 35-49, WLWH had a lower birth rate (OR=0.57, 95%CI=0.44-0.72, p< 0.0001).In the CARMA cohort, WLWH reported more live births *vs.* controls [2 (1-3) vs. 1 (0-2), p=0.003]. Even when the model was adjusted for confounding variables (above), the IRR for live births for WLWH was 1.54 *vs.* controls (p<0.0001).

Conclusions: Overall, WLWH have a lower birth rate than the general population, with greater differences seen as women age. However, when comparing WLWH with similar HIV negative controls (CARMA), WLWH had more children. Explanations may include that WLWH seen at our women-centered clinic (hence in CARMA) are more likely to desire/feel confident having children, or that WLWH who do conceive, have more children than their HIV negative peers.

CSP9.07

Placenta Progesterone Levels are Negatively Associated with Placenta Mitochondrial DNA Content among HIV+ and HIV- women in the CARMA-PREG cohort

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Background: Women living with HIV are at increased risk of preterm delivery, a contributor to infant morbidity and mortality. Synthesis of pregnenolone, the precursor of progesterone which is central to pregnancy maintenance, is dependent on placental mitochondrial function. Given that many antiretrovirals can affect mitochondrial (mt) function, we investigated the relationship between placenta mtDNA content, a marker of mt function, and placenta progesterone levels, as these may be linked with risk of preterm delivery.

Methods: Placental tissue, clinical and sociodemographic data were collected for pregnant women enrolled in the prospective Canadian cohort CARMA-PREG. Placental progesterone levels were measured by ELISA while mtDNA content was quantified by monochrome multiplex qPCR. Univariate associations between progesterone, mtDNA, and preterm delivery (<37w gestation, any etiology) were investigated by Mann-Whitney, Chi2 or Spearman's correlation tests.

Results: Placenta tissue was obtained from 136 HIV-infected and 60 HIV-uninfected participants aged 18-45y, of whom 24 (17.6%) and 9 (15%) had a preterm delivery, respectively. Infants of mothers living with HIV had lower gestational age (p=0.017) and weight (p=0.011) at birth compared to controls. Within this cohort sample, preterm delivery showed no association with HIV status, placenta mtDNA or progesterone. However, placenta mtDNA and progesterone levels were significantly negatively correlated to one another (n=196, rho=-0,242, p<0.0001). In addition, women who delivered by caesarean section (38%) had higher placenta mtDNA than women who had a vaginal delivery (62%, p=0.032).

Conclusions: Our preliminary results suggest an association between lower levels of progesterone in the placenta and increased levels of mtDNA, possibly reflecting a compensatory mechanism for mitochondrial dysfunction. Placenta mtDNA association with mode of delivery may be related to the stress/energy demand during labour and/or placental insufficiency. Possible associations with preterm delivery will be examined once the sample size is larger.

CSP9.08

Adequacy of Cervical Cancer Screening in HIV Positive Women Living in Manitoba

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Introduction: HIV positive women are at increased risk of infection with human papilloma virus (HPV), have higher rates of cervical cytologic abnormalities, and more rapid progression from cervical dysplasia to invasive cervical cancer. Current guidelines recommend yearly Papanicolaou (Pap) testing in sexually active HIV positive women.

Objectives: This study aimed to determine the adequacy of cervical dysplasia screening (Pap testing) among HIV positive women receiving care in Manitoba, to compare screening rates in primary versus specialist care, and to determine if increasing accessibility of gynecologic services in a specialist care model improved rates of Pap testing.

Methods: We conducted a retrospective cohort study of women receiving HIV care in the Manitoba HIV program. Medical records were reviewed from January 1, 2002 to December 31, 2015. Adequate screening was defined as at least one Pap test in a 15-month person-interval. In the specialist care model, we examined adequacy of screening in three intervals: A) prior to linkage to HIV care; B) after linkage to HIV care, but before the availability of on-site gynecologic care and C) after linkage to HIV care and after the availability of on-site gynecologic care. In the primary care model, we examined adequacy of screening in two intervals: A) prior to linkage to HIV care and B) after linkage to HIV care.

Results: Of 195 women included in the study, 122 were receiving care at a specialist care centre and 73 were receiving care at a primary care centre. In the specialist care model, adequate screening was completed in 102 of 488 (20.9%) person-intervals during Period A, 150 of 392 (38.2%) during Period B and 175 of 366 (47.8%) during Period C. In the primary care model, adequate screening was completed in 54 of 292 (18.5%) person-intervals during Period A and 232/400 (58%) during Period B.

CSP9.09

The importance of trauma-informed care provision for HIV-positive pregnant women

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Background: Women living with HIV (WLWHIV) have higher rates of histories of trauma compared to HIV-negative women. The Positive Pregnancy Program (P3) is a multidisciplinary program caring for HIV-positive pregnant women in Toronto, Canada.

Materials and Methods: We performed a retrospective review of all women cared for in P3 from January 2011-December 2016. We assessed rates and categories of trauma among this population, and demographic characteristics associated with having a history of trauma.

Results During the study period there were 139 pregnancies, of which 18 were repeat pregnancies in the same individual. Therefore 121 pregnancies were used for this analysis. The women came from 36 different countries worldwide. Ninety-eight women were Black (86 of African descent and 12 Caribbean), 16 Caucasian, four Asian and three Hispanic. Within the total cohort, 67/121 (55%) of women had self-disclosed histories of trauma. Categories included trauma resulting from migration, living in conflict zones, human trafficking, rape as a tool of war, sexual trauma, loss of family members, and intergenerational trauma resulting from racism within the residential school system. Black women were significantly more likely to have a history of trauma compared to non-Black women (49% vs. 7%, p=.027), with an odds ratio of 2.85 (95% CI 1.10, 7.32). Within racial groups, 60% of Black women and 39% of non-Black women had a history of trauma.

Conclusions: Pregnant WLWHIV in Toronto have a high likelihood of a history of trauma. Although more commonly seen in Black women, trauma affected all racial groups. Provision of trauma-informed care is paramount in this population, and formal tools to elicit these histories should be considered.

HIV Prevention

Prévention du VIH

CSP10.01

Treatment as prevention (TasP) and pre-exposure prophylaxis (PrEP) among female sex workers (FSWs) in Benin: a demonstration project

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Background: Within a combination prevention program offered to FSWs in Benin, we are carrying out a demonstration project on TasP among HIV-positive FSWs and PrEP with Truvada® among HIV-negative FSWs. The study is conducted at Dispensaire IST (DIST), a clinic dedicated to FSWs in Cotonou. It aims to assess the feasibility and usefulness of integrating TasP and PrEP into the combination prevention package already offered to FSWs in Benin.

Methods: The recruitment visit was preceded by a screening visit two weeks earlier in order to determine HIV status and assess other eligibility criteria. Follow-up visits were at day-14 and then quarterly. The target sample sizes were 100 for TasP and 250 for PrEP, respectively. We report on the completed recruitment phase of the study and on retention up to three months prior to completion of follow-up.

Results: Recruitment was carried out from October 2014 to January 2016 and follow-up will be completed in December 2016. The table shows screening coverage, HIV prevalence, as well as recruitment and retention indicators as of October 31, 2016. At month-12 of follow-up, 65.2% of PrEP participants had a detectable tenofovir blood level, whereas 72.5% of TasP participants had an undetectable viral load (82.4% with viral load <1000).

Conclusions: Despite high uptake of both TasP and PreP, retention was problematic in this highly mobile population, although both uptake and retention were better for TasP than for PrEP. Retention issues could be minimized with broad geographical access to TasP and PrEP in West African countries.

Number of FSWs in catchment area	442	
Number who came to DIST for HIV testing	422 (95.5%)	
HIV status	HIV+: 111(26.3%)	HIV-: 311 (73.7%)
Eligible to the study[1]	110	298
Enrolled[2]	TasP: 105 (95.5%)	PrEP: 256 (85.9%)
New cases of HIV infection during follow-up[3]	--	2
Final TasP and PrEP numbers	TasP: 105 + 2 = 107	PrEP: 256 - 2 + 254
Number still on TasP/PrEP	62 (57.8%)	109 (42.9%)
Number of participants not on TasP/PrEP but retained in study	21 (19.6%)	37 (14.6%)
Retention in cohort[2]	83 (77.6%)	146 (57.5%)
Number of withdrawals from the study[4]	21 (19.6%)	105 (41.3%)
Number of losses to follow-up	3 (2.8%)	3 (1.2%)

1. One TasP exclusion because of HIV-2 infection and 13 PrEP exclusions due to active hepatitis B or breastfeeding;
2. TasP>PrEP, p≤0.01, chi-square;
3. New infections occurred while not being on PrEP and temporarily lost to follow-up;
4. 58% of all withdrawals due to moving out of Cotonou and 19% due to becoming ineligible (mostly pregnancy among PrEP participants).

CSP10.02

Evaluation of an interprofessional PrEP Clinic

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Health Canada approved once daily Truvada to reduce the risk of HIV acquisition as a part of a comprehensive risk reduction program for people at high-risk. The relative efficacy of Truvada was greater among subjects using it correctly and consistently. Use of PrEP implies regular medical appointments for monitoring and support.

In order to increase accessibility and uptake of PrEP, our clinic, Clinique PrEP, will take place in a family medicine unit, an inter professional primary care setting. Every professional will have a specific role in screening, prescribing PrEP, educating patients, verifying adherence and following drug's side effects. Collective prescriptions (ordonnances collectives) will be used by the nurses and pharmacists in order to increase professional autonomy.

Objectives: Our primary objective is to obtain a 96% efficacy of PrEP for HIV acquisition, between January and December 2017. Our secondary objective is to optimize patient adherence in combination with safer sex practices and evaluate patients' perceptions of our clinic. We want to demonstrate that PrEP can be effectively prescribed outside of traditional sexually transmitted infection clinics using collective prescriptions.

Methods: To increase the efficacy of our clinic, we address all aspects of PrEP care in our protocol. We trained all our staff to standardize our services. To assure effectiveness, all screening will be done every three months and statistics will be provided. The average adherence rate will be calculated using patient information and pharmacy renewal dates. Counselling patients on the importance of having safer sex will be emphasized and we will compare the percentage of using barrier protection during sex before and after taking care of the patient. A questionnaire will be completed by patients to rate their level of satisfaction and to see if there is any change in their risk taking behaviours.

CSP10.03

An implementation science approach to decentralizing the delivery of HIV pre-exposure prophylaxis through family physicians and sexual health clinic nurses

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Background: Pre-exposure prophylaxis (PrEP) holds potential for decreasing HIV incidence among gay, bisexual, and other men who have sex with men (gbMSM), but rollout in Canada is limited by inadequate numbers of HIV specialists to meet growing demand. Decentralizing PrEP services across front-line healthcare providers may alleviate this critical bottleneck.

Methods: We will evaluate two strategies to decentralizing PrEP delivery in Toronto, Canada: (1) We will empower gbMSM to connect their family doctors with evidence-based, online, accredited, patient-initiated continuing medical education (PICME) training on how to provide PrEP; (2) We will pilot nurse-led PrEP delivery in Toronto Public Health sexual health clinics. gbMSM interested in PrEP will obtain uniquely-coded information cards from local community-based organizations or social media, directing them to an online module with information on PrEP and HIV risk. The module will prompt patients to visit their family physician to share the card, which provides a link to the PICME module, and encourages a follow-up visit to discuss and potentially prescribe PrEP. The strategies will be evaluated through 1) questionnaires administered to patients and physicians at baseline and at six months, 2) focus groups with patients, family doctors, nurses and other sexual health clinic staff, and 3) review of patient charts at the sexual health clinics. The primary objective is to quantify the uptake of PrEP achieved using each strategy. Secondary objectives within each strategy include a) characterizing barriers and facilitators to PrEP uptake, b) assessing fidelity to core components of PrEP delivery, c) preliminary costing analysis, and d) measuring patient-

reported outcomes including satisfaction with clinician-patient relationships.

Discussion: This multi-component program will use both dissemination (PICME) and implementation (nurse-led PrEP) strategies to scale-up PrEP access and delivery. Findings will inform scale-up of the PICME and nurse-led PrEP strategies to other Canadian settings and at-risk populations.

CSP10.04

Preferences regarding emerging HIV prevention technologies among Toronto men who have sex with men (MSM)

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Background: New HIV prevention technologies (NPTs) currently in development include long-acting injectables and topical microbicides, and have unique attributes that may appeal differently to different users. We used a discrete choice experiment (DCE) to characterize NPT preferences among Toronto MSM.

Methods: MSM undergoing anonymous HIV testing completed a DCE with 12 'choice sets' by selecting their preferred option within each set. Each set included "usual methods to prevent HIV infection" (excluding pre-exposure prophylaxis) as one option and two hypothetical NPT options which differed according to HIV prevention efficacy (50%, 65%, 80% or 99% risk reduction), route of administration, side effects (none/mild), and risk of drug resistance (none/low/moderate). We used mixed logistic regression to infer relative preferences for NPT attributes and latent class analysis to determine patterns of responses.

Results: 306 men with median (IQR) age=30 (25, 38) participated, and reported 6 (3, 10) partners and 0 (0, 2) condomless receptive anal sex-acts in the preceding six months. Most knew of post-exposure prophylaxis (80%) and pre-exposure prophylaxis (91%), but only 11% and 5% respectively had used them. An on-demand pill was the most preferred NPT, followed by a daily pill, monthly injection and on-demand rectal gel. Resistance was an important determinant of NPT preference if the risk was moderate, but not if low. Minimum NPT efficacy required for an on-demand pill to be preferred over usual methods was 52.8% (95%CI=46.9-58.7); for a daily pill, injections, and rectal gel, estimates were 60.1% (95%CI=53.8-66.5), 67.0% (95%CI=61.0-73.0), and 78.3% (95%CI=70.9-85.7), respectively. Latent class analysis identified one subset of participants clearly favouring on-demand PrEP (40.5%), and three others preferring usual methods but with an aversion to injections (20.7%), aversion to rectal gels (21.9%), or relative indifference to NPTs (16.9%).

Conclusions: Attitudes towards NPTs among MSM are heterogeneous. Understanding these preferences may help predict NPT uptake.

CSP10.05

PEP/PrEP Awarness Among Crystal Meth users in Montreal

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Introduction: Growing evidence suggests that use of stimulant like Crystal Methamphetamine increase significantly the risk for HIV. We aimed to assess the awareness and knowledge of this core group about the chemo prophylactic tools available to prevent HIV-infection.

Methods: A survey at Clinique médicale Quartier Latin, a Montreal's urban center specialized in sexual health run since Oct 2016. Data on socio-demographics, drug & sexual behaviour, health and knowledge about PEP/PrEP were collected by auto-administered questionnaire completed by patients while waiting to see a clinician. The determinants of were obtained by logistic regression using SPSS-20.

Results: Since October 2016, 504 patients participated to the study. 72% were male, median age was 49y (IQR 36-60), 53% were MSM, 35% heterosexual and 12% had relation with both sex. Lifetime and recent prevalence of chemsex were 56% and 19% respectively. 68 patients (14%) reported having used crystal lifetime and 7% during the last year. Overall, only 53% of patients were aware of PEP and 48% of PrEP, however these proportion were significantly higher among crystal meth users (79% and 83% respectively,p<0.001). HIV infected patients (OR=1.83, 95%CI:1.01–3.31), crystal users (OR=2.18; 95%CI:1.07-4.47) and MSM (OR=7.22; 95%CI:4.33-12.05) were more likely to be aware of PEP treatment. Regarding PrEP treatment, the patients who already heard about PrEP were more likely to have been diagnosed with STI during the last 12 months (OR=2.17;95%CI:1.18-4.04), to be MSM (OR=10.82; 95%CI: 6.14-19.09) and crystal user (OR=4.48; 95%CI:1.98-10.12). Over 65% reported knowing where to go to have access to PEP and PrEP, 22% had already taken PEP and 20% had already had PrEP.

Conclusion: Most of the chemsexers, who are at high risk for HIV infection seems be aware of the new prevention tools available in Montreal, but we have to continue working with them and raise awareness about the entire prevention continuum

CSP10.06

Toronto's HIV prevention service organizations for gay, bisexual and men who have sex with men: A mixed-methods study

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Background: Gay, bisexual and men who have sex with men (GBMSM) continue to be disproportionately represented among new HIV infections in Canada. Many health and community organizations provide HIV prevention services to GBMSM in Toronto. However, it is unclear how services coordinate efforts and how GBMSM engage with these services. Our objective was to characterize HIV service organizations (HSO) in Toronto regarding prevention services, populations served, barriers and facilitators to access, and partnerships.

Methods: An advisory group made up of HSO representatives' supports this study. We conducted a mixed-methods study, beginning with an environmental scan of HSO, followed by an online survey and 11 key informant interviews. Quantitative data was analysed used descriptive statistics and qualitative data was analysed using thematic content analysis.

Results and Discussion: Of 64 HSO identified in Toronto, 44 (69%) responded to the survey. HSO reported focusing on new immigrants or refugees (64%), youth and adolescents (64%) and African-Caribbean Black men (59%). Fewer focused on Indigenous (38%) and Two-Spirited (13%) communities. 69% of organizations reported no programming for gender non-conforming populations. Barriers included a lack of consistent funding, the cost of PrEP, and inconsistent adherence to evidence-based HIV prevention practices. Many informants reported challenges in collaborating with health providers. Facilitators included adopting a client-centred model and using a syndemic, context-based approach. Social media was identified as a novel platform to deliver HIV prevention services to GBMSM. Diverse services are available to several GBMSM sub-populations. Few formal partnerships are currently established among HIVSOs in Toronto.

Conclusion: We have characterized a majority of HSO in Toronto serving GBMSM. Our results point to opportunities for HSO to expand collaboration, both to serve the general population and sub-populations. Next steps include carrying out focus groups with GBMSM in Toronto and developing a list of actionable strategies to improve HIV prevention.

Opportunistic Infections and Malignancies

Infections opportunistes et pathologies malignes

CSP12.01

HIV-infected Individuals Have Reduced Levels of Nasal Nitric Oxide Despite Effective ART

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Background: Produced by respiratory airway epithelial cells and macrophages, nasal nitric oxide (NO) results in cellular cytotoxicity through either direct or indirect killing of intracellular pathogens. Low levels of nasal NO have been associated with increased propensity to rhinosinusitis and respiratory tract infections in certain conditions. Our objective was to describe nasal NO levels in HIV-infected individuals on effective antiretroviral therapy (ART) and to determine possible risk factors for reduced nasal NO levels.

Methods: HIV-infected adults with suppressed viral load for ≥1 year on ART were recruited. Exclusion factors included acute viral illness/respiratory infection, current use of nasal/inhaled steroids/decongestants or chronic pulmonary disease. Individuals underwent nasal NO testing by standardized methods using a CLD88 chemiluminescence analyzer and completed the Sino-Nasal Outcome Test 20(SNOT-20) questionnaire on symptoms of rhinosinusitis. Clinical and lab parameters were collected. Descriptive analyses were performed (SPSS).

Results: 26 individuals participated. Mean age was 47 years(std dev±11), 9(34%) were current tobacco and 9(34%) were marijuana smokers. Mean CD4 count was 566(±280) cells/mm^3. Individuals were HIV-infected for a mean duration of 15(±9) years and had viral load suppression for 5(±3) years. Mean total points on the SNOT-20 questionnaire was 17(±15)/100 (higher scores suggesting greater symptomatology). Mean nasal NO level was

256(±78) nL/min[mean in healthy controls=305(±119) nL/min](p=0.02). 18 individuals(69%) had nasal NO<300 while 8(31%) had levels≥300 nL/min. There was no association between nasal NO levels and CD4 count/%, CD4/CD8 ratio, CD4 nadir, smoking status, ART regimen or SNOT-20 score. A trend was found between lower NO and longer duration of HIV infection(Pearson correlation -0.639, p=0.064).

Conclusion: HIV-infected individuals have significantly lower levels of nasal NO than the general population which may in part explain their ongoing propensity to respiratory tract infections, including rhinosinusitis. Longer duration of HIV infection, but not current or nadir CD4 count, may be a risk factor.

CSP12.02

JC Virus Progressive Multifocal Leucoencephalopathy Clinical Presentation and Prognosis in HIV and Non-HIV Patients: A Case Series

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Background: Human polyomavirus JC (JCV) is responsible for progressive multifocal leucoencephalopathy (PML). Introduction of combined antiretroviral therapy (cART) and increased use of immunosuppressive and oncologic therapies have modified the epidemiology and prognosis of PML. This study objective was to evaluate and compare the prognosis, diagnostic delays and clinical and radiological presentation of PML in HIV and non-HIV patients.

Methods: This retrospective observational multicentre study was performed in 4 university-affiliated hospitals of Montreal (Quebec). Patients were recruited through laboratory information systems and clinical archives interrogation. Patients with positive JCV polymerase chain reaction on cerebrospinal fluid and/or with a clinical diagnosis of PML during a hospitalization episode between January 2009 and December 2016 were included. Clinical data were collected through medical chart review following institutional review board approval. Fisher's exact test and Mann-Whitney tests were used for comparative analysis of categorical and continuous variables.

Results: The study includes 13 HIV-infected-patients and 8 non HIV-infected-patients. One-year survival and time to diagnosis delay data were respectively available for 13 and 10 patients in the HIV positive group and for 6 and 8 patients in the HIV negative group. One-year survival was 91.7 and 16.7 percent in the HIV positive and negative groups respectively (p=0.0039). Median time between initial symptoms and PML diagnostic was 70.5 (IQR: 32-147) and 31.5 (IQR 20-133.5) days in the HIV positive and negative groups respectively (p=0.45). No differences between groups were noted in clinical and radiological presentations.

Conclusions: Preliminary data suggest that PML prognosis is significantly better among HIV positive patients. Modern cART and immune status restoration could explain this finding. Whether PML or the underlying neoplastic or immunosuppressive condition is responsible for high mortality rates in the non-HIV population needs further exploring. Diagnostic delays, clinical and radiological presentations between HIV positive and negative patients showed no significant differences.

CSP12.03

Warts and All! Design Considerations in a Study to Evaluate Screening Tests for Anal Cancer in HIV-Positive Men Who Have Sex with Men.

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Background: High-risk types of human papillomavirus (HR-HPV) are the main cause of anal, and some penile and oral cancers in men. HR-HPV infection and anal cancer rates in HIV-positive gay, bisexual, and other men who have sex with men (MSM) are much higher than historic rates of cervical cancer prior to the adoption of routine screening. There are no universally-accepted guidelines for screening and treatment of anal pre-cancer. At present, anal cancer is usually diagnosed late in its course and is symptom-based; anal pre-cancers are asymptomatic and diagnosed via high resolution anoscopy (HRA). Few clinicians are trained in HRA making it a limited resource. Therefore, it is crucial to optimize decision making about whom to refer for diagnostic HRA.

Description and Objectives: One aim of the HPV Screening and Vaccine Evaluation (HPV-SAVE) study is to determine how best to screen HIV-positive MSM for anal

pre-cancer. Enrolling ~3000 men, this study will assess the utility of combining HPV DNA type testing (Types 16/18/31, other HR-HPV, no HR-HPV) with anal cytology (Normal, ASCUS, LSIL, HSIL) to screen for anal pre-cancer, determining the most effective screening test criteria. Our screening algorithm will randomly sample participants who screen negative on Pap cytology to undergo HPV testing and HRA to mitigate verification bias, with sampling proportions chosen according to clinically relevant detectable upper bounds for the prevalence of disease in those who screen negative. We will also discuss selection bias, misclassification of cytology and histology results, and precision of performance estimates while confined by capacity for HRA.

Significance: By appropriately designing the sampling scheme, the HPV-SAVE study will ascertain unbiased estimates of sensitivity, specificity, and predictive values of the optimal screening criteria to aid both patients and physicians in clinical decision-making around screening and follow-up of anal pre-cancer.

CSP12.04

Co-infection leishmaniose viscérale-infection VIH : à propos de 15 cas K.Otmani Service des maladies infectieuses et tropicales CHU de SIDI BEL ABBES, ALGERIE

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Objectifs : La leishmaniose viscérale (LV) est une anthropozoonose endémique dans le nord de l'Algérie. Considérée comme une maladie infantile, les formes de l'adulte sont en augmentation du fait de l'épidémie liée au VIH. L'objectif est de préciser les aspects épidémiologiques, cliniques et biologiques de la LV chez des adultes infectés par le VIH-1.

Matériels et méthodes : Étude rétrospective de 15 malades présentant une co-infection par Leishmania et le VIH-1, hospitalisés entre 2010 et 2015 dans un service des maladies infectieuses de Sidi Bel Abbes . Le diagnostic de la LV a été fait par la mise en évidence de formes amastigotes de Leishmania dans les frottis de moelles osseuses et/ou par la sérologie.

Résultats : Il s'agit de 12 hommes et de 3 femmes ; l'âge moyen est de 41 ans. Le mode de contamination par le VIH-1 était hétérosexuel dans 87 % des cas (13 malades). Une fièvre était présente chez 10 patients (67 %), une splénomégalie chez 11 (73 %), une hépatomégalie chez 5 (45 %), une pancytopénie chez 9 (60 %), une bicytopénie (leucopénie et anémie) chez 6 (40 %). Un malade a présenté une localisation cutanée associée ; un cas était une rechute. Cent pour cent avaient un taux de lymphocytes CD4 < 200 x 106/l (moyenne 39 x 106/l). Le frottis médullaire montrait la présence d'amastigotes chez 14 malades (94 %) ; un malade avait un frottis médullaire négatif et une sérologie de la LV positive. Le traitement utilisé est l'amphotéricine B classique : la réponse était satisfaisante avec une négativation des frottis médullaires chez 14 malades (93 %) ; il y a eu un décès précoce, deux rechutes tardives.

Conclusion : La LV de l'adulte est plus fréquente chez les personnes infectées par le VIH. Comme rapporté dans de rares études, elle touche les sujets très immunodéprimés et revêt le profil d'une authentique infection opportuniste du SIDA

Resistance

Résistance

CSP14.01

Longitudinal Trends of HIV Drug Resistance in a large British Columbia Cohort; 1996-2015

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Background: Human immunodeficiency virus (HIV) resistance to combined antiretroviral therapy (cART) drugs has hindered HIV treatment. We aim to identify long-term trends in drug resistance; before and after cART initiation, time to development of resistance, and the association of clinical variables to resistance.

Methods: IAS-USA (2015) mutations were identified in 23,271 HIV protease-reverse transcriptase sequences from 6543 treatment naïve British Columbia (BC) adults starting cART between 1996 and 2015. Kaplan-Meier time to resistance in four drug resistance categories was calculated, and separately, multivariable regression odds ratios (OR) for clinical variables were associated with developing resistance in each five-year era (1996-2000, 2001-2005, 2006-2010, 2011-2015).

Findings: Resistance detected after therapy initiation declined drastically (39% to 3%) in 1996-2015, as resistance prior to therapy increased (12% to 18%). Drug resistance rose to 31% (NNRTI), 30% (3TC/FTC), 17% (other nRTI), and 10% (PI) after >16 years of therapy. Participants initiating cART in 1996-2000 had 6.3-times more 3TC/FTC resistance, 5.5-times more other nRTI resistance, 4.6-times more NNRTI resistance, and 10-times more PI resistance than those starting in 2011-2015 after 5 years on therapy. The highest odds of developing resistance shifted from 60-<80% and 80-<90% adherence in 1996-2010, to 40% in 2011-2015.

Interpretation: In the past two decades, HIV drug resistance in the clinic has transitioned from primarily being selected de-novo in patients to being primarily driven by transmitted resistance. Resistance selected in treated indi-

viduals is rare in the past five years, and observed mostly in those in the lowest adherence strata.

Substance Use and HIV

Toxicomanies et VIH

CSP15.01

Prevalence of HIV virologic failure in a multidisciplinary centre treating high-risk vulnerable populations

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Introduction: Current antiretroviral therapies are associated with a high degree of long-term efficacy. However, these results are more challenging to achieve among people who inject drugs (PWID), due to reduced engagement in care and adherence to treatment. Provision of care in a dedicated multidisciplinary setting may help increase the success of HIV treatment and limit the risk of virologic failure.

Methods: An observational, retrospective study was conducted among HIV-infected patients seen at the Vancouver Infectious Diseases Centre (VIDC). All individuals had access to medical, psychiatric, addiction-related, and social care with maintenance in long-term follow-up. The endpoint of this analysis was virologic failure, defined as initial suppression of HIV viral load, followed by a measure >200 copies/mL, comparing rates of failure between PWID and non-PWID.

Results: Since 2013, 521 HIV+ patients have been maintained on antiretroviral therapy at VIDC (mean age of 51.6 years, 11% female). Overall, 179 (32%) are active/recent PWID (63% heroin, 59% cocaine, 70% other stimulants, 49% on opiate substitution therapy), 94% with HIV/HCV co-infection in this sub-group. Rates of maximal virologic suppression were 77% and 84% in PWID and non-PWID subgroups ($p > 0.05$). Only 5 PWID and 2 non-PWID had documented virologic failure while on treatment. All individuals who experienced virologic failure were switched to new regimens and successfully achieved virologic suppression.

Conclusion: When HIV care is implemented in a multidisciplinary setting, high-risk populations are as likely to achieve maximal virologic suppression, at rates nearly comparable to those achieved in the general population. Those who did not were all successfully treated with readily available second line regimens. Novel models of care such as ours will be needed to allow HIV-infected PWID to achieve the promise of "90-90-90" within the global response to the HIV pandemic.

CSP15.02

What leads to discharges against medical advice from hospital by people living with HIV who use substances? The health care provider perspective

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Background: Many people living with HIV/AIDS (PHAs) use illicit and prescription drugs in a non-medically indicated manner, and drink hazardously, for a range of reasons. Substance use by PHAs is associated with higher rates of emergency room visits, poor health outcomes, and repeat hospital admissions. In hospital, PHAs who use substances often encounter stigma, receive substandard care, and are more likely to leave against medical advice. This qualitative study explores what leads to discharges against medical advice (DAMA) from the health care provider perspective.

Methods: Twenty-six health care providers (11 physicians, 6 nurses, 4 social workers, 4 pharmacists, and 1 dietician) who provide acute care for individuals living with HIV and/or HCV were recruited from three Toronto and Ottawa hospitals. Data were collected through semi-structured interviews which were audio-recorded and transcribed verbatim. An inductive approach was used to analyze the data.

Results: Participants conceptualized DAMA as part of a longer process that can begin at the time of admission (or a previous admission) and is influenced by a range of medical, interpersonal, organizational and structural factors. In particular, participants identified the following factors that contribute to DAMA among substance using PHAs: poor pain and withdrawal symptom management; conflict between providers and patients about treatment plans, procedures, behaviours and attitudes; patient boredom and frustration; and patients deciding they feel well enough to leave. Participants had mixed feelings about their level of responsibility for patients leaving. However, many described strategies they use when they anticipate PHAs may leave early, including having pharmacy prescriptions ready, following up with primary or community care providers, and under extreme circumstances engaging security or law enforcement to retrieve patients.

Conclusion: Our study advances the limited research on DAMA by identifying important factors beyond individual patients or a single hospital stay that contribute to early and unplanned discharges.

Clinical Sciences: Other

Sciences cliniques : Autre

CSP16.01

Cognition, Mood and Quality of Life in the Brain Health Now Canadian cohort: Good News and Red Flags

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Background: Chronic HIV infection commonly affects cognition and mental health. The Positive Brain Health Now cohort study aims to provide a better understanding of the relationship between cognition, mood, and quality of life.

Methods: Among cohort participants (N=833, ≥ 35 years of age and HIV+ ≥ 1 year), we documented cognitive ability (computerized B-CAM), self-reported cognitive difficulties (PDQ), depression and anxiety (HADS-D and HADS-A), sleep, physical activity and quality of life (RAND-36, WHO-QOL). Findings of potential health importance, "Red flags", are computed.

Results: Cohort members are mostly educated males with a median age of 53. 44% are gainfully employed. Health-related quality of life is below Canadian norm in all domain except physical function. Most participants (71%) are satisfied with their quality of life and find their life to be meaningful (70%). Clinically significant anxiety (23%) is more common than depression (9%). Both depression and anxiety are associated with lower cognitive ability but only anxiety is associated with more self-reported cognitive difficulties. Dissatisfaction with sleep in common (35%). The most common "red flags" are related to negative mood and health problems interfering with social activities. Surprisingly, pain is also identified as severe and disabling among 7% of participants. Three or more symptoms of potential clinical importance are reported in 11%.

Conclusions: Most participants report satisfaction with their quality of life. However, health-related quality of life is below Canadian norms in most domains. Mental health symptoms are common and 10% experience significant health difficulties that warrant clinical attention.

Characteristics of the cohort	
Age (mean ± SD)	52.8 (8.2)
> 60 years, N (%)	147 (17.6)
Men	718 (86.2)
Education	
High school or less	32%
College	34%
University	34%
Working (%)	44%
Nadir CD4 (median)	220 cells/mm^3
Current CD4 (median)	610 cells/mm^3
Red Flag, N (%)	
Red Flag- Physical	
Today: extreme pain or discomfort	27 (3%)
Last 2 weeks, very dissatisfied with health :	17 (2%)
Past 4 weeks, bodily pain severe or very severe	58 (7%)
Red Flag- Emotional	
Health today: extremely anxious or depressed	30 (4%)
Last 2 weeks, negative feelings always or very often	88 (10%)
Last 2 weeks, enjoy life not at all or little	89 (11%)
Past 4 weeks, felt downhearted and blue : all or most of the time	46 (5%)
Past 4 weeks, nothing could cheer you up all or most of the time	32 (4%)
Red Flag- Function	
Past 4 weeks, physical health or emotional problems interfered with social activities all or most of the time	91 (11%)
Past 4 weeks, pain interfered with normal work quite a bit or extremely	58 (7%)
Red Flag- Quality of Life	
Last 2 weeks, very poor quality of life	9 (1%)
I have lots of reasons for living : disagree or strongly disagree	61 (7%)
Number of Red Flags	
Number of "Red Flags"	
1	86 (10%)
2	53 (6%)
3-5	72 (9%)
6+	20 (2%)

CSP16.02

Does HIV Infection Compromise the Integrity of the Oral Mucosa and Increase the Immune Activation Markers Associated with Accelerated Aging?

Samantha E. Heron, Stan Houston, Shokrollah Elahi

University of Alberta, Edmonton, AB

The rate of HIV infection continues to rise globally, with an estimated 36.7 million people living with HIV in 2015. Even with antiretroviral therapy (ART), HIV-infected individuals have a shorter life expectancy and experience non-HIV re-

lated comorbidities such as cardiovascular disease, osteoporosis, cancer, and neurocognitive decline. This concept of "accelerated aging" has been associated with systemic hyper-immune activation in these individuals. HIV disrupts the epithelial lining of the gut associated lymphoid tissue, resulting in translocation of bacterial byproducts into the periphery causing generalized immune activation.

We proposed that the integrity of oral mucosa could be influenced by HIV infection and subsequently inflammatory conditions in the oral cavity might play a role in generalized immune activation in these patients. In this study, we investigated the immune cells in saliva as well as from buccal mucosal swab samples from HIV-positive patients. The samples from a control group of HIV-negative individuals will be compared against four populations: a long-term non-progressor (LTNP) population; a HIV-positive population taking ART with a CD4 count less than $200ul^{-1}$; a HIV-positive population taking ART with a CD4 count greater than $500ul^{-1}$; and a recently diagnosed HIV-positive but ART naive. Each patient will be age and gender matched to healthy controls. Our preliminary data indicate significantly lower proportion of langerhans and activated T cells in the oral cavity of LTNP group compared to healthy controls, the HIV group with a CD4 count greater than $500ul^{-1}$, and the group with a CD4 count less than $200ul^{-1}$. In addition, a comprehensive immunophenotyping was conducted on the saliva and buccal mucosal specimens.

These studies will assist us to better understand how HIV-infection impacts the oral mucosal immunity, and identification of certain immune signatures associated with HIV in the oral cavity may assist us for developing potential therapeutic and preventive interventions.

CSP16.03

Abdominal Fat Accumulation in a Cohort of HIV-Infected Patients Attending an Outpatient Clinic in Montreal

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Objective: Increased waist circumference due to excess abdominal fat (subcutaneous (SAT) and visceral (VAT)) is associated with the metabolic syndrome, cardiovascular disease and increased morbidity and mortality in the general population.

Increased WC in treated HIV+ patients is a frequently documented finding trending upward. HIV+ patients with history of Thymidine analog drug exposure and the clinical phenotype known as Lipodystrophy (Peripheral fat atrophy|Central fat hypertrophy) and increased WC are presumed to have clinically significant increases in VAT. A retrospective analysis of medical records of this population was undertaken in patients attending an HIV Clinic to assess these assumptions.

Methods: Retrospective analysis of medical health records and an electronic database. Patients identifiers: Any thymidine analog drug exposure (D4T|AZT) and or clinical diagnosis of Lipodystrophy and for whom WC measurements were captured recently : Feb. 1st to Nov. 1st 2016. Excess abdominal fat was defined as a WC ≥ 95 cm in men and ≥ 94 cm in women.

Visceral Abdominal Tissue (VAT) was determined by Abdominal Computed Tomographic Single Slice L4-L5 intervertebral level imaging. Excess VAT has been defined as a measurement > than 130 cm^2.

Results: 70 patients (66 male, 4 females) met the search criteria. Of these patients, 29 underwent radiologic imaging and 22/29 met the definition of excess VAT while 7/29 had SAT. The mean VAT level in the group with excess VAT was 223 cm^2.

We plan an analysis of the demographic and clinical characteristics of both groups to determine the differences.

Conclusion: Waist circumference alone is an insufficient single predictor for excess VAT. CT abdominal imaging identified 7 patients who did not have excess VAT. That shows that it's necessary to confirm the presence and determine the precise volume of VAT in HIV+ patients for whom VAT treatment therapies could be considered and therapeutic effectiveness assessed.

CSP16.04

Examining Cause-Specific Mortality for Patients Enrolled in an Outpatient HIV Primary Care Clinic in a Tertiary Referral Hospital in a Canadian Setting

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Introduction: Engagement in care and access to highly active antiretroviral therapy (HAART) have significantly decreased morbidity and mortality among people living with HIV/AIDS. In this study, we examine patterns of cause-specific mortality for individuals enrolled in a comprehensive, interdisciplinary HIV Primary Care clinic in Vancouver, British Columbia.

Methods: A retrospective study was conducted on HIV-infected individuals age ≥ 19 years enrolled in the John Ruedy Immunodeficiency Clinic (IDC), a specialized HIV clinic in a tertiary referral hospital. Patients were included if they were deceased between 01-Jan-2004 and 31-Dec-2015. Data on medical history, clinical laboratory tests and mortality were obtained from the clinic's database and from individual medical records. Causes of death were independently reviewed by two physicians and recorded

utilizing a previously validated algorithm. A Poisson regression model was used to examine trends for AIDS- and non-AIDS-related mortality.

Results: From January 2004 to December 2015, out of 2244 patients enrolled in the IDC, there were 271 deaths (12%). AIDS-related mortality decreased from 36.18 per 1000 person-years (PY) in 2005, to 2.49 per 1000 PY in 2015 ($p < 0.001$). Non-AIDS-related mortality decreased from 37.38 per 1000 PY in 2004, to 13.72 per 1000 PY in 2015 ($p = 0.01$). The most frequent underlying causes of death were AIDS-related events (n=74, 27%), causes related to substance abuse (n=44, 16%), non-AIDS-related malignancies (n=44, 16%) and progression of chronic viral hepatitis (n=16, 6%).

Conclusion: We observed a significant decreasing trend for both AIDS- and non-AIDS-related mortality over the study period. Advances in clinical care and treatment are showing significant benefits for people living with HIV/AIDS; better screening and management of non-AIDS-related causes of death are needed.

CSP16.05

Feasibility and Acceptance of HIV Point-of-Care Testing on an Internal Medicine Inpatient Unit

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Introduction: It is estimated that 25% of people living with HIV in Canada are unaware of their status. HIV point of care (POC) tests provide an alternative to standard laboratory testing, which may decrease barriers to testing for some individuals.

Objective: The objectives of this study were to evaluate feasibility and patient acceptance of HIV POC testing for patients admitted to the internal medicine unit and to evaluate physician testing patterns before and after implementation of this study.

Methods: Patients admitted to internal medicine over a 3-month period were invited to participate in the study. Those who agreed to participate were administered a questionnaire on sociodemographic data and risk factors for HIV by the study staff. After administration of the questionnaire, the study staff provided pre-test counseling, performed an HIV POC test, then provided post-test counseling based on the results. Participants were given a post-test questionnaire to evaluate patient satisfaction with the testing experience.

Results: Of 455 patients admitted to internal medicine during the study period, 144 consented to participate in the study. Reasons given for declining testing included lack of perceived risk, fear of test results, and lack of interest. Of the study participants, 138 (95.8%) tested negative. Four patients (2.8%) had indeterminate test results, but went on to test negative by fourth generation ELISA. Two patients (1.4%) had reactive HIV POC tests. Of these, one subsequently tested negative by fourth generation ELISA and one was previously known to be HIV positive. Overall, 133 (92.3%) of patients indicated that they were satisfied with the testing experience, and 133 (92.3%) stated that they would choose a rapid HIV test. In the three months prior to the study period, 65 patients were tested for HIV, with one reactive. Rates of testing for the 3-month period following the intervention are pending.

Epidemiology and Public Health

Épidémiologie et santé publique

Data Science: Use of Administrative Data, New Measurement Tools other Novel Data Sources in HIV Public Health Research

Science des données : Utilisation des données administratives, nouveaux outils de mesure, autres sources originales de données en recherches sanitaires publiques sur le VIH

EPHP1.01

A Cohort Study Examining Emergency Department Visits and Hospital Admissions Among People Who Use Drugs in Ottawa, Canada

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The health of people who use drugs (PWUD) is characterized by multimorbidity and chronicity of health conditions, necessitating an understanding of their health care utilization. The objective of this study was to evaluate emergency department (ED) visits and hospital admissions among a

cohort of PWUD. We used a retrospective observational study design between 2012 to 2013 in Ottawa, Ontario. The population was a marginalized cohort of PWUD (the PROUD study) for whom survey data was linked (n=663) to provincial health administrative data housed at the Institute for Clinical Evaluative Sciences. We constructed a 5:1 comparison group matched by age, sex, income quintile, and region. We used multivariable logistic regression analyses to identify factors associated with ED care and hospitalization. Compared to the matched cohort, PWUD had higher rates of ED visits (rate ratio [RR] 7.0; 95% confidence interval [95%CI] 6.5 to 7.6) and hospitalization (RR 7.7; 95%CI 5.9 to 10.0). After adjustment, factors predicting two or more ED visits were receiving disability (odds ratio [OR] 3.0; 95%CI 1.7 to 5.5) or welfare payments (OR 2.7; 95%CI 1.5 to 5.0), injection drug use (OR 2.1; 95%CI 1.3 to 3.4), incarceration within 12 months (OR 1.6; 95%CI 1.1 to 2.4), mental health comorbidity (OR 2.1; 95%CI 1.4 to 3.1), and a suicide attempt within 12 months (OR 2.1; 95%CI 1.1 to 3.4). Receiving methadone (OR 0.5; 95%CI 0.3 to 0.9) and having a regular family physician (OR 0.5; 95%CI 0.2 to 0.9) were associated with lower odds of having more ED visits. Similar and additional factors were associated with having one or more hospital admissions, including comorbid HIV (OR 2.4; 95%CI 1.2 to 5.6). Improved post-incarceration care and access to integrated primary care services including opioid replacement therapy may be effective interventions to decrease acute care use among PWUD.

EPHP1.02

Development and validation of a case-finding algorithm for the identification of people who inject drugs from administrative health data in British Columbia

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Background: The purpose of this analysis was to develop and validate a case-finding algorithm to identify PWID from the Comparative Outcomes and Service Utilization Trends (COAST) study.

Methods: COAST is a population-based retrospective cohort of all known people living with HIV/AIDS (PLWH) and a 10% sample of the general population in British Columbia (BC), with data from 1996 to 2013. COAST contains longitudinally collected demographic and clinical data from the BC Centre for Excellence in HIV/AIDS provincial Drug Treatment Program (DTP) and linked administrative health data from Population Data BC (including Medical Services Plan (MSP), Discharge Abstract Database (DAD), and PharmaNet data). MSP captures insured medical services billed in the province of BC by physicians. DAD captures all discharges, transfers and deaths from acute care hospitals in BC. PharmaNet captures all prescription dispensations in BC. The case-finding algorithms developed were validated using DTP and Longitudinal Investigation into Supportive and Ancillary Health Services (LISA) datasets. DTP has an injection drug use (IDU) flag if the physician has ever identified the patient as a PWID. LISA has an IDU based on face-to-face interview questionnaire responses.

Results: The case-finding algorithm selected to identify history of IDU required the presence of at least one IDU related International Classification of Disease (ICD) 9 or 10 code from MSP or DAD data (e.g. ICD-9 304) or one PharmaNet record for methadone. When validated against the DTP dataset, the algorithm had a sensitivity, specificity and PPV of 72%, 90% and 85%, respectively. When validated against the LISA dataset, the algorithm had a sensitivity, specificity and positive predictive value (PPV) of 83%, 80%, 86%, respectively.

Conclusions: The '1 MSP or 1 DAD or 1 PharmaNet' algorithm can be applied as a framework to assemble population-based IDU cohorts and assist subsequent hypothesis testing using administrative health data.

EPHP1.03

Trends in Engagement in HIV Care Among Diagnosed People Living with HIV in the Ontario HIV Laboratory Cohort: a Retrospective, Population-based Cohort Study

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Introduction: Measurement of the HIV cascade is a global priority yet is often limited by available data sources and their representativeness of entire jurisdictions. Using a province-wide database, we measured trends in HIV care engagement from 2000-2015 among diagnosed people living with HIV (PLWH) in Ontario.

Methods: We developed a retrospective population-based cohort of diagnosed PLWH using a centralized diagnostic and viral load (VL) laboratory database with records linked at the individual-level. We included individuals with a nominal HIV-positive diagnostic test (1985-2015) or a VL test (1996-2015). Individuals were administratively lost-to follow-up (LTFU) and removed from the cohort if they had no VL test for 2 consecutive years, and no VL test in later years. Outcomes included the annual proportion of

diagnosed PLWH (cohort individuals not LTFU) meeting the following indicator definitions in a given calendar year from 2000-2015: in care (≥1 VL test); on antiretroviral treatment, ART (documented on last VL test requisition); and VL suppressed (<200 copies/ml on last VL test).

Results: Between 1985-2015, 29,587 individuals were followed for 244,543 person years and 552,855 VL tests. The number of diagnosed PLWH increased from 8,859 in 2000 to 16,110 in 2015, of whom 14,065 were in care in 2015. Estimates of all cascade indicators increased over time, with the proportion of diagnosed PLWH who were in care (87.3%), on ART (81.1%), and virally suppressed (79.5%) reaching highs in 2015. The proportion suppressed doubled by 2015 (from 40.7% in 2000) and increased faster than other indicators.

Conclusion: Population-based estimates of HIV cascade engagement indicate improvement over time in Ontario. This centralized laboratory database is a powerful tool for analyzing the cascade, despite challenges with non-nominal diagnoses, missing ART information, and accounting for migration/death. Further work is needed to explore estimates by age, sex, population and region.

EPHP1.04

Mortality risk among people with HIV in Ontario, 1995-2014

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Background: Our aims were to compare mortality risk between participants and non-participants of an HIV clinical cohort over time, identify mortality risk factors, and determine whether these differed between participants and non-participants.

Methods: We constructed a retrospective cohort of people in HIV care in Ontario from 1995 to 2014 using administrative population-based health records. Within this cohort, we used record linkage to identify participants of the Ontario HIV Treatment Network (OHTN) Cohort Study (OCS), a multi-site clinical cohort of people attending specialty HIV clinics since 1995. We used Cox proportional hazard models and time-updated covariates, including interaction terms where appropriate, and report these as adjusted hazard ratios (HR) with 95% confidence intervals (CI).

Results: A total of 4,407 OCS participants and 15,185 non-participants were followed 165,689.96 person-years (PY); there were 3,582 deaths. Mortality declined from 5.47 (5.23-5.72) per 100PY in 1995-99 to 1.32 (1.24-1.41) per 100PY in 2010-14. The gap in mortality risk between OCS participants compared to non-participants increased with time (1995: HR 1.02, 0.92-1.13; 2000: 0.71, 0.64- 0.80; 2005: 0.50, 0.41-0.61; 2010: 0.35, 0.26-0.45). Among OCS participants, there was no difference in mortality by care pattern. Among non-participants, compared to those having only HIV specialist care, mortality risk was higher for those receiving no care (HR 1.87, 1.69-2.07) or both HIV specialist and family physician care (HR 2.20, 1.85-2.60), and lower among those receiving only family physician care (HR 0.77, 0.69 to 0.85). Additional mortality risk factors were older age, male sex, lower income, higher comorbidity, non-urban residence, and non-immigrant status.

Conclusion: Mortality risk among people with HIV decreased over time and was generally lower among research volunteers in a clinical cohort, for whom care pattern was unassociated with mortality. Our findings suggest that people not participating in research studies may require improved coordination of care between providers.

EPHP1.05

Mortality and care-seeking behaviour after loss to follow-up from a cohort study

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Background: Knowledge of health outcomes of cohort study participants after loss to follow-up (LTF) is necessary for interpretation of research findings from those studies. Time to event analyses of clinical outcomes or death in cohort studies often assume that censoring due to LTF is independent of the outcome under study. Estimates of life expectancy require assumptions about survival after LTF.

Methods: Participants in the Ontario HIV Treatment Network (OHTN) Cohort Study (OCS) were linked to administrative population-based health records. Rates of mortality were summarized by calendar period.

Results: 5568 OCS participants were enrolled between 1995 and 2014 and were linked to administrative health records. As of Dec 31, 2014, 3300 of these participants were active, 860 had died, 229 were enrolled at a site that had closed, and 1179 were LTF. After linkage with administrative health records, the median person years (PYRS) of follow-up in Ontario after LTF from the OCS was 10.88, 10.97, 5.59 and 3.66 for participants who were LTF in the calendar year periods 1996-99, 2000-04, 2005-09 and 2010-14. 5.6% had no outpatient visits after LTF from the OCS. After LTF from the OCS, 267 participants were recorded as having died according to administrative record (3.3 deaths per 100 PYRS of follow-up). Rates of death among OCS participants and non-OCS participants were 2.52 and 2.20 per 100 PYRS of follow-up. Age-adjusted rates are shown below.

Discussion: Participants who were LTF from the OCS had higher rates of mortality than participants who continued under follow-up in the cohort.

	Age-adjusted mortality rates		
	Non-OCS	Active OCS participants	OCS after LTF
1996-99	6.49 (5.98-7.03)	7.46 (6.32-8.73)	14.98 (6.88-27.29)
2000-04	2.60 (2.34-2.88)	3.66 (3.03-4.37)	4.04 (2.63-5.89)
2005-09	2.13 (1.95-2.32)	1.60 (1.30-1.94)	4.62 (3.55-5.90)
2010-14	1.66 (1.53-1.80)	1.04 (0.87-1.23)	2.06 (1.50-2.73)

EPHP1.06

Excess Burden of Infections Among HIV Positive Individuals Prior to HIV Diagnosis and Care

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Background: Successful engagement in the HIV treatment cascade involves understanding the complex health needs of HIV-positive individuals. Knowledge of pre-existing/concurrent infectious conditions can inform engagement/treatment strategies used by HIV care programs. We compared diagnoses of common infections between HIV cases and HIV-negative controls, five years prior to HIV diagnosis.

Methods: Data were from a retrospective cohort from Manitoba**.** Participants included HIV-positive individuals presenting to care between 2007-2011 to the Manitoba HIV program, and HIV-negative controls, matched (1:5) by age, sex and region. Clinical information was linked to population-based administrative databases, including physician visits, hospitalizations and pharmaceutical dispensations. Diagnoses for tuberculosis (TB), pneumonia, thrush, cellulitis and influenza were classified according to International Classification of Diseases codes, and where appropriate, drug dispensation information. Conditional logistic regression was used to compare diagnoses between cases/controls; odds ratios (ORs) and 95% confidence intervals (95%CI) are reported.

Results: A total of 193 cases and 965 controls were included. HIV cases were more likely to have a diagnosis for TB (OR: 4.1, 95%CI: 2.2-7.7), thrush (OR: 2.0, 95%CI: 1.3-3.0), cellulitis (OR: 1.5, 95%CI: 1.1-2.1), and pneumonia (OR: 1.7, 95%CI: 1.2-2.4), but not influenza (OR: 0.9, 95%CI: 0.6-1.3). Having diagnoses for cellulitis (p=.045) and pneumonia (p=.027) were associated with CD4 counts <350 cells/mm3 at program entry. Results were similar at 2 years prior to diagnosis.

Conclusion: HIV positive individuals had an excess burden of infections prior to their HIV diagnosis. Complex care needs of HIV-positive individuals highlight the need for strongly-linked, interdisciplinary care.

Table 1: Prevalence of Infectious Conditions and Odds Ratios (OR) and 95% Confidence Intervals from Conditional Logistic Regression Models Comparing HIV-Positive Individuals and Their HIV-Negative Controls

Infectious Conditions	Controls (n, %) N: 965	Cases (n, %) N: 193	OR (95%CI)
Thrush	126 (13.1)	41 (21.2)	2.0 (1.3-3.0)
Cellulitis	526 (54.5)	124 (64.3)	1.5 (1.1-2.1)
Pneumonia	220 (22.8)	64 (33.2)	1.7 (1.2-2.4)
Influenza	293 (30.4)	54 (28.0)	0.9 (0.6-1.3)
Tuberculosis	24 (2.5)	19 (9.8)	4.1 (2.2-7.7)

EPHP1.07

Mapping uncertainty: A Case Study of Mapping STBBI Epidemiological Data Relative to Testing Locations in Nova Scotia

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Objectives: 1. To create a visual map of the incidence rates of sexually transmitted and blood-borne infections (STBBIs) in Nova Scotia relative to testing locations between 2008 and 2015. 2. To undertake in-depth interviews with a sample of policy and programming decision-makers about STBBIs in Nova Scotia based on the mapping exercise findings. 3. To use these data to frame evidence-based recommendations in relation to scaling-up of STBBI testing programs and interventions in Nova Scotia.

Methods: Although many efforts have been made to prevent, or at least mitigate, the rise in STBBIs, current approaches have not been fully successful in reducing new infections. Our team has undertaken a mapping study of STBBI (e.g., HIV, HCV, chlamydia, syphilis, gonorrhea) incidence and prevalence rates in Nova Scotia to map the burden of STBBIs relative to STBBIs testing locations.

Results: Several recent outbreaks of STBBIs suggest more is needed to ensure those at risk are able to access testing in Nova Scotia. However, as indicated by our data, gaps continue to exist in relation to access to testing in particular regions and among particular at-risk, priority populations.

Conclusions: Given that testing is a key intervention to help stem the tide of STBBIs, addition attention is needed to ensure maximum synergies between sectors, including testing sites, community-based programs, laboratory services, and public health. The findings from this research will assist in realigning Nova Scotia's policy and programming responses to the burden of STBBIs in the province.

EPHP1.08

PHIRST Trial - Pharmacist Consults: Prioritization of HIV-Patients with a Referral Screening Tool

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The role of pharmacists in HIV outpatient clinics has greatly increased in the past decades. Given the limited resources of the health system, the prioritization of pharmacist consults is now a main concern. This study aimed to create a scoring system allowing for standardized prioritization of pharmacist consults for patients living with HIV. Data was retrospectively collected from 200 HIV patients attending the Chronic Viral Illness Service at the McGill University Health Center. An expert panel consisting of four pharmacists working in the field of HIV prioritized each patient individually, after which a consensus was established and was considered as the gold standard. In order to create a scoring system, two different methods (Delphi, statistical) were used to assign a weight to each characteristic considered to be important in patient prioritization. A third method (equal weight to each characteristic) was also evaluated. The total score per patient for each method was then compared to the expert consensus in order to establish the score cut-offs to indicate the appropriate categories of delay in which to see the patient. All three systems failed to accurately prioritize patients into urgency categories ("less than 48 hours", "less than 1 month", "less than 3 months", "no consult required") according to expert pharmacist consensus. The presence of high level interactions between patient characteristics, the limited number of patients and the low prevalence of some characteristics were hypothesized as the main causes for the results. Creating a prioritization tool for pharmacy consults in HIV outpatient clinics is a complex task and developing a decision tree algorithm may be a more appropriate approach in the future to take into account the importance of combinations of patient characteristic.

Epidemiology and Surveillance of HIV Co-infections

Épidémiologie et surveillance des coinfections au VIH

EPHP2.01

Profile of Patients Living with HIV in Newfoundland and Labrador, Canada

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Introduction: The complexity of HIV affects its patients in all aspects of life. Currently, patients living with HIV (PLHIV) access healthcare primarily through HIV specialists; however, the transition towards primary care is necessary to help bridge the gaps evident in the current system. This multiphase project aims to advance PLHIVs access to primary healthcare. This phase will develop a comprehensive profile of PLHIV in Newfoundland and Labrador (NL) to better understand where to prioritize change.

Methods: This is retrospective cohort study. De-identified data of PLHIV in NL was collected from a number of different databases and assembled and linked by NL Centre for Health Information (NLCHI). Patients were identified as having HIV from three different sources: laboratory, HIV clinic or medico-administrative data. The finalized database includes information surrounding patient demographics, comorbidities, mortality, HIV exposure type, risk level, AIDS status, pregnancy information, year of diagnosis and cancer status, medications. STATA software was used to perform a descriptive analysis on the data.

Results: A total of 316 patients in NL have been diagnosed with HIV. 65 of these patients (20%) died during 1995-2014, leaving 251 active PLHIV. Of those alive, 237 (94%) were sourced by the HIV clinic database, meaning 94% of patients are linked to HIV clinic care and have received services at some point. On average, these patients have had HIV for 12.68 years (σ=8.72 years) and 20.88% have been diagnosed with at least 1 comorbidity. Study is in progress and the analysis will be completed for the presentation at conference.

Conclusion: This comprehensive profile of PLHIV in NL, will enable policy makers and researchers to advance primary healthcare and target changes towards the most appropriate cohort of individuals. This knowledge will help guide and prioritize the subsequent phases of this study.

EPHP2.02

An Upward Trend in Ocular Syphilis Cases in British Columbia, 2013-2016: A Descriptive Analysis

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Introduction: HIV-positive individuals are generally considered higher risk for early and more serious neurologic complications related to syphilis. In 2014-2015, clusters of ocular syphilis cases were reported in the US. Simultaneously, British Columbia (BC) saw a dramatic rise in syphilis cases by 40%. Here we describe ocular syphilis cases diagnosed in BC.

Methods: All neurosyphilis cases diagnosed in BC since 2013 were reviewed to identify ocular cases. Ocular syphilis was defined as having signs/symptoms of ocular disease (e.g. uveitis) and syphilis of any stage, as defined by the Centers for Disease Control.

Results: Between January 1st, 2013 and October 31st, 2016, 35 cases of ocular syphilis were recorded in BC. Most were male (32/35; 91.4%) and identified as white (20/35; 57.1%). The mean age was 49.7 years. A majority (18/35; 51.4%) were living with HIV. The most frequent ophthalmologic diagnoses were uveitis (41.9%), optic neuritis (12.9%), and retinitis (9.7%). Twenty-three cases had lumbar puncture data available: 13 (56.5%) had elevated cerebrospinal fluid (CSF) protein, 15 (65.2%) had elevated CSF cell count, and 6 (26.1%) had positive CSF VDRL. As a proportion of all syphilis cases, ocular syphilis accounted for 0.80% of all cases during the 2013-2015 period, versus 1.54% for 2016 ($p = 0.05$). Stratified by HIV serostatus, there was a significant increase in the proportion of ocular syphilis cases in those living with HIV between the 2013-2015 and 2016 time periods (1.17% vs. 3.21%, $p = 0.03$).

Conclusion: Paralleling trends observed in some US jurisdictions, BC is experiencing an increase in ocular syphilis cases, and an increasing proportion of syphilis cases in those living with HIV are being diagnosed with ocular findings. These results further highlight the importance of continuing efforts to respond to the syphilis epidemic, and focused screening for ocular symptoms, particularly in those at highest risk.

EPHP2.03

Hepatitis C re-clearance and lack of cross-genotype immunity in a large population cohort

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Background: Data on spontaneous clearance of Hepatitis C (HCV) after reinfection (re-clearance) in humans are very limited. We examined HCV re-clearance in a large population-based cohort in British Columbia, Canada.

Methods: We identified people with HCV reinfection who had at least one follow-up HCV-RNA testing (n=357) to examine HCV re-clearance using the BC Hepatitis Testers Cohort that includes all British Columbians tested for HCV during 1990-2013. Multivariable Cox proportional hazards (PH) model was used to identify potential predictors of re-clearance.

Results: Confirmed (two consecutive negative PCR ≥28 days apart), and probable re-clearance (only one negative PCR, or two consecutive negative PCR <28 days apart) were observed in 34% (n=121) and 15% (n=54) of the participants, respectively. The rate of confirmed re-clearance was 12.36 (95% CI: 10.26-14.77) per 100 person-year. In adjusted Cox PH model, the reinfection with a heterologous HCV genotype (adjusted Hazard Ratio [aHR]: 0.45, 95% CI: 0.25-0.84), and ongoing problematic alcohol use (aHR: 0.47, 95% CI: 0.29-0.78) were significantly associated with re-clearance. Among those who cleared their first infection spontaneously, the likelihood of re-clearance was 49% lower (aHR: 0.51, 95% CI: 0.27-0.94) when reinfected with a heterologous HCV genotype.

Conclusions: Alcohol abuse and reinfection with a heterologous HCV genotype are associated with lower HCV re-clearance. Lack of cross-genotype immunity lends support to the literature on prophylactic vaccine development boosted with multiple HCV genotypes.

EPHP2.04

Prevalence and Incidence of Hepatitis C Virus Infection Among HIV-Negative and HIV-Positive Gay and Other Men Who Have Sex With Men in Vancouver

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Background: We sought to identify factors associated with past/current and incident HCV infection within a prospective cohort of gay and other men who have sex with men (MSM) in Vancouver.

Methods: MSM aged ≥16 years were recruited from 02/2012-08/2015 to complete study visits every 6 months, which included self-completed behavioural questionnaires, nurse-administered rapid HIV tests, and venous blood sample collection for HCV-antibody serology. We used logistic regression and generalized estimating equations to identify factors associated with prevalent HCV antibodies at enrolment and incident HCV infection at follow-up, respectively.

Results: Of 774 participants, 2.0% (15/551) of HIV-negative and 28.3% (50/223) of HIV-positive MSM were HCV-positive at enrollment (see Table 1 for associations with prevalent infections). Of these, 56 (86.2%) were aware of their diagnosis, but only 5 (54.6%) of these HIV-negative MSM and 17 (45.9%) of these HIV-positive MSM reported prior HCV treatment (2 and 7 reported treatment success, respectively). Of 534 HCV negative participants with a median follow-up of 1.86 years, we observed 5 incident HCV cases (incidence rate=0.50/100 person-years). All incident HCV infections were among single, HIV-positive, gay-identified MSM. Incident HCV was associated with older age (median 48 versus 24; RR=1.06, 95%CI:1.01-1.12), recent crystal methamphetamine use (60% versus 11.7%; RR=10.62, 95%CI:1.77-63.64), and greater numbers of recent anal sex partners (median 10 versus 2; RR=1.01, 95%CI:1.01-1.02); incident HCV was not associated with recent injection drug use (20% versus 7.2%; RR=3.01, 95%CI:0.35-26.15; p=0.318).

Conclusions: Sexual and substance use factors were associated with HCV serconversion, but injection drug use was not.

Table 1. Multivariable logistic regression of prevalent HCV-antibodies at enrollment separately for HIV-negative and HIV-positive MSM

	HIV-Negative AOR (95%CI)	HIV-Positive AOR (95%CI)
Race/ethnicity		
White	1.00	1.00
Indigenous	**7.76(1.88-31.99)**	2.92 (0.96-8.88)
Other	N/A	0.30 (0.04-2.29)
Sexual identity		
Gay	1.00	1.00
Other	6.51 (1.73-24.52)	**3.74 (1.23-11.40)**
Injection drug use		
No	1.00	1.00
Yes	**6.56 (1.59-27.12)**	**9.94 (3.75-23.78)**
Currently lives in downtown core		
No	Not selected	1.00
Yes		**5.00 (1.16-20.00)**
Any condomless anal sex with an unknown HIV status partner, P6M	Not selected	
No		1.00
Yes		**3.04 (1.20-7.67)**

EPHP2.05

Spatial and temporal trends of HIV and HCV diagnoses in British Columbia

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Background: The co-occurrence of HIV and HCV underscores the need for coordinated prevention and treatment strategies. Such strategies could be informed by detailed analysis of temporal-spatial patterns. We aimed to identify geographic clusters and persistent areas of HIV and HCV infection in British Columbia during the years 1990-2013.

Methods: The British Columbia Hepatitis Testers Cohort (BC-HTC) includes approximately1.5 million individuals tested for HCV or HIV at the BC Public Health Laboratory or reported as a case of HCV, HIV, hepatitis B, or tuberculosis linked to healthcare administrative databases. For geographic analysis, we created annualized diagnosis rate maps of HIV, HCV and HIV/HCV aggregated at the Canada Census Enumeration or Dissemination Area level over five time periods (1990-1993, 1994-1998, 1999-2003, 2004-2008 and 2009-2013).

Results: A higher diagnosis rate of HIV and HCV was persistently found in the Downtown core and downtown eastside (DTES) neighbourhood of Vancouver across all time periods. Geographic diffusion of HIV infection was observed in suburban and rural areas of Greater Vancouver

in recent years (2009-2013). HCV diagnoses peaked during the 1994-1998 time period, and it has since been trending downwards. Spread of HCV infection outside of the Greater Vancouver area to major cities on Vancouver Island, interior and northern regions of BC was noted. HIV-HCV co-infection was persistently clustered in DTES over the entire time period and spread throughout Greater Vancouver with pockets of high diagnoses in Surrey in recent years.

Conclusions: Small area geographic mapping identified distinct 'core' areas of persistent HIV and HCV infection over 24 years in the Greater Vancouver area. Our findings delineate areas where possible infections, risk factors and social disparities converge suggesting a complex interplay of social conditions and disease transmission. Targeted prevention, care and support services are needed to tackle HIV and HCV infections.

EPHP2.06

Characteristics and Clinical Outcomes in Antiretroviral-Treated HIV-HBV Co-Infection

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Objective: Shared routes of transmission make HIV-HBV co-infection common. We describe socio-demographic characteristics of Canadian HIV-HBV co-infected individuals and evaluate factors associated with advanced hepatic fibrosis in this population.

Methods: HIV-HBV co-infected participants were identified from the multi-site Canadian Observational Cohort of individuals who initiated ARV after January 2000. This analysis includes data collected until 31 December 2014. HBV was defined as surface antigen or HBV-DNA positive. Participants with unknown HBV status were excluded. Multinomial logistic regression models were developed to investigate socio-demographic and clinical variables' association on liver fibrosis determined by AST-to-Platelet-Ratio-Index (APRI). Advanced fibrosis was defined as APRI>2.0.

Results: HBV status was known in 7971/10477 (76%) participants. 783 (7%) were HBV co-infected. Compared to HIV mono-infection, co-infected individuals were older at first ARV initiation (mean age 41 vs. 39 yrs, p<0.001), more frequently males (88% vs. 83%, p<0.001), MSM (59% vs. 53%, p=0.004), IDU (21% vs. 18%, p=0.04), and had higher mean APRI scores at baseline (<1 year pre-ARV initiation; 0.47 vs. 0.37, p<0. 001) and end of evaluation (0.31 vs. 0.29, p<0.011). In multivariate analyses, HBV coinfection was independently associated with having advanced fibrosis/cirrhosis prior to and after initiating ARV therapy. HIV-HBV co-infected participants were 2.89 (95% CI: 1.84, 4.54) and 2.53 (95% CI: 1.52, 4.23) times more likely to have APRI>2.0 compared to APRI≤0.5 at baseline and end of evaluation respectively. HIV-HBV individuals did not differ from HIV mono-infected individuals with regards to poverty (p=0.30) and socio-economic status. A single site inadvertently misclassified HBV vaccine antibody response as evidence of HBV infection. Removal of this site did not alter the reported demographic characteristics of our cohort.

Conclusion: The prevalence and demographic characteristics of Canadians with HIV-HBV co-infection is similar to other developed nations. The effect of ARV on fibrosis progression/regression in HIV-HBV is currently being evaluated.

EPHP2.07

Risk Profiles in Mono Infected TB Patients and Those Co-infected with HCV and/or HIV

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Background: Mono-infected TB cases may be different subpopulations with respect to demographic and risk characteristics than are those co-infected with HIV or HCV. Better understanding these subpopulations is the first step in developing targeted prevention strategies.

Methods: We used diagnostic testing, co-infection and risk factor data for cases of active TB diagnosed in BC between 1990-2013 in the BC-Hepatitis Testers Cohort (BCHTC). The BCHTC includes ~1.5 million individuals tested for HCV or HIV, or reported as a case of HCV, HIV, HBV, or TB. Demographic and risk behaviors were compared between: 1) TB mono infected, 2) TB/HIV coinfected, 3) TB/HCV coinfected, and 4) tri-infected (TB/HIV/HCV). Co-infection is defined over the study period, and is not necessarily concurrent in time.

Results: A total of 5927 individuals were identified with TB only, 144 with TB/HIV, 294 with TB/HCV, and 222 with TB/HIV/HCV. TB mono infected cases were primarily foreign-born (FB) (73.5%) with low injection drug use (IDU) (3.2%), problematic alcohol use (10.1%), and mental illness (12.4%). TB/HIV cases were evenly distributed between Canadian born (CB) (47.9%) and FB (47.9%), and showed moderate IDU (22.2%), alcohol use (27.8%), and mental illness (29.2%). In contrast, those with TB/HCV or TB/HIV/HCV infection were primarily CB (74.5% and 88.3%, respectively), and showed high IDU (TB/HCV: 45.2%, TB/HIV/HCV: 86.5%), mental illness (TB/HCV 33.0%, TB/HCV/HIV: 58.1%) and alcohol use (TB/HCV: 59.5%, TB/HIV/HCV: 64.4%). Approximately 20.3% of TB cases belonged to the lowest quintile of the social deprivation index, compared to 45.8% of TB/HIV, 48.6% of TB/HCV, and 60.4% of TB/HIV/HCV.

Conclusions: Results suggest commonality of social disparities, mental illnesses and substance use across those with co-infections, especially in those with HCV. Public health approaches that provide support for these co-morbidities, like harm reduction and mental health interventions, may be particularly beneficial for this subgroup.

EPHP2.08

Z-PROFILE: Real-World Utilization Of The New Combination Elbasvir/Grazoprevir In Adult Patients With Chronic Hepatitis C In Canada

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Background and Purpose: Direct-acting antivirals represent the standard of care for chronic hepatitis C infection. Canada was the first country worldwide to approve elbasvir/grazoprevir (EBR/GZR) for genotypes (GT) 1 and 4, with/without ribavirin, and for GT3 with sofosbuvir. Currently, reimbursement is available through private payers, with public reimbursement anticipated soon. The aim of this study is to describe the profile of hepatitis C patients selected for treatment with EBR/GZR and to analyze the treatment utilization patterns in a Canadian real-world setting.

Methods: A multicenter retrospective chart review of HCV-infected patients treated with EBR/GZR in selected Canadian health care providers. This interim analysis included patients initiating EBR/GZR treatment between January and November 2016.

Results: In this interim analysis, 102 patients from 8 sites were included. The mean age was 52.6 years, 60.8% were male, 78.4% Caucasian and 5.9% Aboriginal. Genotype distribution included patients infected by GT1a (n=58, 56.9%), GT1b (n=18, 17.6%), GT2 (n=1, 1%), GT3 (n=15, 14.7%), GT4 (n=3, 2.9%), and GT6 (n=1, 1.0%). HIV co-infection was reported for 11 (10.8%) patients. Pre-treatment fibrosis evaluation revealed a fibrosis stage of F0-1 (n=60, 58.8%), F2 (n=15, 14.7%), F3 (n=8, 7.8%), F4 (n=18, 17.6%) and 1 missing. Prior HCV treatment was reported for 22 (21.6%) patients. Of these, 21 (95.5%) were previously treated with an IFN-containing regimen. Baseline resistance-associated substitutions (RAS) testing was performed for 13 (12.7%) patients. No NS5A substitutions were identified. 89 patients (87.3%) were prescribed 12 weeks of EBR/GZR and the other 13 patients received 16 weeks of EBR/GZR with RBV. Sofosbuvir was prescribed with EBR/GZR for all 15 patients with GT3.

Conclusion: In this Canadian cohort, the majority of individuals treated had early stage fibrosis and were predominantly infected by GT1 as reflected by the distribution in Canada. A significant proportion of persons were co-infected with HIV.

EPHP2.09

New Insights into Circulating Neisseria gonorrhoeae Sequence Types using Non-Cultured Clinical Specimens in British Columbia

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Background: From 2014 to 2015, there was a 114% and 56% increase in gonorrhea reports in females and males, respectively, in British Columbia (BC). Historically, culture-based *Neisseria gonorrhoeae* multi-antigen sequence type (NG-MAST) surveillance is over-represented by males attending STI clinics. We sought to understand trends in NG-MAST of gonorrhea cases among females in relation to this recent increase.

Methods: From October to December, 2015, the first 30-40 gonorrhea positive nucleic acid amplification test (NAAT) samples each month in BC females were characterized by NG-MAST based on the sequence of the *porB* and *tbpB* genes. Sequence type was determined using the NG-MAST website (www.ng-mast.net) and compared against the prevalent strain types as routinely reported in the National Surveillance of Antimicrobial Susceptibilities of *Neisseria gonorrhoeae* Annual Summary 2014. Descriptive statistics were completed using Microsoft Excel.

Results: Of 112 NAAT samples analysed, 35 were non-typeable. Of the remaining 77 samples, the most common NG-MASTs identified were ST-5985 (32%), ST-7638 (21%) and ST-4637 (10%). For comparison, ST-5985, ST-7638, and ST-4637 comprised of 52%, 0%, and 0.3%, respectively, of prevalent NG-MASTs in 2014. ST-7638 and ST-4637 have rarely been identified in BC cultures in prior years, but have been commonly seen in neighbouring provinces. The vast majority of ST-5985 cultures from BC demonstrated a high level of resistance to tetracycline while cultures of ST-7638 and ST-4637 have been virtually all susceptible.

Conclusion: A substantial number of gonorrhea diagnoses were identified as NG-MASTs not previously known to be circulating in BC. Whether this represents strain replacement (which may in turn contribute to increases in incidence) or is due to undersampling of females in prior years requires further study. Ongoing strain typing surveillance of both sexes, now feasible with NAAT-based NG-MAST, will help improve our understanding of the changing epidemiology of *N gonorrhoeae*.

Evaluations of Public Health Programs and Interventions

Évaluation des programmes et des interventions en santé publique

EPHP3.01

HIV and Rehabilitation: Evaluation of a community-based initiative and looking to future directions

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A 2014 survey of rehabilitation professionals found that less than one-third felt they had the skills and knowledge to treat people living with HIV (PLWHIV) (Worthington, 2014). However, as HIV is now considered a chronic health condition and more than 30% of PLWHIV are also living with at least one other physical condition, there is a need for rehabilitation for PLWHIV (Kendall, 2014). In Canada there is only one community-based HIV organization that provides occupational therapy with another slated to begin offering physiotherapy and occupational therapy in 2017. This further exaggerates the gap in knowledge of rehabilitation for PLWHIV and actual services available, and the need for rehabilitation.

Realize has been working with university-based rehabilitation programs and community-based HIV organizations across Canada to try and increase knowledge, perceived efficacy, and practice to encourage rehabilitation professionals to work with PLWHIV. Over 30 students have participated in role-emerging practicums at HIV organizations across Canada. While occupational therapy students have been placed most often, we recently facilitated a physiotherapy placement for two students and are exploring options for other rehabilitation disciplines.

Evaluation results show that HIV organizations reported increased knowledge about the role of rehabilitation and increased capacity to serve their clientele as a result of participating. Additionally, over 85% of students surveyed in 2015 reported an increase in knowledge related to their profession and HIV, and would recommend this placement opportunity to other students.

By facilitating rehabilitation practicums at community-based HIV organizations, we are educating future health professionals about the important role they play in the lives of people living with HIV, and increasing the awareness of the role of rehabilitation in the lives of PLWHIV among community-based organizations and health professionals. Future directions for this project include more physiotherapy placements and exploring opportunities to involve students studying in other health disciplines.

EPHP3.02

Perspectives of People Living with HIV on Access to Healthcare: Scoping Review of Canadian Literature

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Introduction: Despite attempts to improve access to healthcare for people living with HIV (PLHIV), gaps in the current system persist. Previous work has focused on the perspectives of healthcare workers and policy makers in the hopes of identifying opportunities for improvement. Instead, this project focuses on the perspectives of Canadian patients and their perceived access to care.

Objective: To analyze themes within the Canadian literature with respect to the perspectives of PLHIV on their access to healthcare.

Methods: We performed a scoping review of peer-reviewed and grey Canadian literature. Two independent researchers reviewed each article and extracted, collated, summarized and thematically analyzed all relevant data. Themes were developed based on their recurrence throughout the literature.

Results: Among the 64 articles eligible and reviewed, four were Canadian studies. Ten initial themes (Acceptability, Accessibility, Accommodation, Affordability, Availability, Other barriers, Communication, Satisfaction, Preferences, and Equity in access) were identified. These were then classified into more specific emerging and final themes. Acceptability and Availability were discussed in all four Canadian studies; whereas, Accessibility, Affordability and Other Barriers were discussed in 3 of the studies, Accommodation in 2 studies and Communication, Satisfaction, Preference and Equity in Access in only 1 study. Five final themes were discussed most frequently in the Canadian literature: Fear of rejection and isolation, Lack of trust regarding confidentiality, Unqualified or not enough HIV training in healthcare workers, Long wait times and Feelings of stigma/discrimination.

Conclusion: Themes arising from the Canadian literature are similar to the broader literature. A focus on Canadian perspectives is critical to ensuring that the needs of Canadians are addressed appropriately. This scoping review will assist with the development of patient-oriented healthcare programs for PLHIV in Canada.

EPHP3.03

The Sex You Want: Preliminary Outcomes of an Online Gay Men's Health Promotion Campaign

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Background: In January 2017 the Gay Men's Sexual Health Alliance launched Ontario's most comprehensive online sexual health promotion campaign for cis and transgender gay, bisexual and other men who have sex with men. The Sex You Want campaign (www.thesexyouwant.ca) was developed in response to the increasing relevance of new HIV prevention technologies in the lives of men who have sex with men and to support a provincial network of AIDS service organizations in communicating complex biomedical information.

Methods: An evaluation framework for The Sex You Want was developed with support from the Ontario HIV Treatment Network. Its purpose was to determine the extent to which: (1) the promotional campaign increased use and awareness of the website amongst men who have sex with men (2) the Sex You Want website met the needs of its users (3) men who have sex with men took action after visiting the website; and (4) the provincial alliance of AIDS service organizations were meaningfully engaged in the development of the campaign.

Results: We present preliminary evaluation data that highlights the effectiveness of the approaches used to promote the campaign and use of the website focusing on the sexual health strategies featured (condoms, pre-exposure prophylaxis, post-exposure prophylaxis and treatment as prevention). Additional website analytics on number of visitors, regional uptake, page visits and shares will also be presented. Finally, an analysis of key themes that emerged from visitor feedback on the website's content and users' experiences will also be discussed. This evaluation will help inform website updates and the development of future campaigns by Ontario's funded Priority-Population Networks.

EPHP3.04

An Innovative Intensive HIV Preceptorship Training Program For Family Physicians And Its Impact On Patient Outcomes

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Background: HIV-positive patients' health outcomes are related to the level of training and expertise of their providers. We evaluated HIV-related outcomes of patients under the care of British Columbia's family physicians who underwent an intensive HIV training program at the BC Centre for Excellence in HIV (BC-CfE).

Methods: We compared the physicians' ART prescriptions and refills, adherence to HIV provincial clinical guidelines, and HIV-related outcomes of patients before and after training. Data was obtained from the Drug Treatment Program's database at the BC-CfE. Statistical analysis was performed using the Wilcoxon Signed-Rank test. Results :From September 2011 to June 2015, 48 family physicians from across BC participated in the preceptorship training program. Their ART prescribing patterns, HIV-related diagnostic test requests, and HIV-related health outcomes of their HIV-positive patients (n=552) were compared 12 months before and 12 months after training. Overall, there was an increase in most parameters:

Conclusion: We showed a significant change in ART prescribing behaviours, adherence to clinical guidelines, and patient outcomes in a limited number of family physicians who completed the Intensive HIV Preceptorship Program at the BC-CfE. This initiative complements the provincial Treatment as Prevention strategy by increasing the number of medical professionals who are trained in HIV treatment and care.

Outcomes (per physician)	Before training (12 mo.) Median	Q1-Q3	After training (12 mo.) Median	Q1-Q3	p-value
# of HIV+ patients	2.5	1.0-10.5	9.0	3.0-18.5	<0.001
# of ART prescription refills	4.0	0.0-19.0	14.0	1.5-35.5	0.004
# of ART prescription initiation/change	0.0	0.0-1.0	0.0	0.0-2.5	0.005
# of viral load test requests	9.0	1.5-28.0	30.5	7.0-65.5	<0.001
Patients' CD4+ cell count at ART initiation (cells/mm3)	248	220-300	390	265-550	0.004
% of patients with viral suppression within 6 months of ART initiation	21	11-28	50	20-60	0.002

EPHP3.05

Reducing Harms for People Who Use Drugs in Atlantic Canada: The Need for Enhanced Harm Reduction and Innovative HIV/STBBI Testing Services

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Background: In contrast to most other regions, Atlantic Canada's harm reduction landscape is very conservative. There is relatively limited access to needle and syringe programs, low threshold methadone maintenance treatment, and opioid substitution therapy. Further, there are no supervised consumption sites, community detox centres, or access to innovative testing technologies, such as rapid

point-of-care testing. Working within this constrained environment, Mainline Needle Exchange has been at the forefront of Atlantic Canada's harm reduction efforts for 25 years. This paper synthesizes the results of the organization's evaluation within the broader context of efforts to reduce harms for people who use drugs (PWUD) in the Atlantic region.

Qualitative and quantitative data was collected from three main sources: (1) Key epidemiological, program and policy documentation providing the federal/provincial/regional context; (2) Mainline's de-identified electronic record system tracking service use, including trends over time; and (3) Key informant interviews with staff, clients and partners.

Results: Reducing barriers to harm reduction and HIV/STBBI testing services has long been a priority among researchers and community-based organizations in the Atlantic Region. Mainline's impact on the health and wellness of PWUD is far-reaching and life-saving. Benefits to the broader community are also evident in terms of increased levels of health and safety, as well as increased knowledge, advocacy and community mobilization. The most notable challenges were related to broader systemic barriers, and the results provide useful information for moving toward equitable access to health promotion and disease prevention, within an integrated harm reduction/population health approach.

Conclusions: The demand and need for effective harm reduction services has increased markedly over the years, and continues to increase. A more comprehensive, evidence-based package of harm reduction initiatives is needed to promote the health, safety and well-being of people who use drugs in Atlantic Canada.

EPHP3.06

Program Evaluation Practices of Online-Based Sexual Health Promotion Outreach to Gay and Bisexual Men in Ontario

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Background: Research on program evaluation of online sexual health outreach services is scarce, due to the fact that such programs and services are relatively new. The main goals of this analysis were to examine evaluation practices and parameters for online outreach work used across agencies serving gay, bisexual, 2-spirit, and other men who have sex with men (MSM) in Ontario.

Methods: From 10/2013 to 04/2014, online outreach service providers and managers from public health agencies and ASOs were recruited to complete a 1-hour in-person/telephone interview to explore in-depth their experiences with, and perspectives on, the delivery of and effectiveness evaluation methods used for online outreach services for MSM. Thematic analysis was conducted using NVivo10.

Results: Participants (*n*=22) commented on the various systems and plans they used to evaluate this service at their agency. Although participants reported that no official evaluations of the effectiveness of online sexual health outreach services had been conducted by their agencies, most participants reported the existence of other evaluation tools, which included counts of contacts made during various times of days, descriptive details of these contacts, and/or the number of referrals. Participants also provided important insights into the unique challenges associated with evaluating online sexual health outreach services for MSM.

Conclusions: Our findings offer the first nuanced understanding of the challenges associated with program evaluation of online sexual health outreach services for MSM. These results suggest that without evaluating the effectiveness of online outreach services, many agencies may be missing a growing opportunity to improve their services in order to effectively engage MSM in the prevention of STI and HIV transmissions. These findings can assist ASOs, public health agencies, and healthcare providers in meeting the needs of online outreach workers as they implement and improve evaluations of service delivery.

EPHP3.07

Short-term Impact of a Blended Learning Intervention to Increase Provider Capacity to Support Older Adults Living with or Vulnerable to HIV

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Older adults, including people with HIV, favour 'aging in place.' For many, residing at home requires access to formal supports like those provided by home care agencies, seniors' services, and chronic disease organizations, with HIV services rounding out the community-based circle of care for people aging with HIV. However, among 232 service providers from diverse settings and sectors who responded to an online needs assessment, the majority reported little training and low to moderate levels of knowledge related to HIV and aging, as well as limited experience caring for older people living with or vulnerable to HIV. A blended learning intervention designed to increase service provider capacity to support the HIV-related needs of older adults, was developed, pilot tested with 90 service providers across Canada, and evaluated using both process and outcome measures. The intervention included four web-based self-study modules and one group-based, interactive workshop. Using a pre/post survey design, self-reported knowledge of: 1) risk factors for HIV among older adults; and 2) the needs and experiences of older adults living with HIV; both increased among participants. Ageist beliefs did not change as a result of the intervention, but HIV-stigma scores decreased. Upon

completion of the intervention, participants self-reported: 1) greater comfort working with older adults living with HIV; 2) increased confidence talking to older adults about their sexual health; and 3) improved ability to identify a resource on HIV and aging. Learners described the course content as trustworthy and engaging, and valued the flexibility of self-study.

This blended learning intervention shows promise as a tool for increasing service provider capacity, and thus improving access to support for older adults living with or vulnerable to HIV. A higher pre/post survey response rate and longer-term follow-up are needed to verify the significance of the findings and the sustainability of intervention impacts.

EPHP3.08

What Gay and Bisexual Men who 'Party-n-Play' Want from Health and Social Care in Toronto?

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Background: The goals of this qualitative study were: 1) to inform the development of health and social care programs, services, and tailored interventions that meet the needs of MSM who Party-n-Play (PNP); 2) examine how MSM who PNP interact with health and social care providers.

Methods: In-depth 1 hour interviews were conducted with 44 substance-using MSM (ages 19-58) in Toronto between October and November 2016. PNP-involved men were asked about their interactions with staff at sexual health clinics, ASOs and other health agencies. They were also asked to comment about these interactions, the care they received and suggestions on the best type of health and social care related to their drug use and sexual health that you they could imagine in Toronto. Interviews were recorded, transcribed verbatim and thematic analysis was used to (a) characterize MSM's interest in health and social services, treatment programs for physical, mental, or sexual health, including HIV prevention, treatment and care services, (b) elicit feedback regarding optimal care formats, and c) identify barriers to accessing healthcare for this population.

Results: MSM expressed an interest in health promotion efforts tailored for them and various other types of support services. MSM who PNP identified key barriers to care: health and social care service fragmentation in Ontario, the judgment and lack of competencies within hospital environments, as well as stigma related to drug use, serostatus disclosure (if HIV-positive) and sexual practices.

Conclusions: The findings highlight important considerations for the development of appealing, effective, and culturally competent health and social care services tailored to the needs of substance-using MSM. Health and social care practitioners, HIV program staff and managers, as well as funders can use these findings to make active decisions about how to improve the health and social care system for substance-using MSM.

EPHP3.09

Canadian Health Professionals' Knowledge and Clinical Practices Related to HIV Screening and Testing

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Background: The Public Health Agency of Canada (PHAC) provides guidance to healthcare providers regarding who, when, and how often to screen for HIV.

Objectives: The objective of this study is to determine the level of healthcare provider knowledge related to HIV and whether their practices are consistent with PHAC's HIV guidance, in order to identify areas for capacity building and knowledge translation.

Methods: Data was collected from a convenience sample of healthcare professionals as part of an open, anonymous online national survey aiming to assess the impact of PHAC guidance on professional practice. The survey was pilot tested with infectious disease experts prior to dissemination through professional associations, listservs and government agencies.

Results: In total, 1075 participants from across Canada responded to the survey, with the majority being nurses and physicians. Knowledge of certain aspects related to HIV screening and testing was good, but some knowledge gaps were evident. Approximately 53% of respondents reported offering HIV testing regularly and 65% offer HIV tests as part of routine care to at least 50% of their patients. Very few reported not having enough time for pre- and post-test counselling and the majority regularly provides important information during counselling. A number of providers are not regularly screening patients as part of routine care, nor using point-of-care testing.

Conclusions: These preliminary results point to some potential areas for capacity building and knowledge translation with respect to HIV testing. This study also provides a baseline for future assessments of PHAC products, and provides key input for the development of future knowledge translation activities based on existing levels of knowledge and practice. Given that undiagnosed HIV cases contribute significantly to HIV incidence, such information is valuable in order to control the transmission of HIV in Canada.

EPHP3.10

Impact of Health Care Utilization on Survival Rates in a Hospital-Based Outpatient HIV Clinic

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Introduction: Retention in care is associated with positive health outcomes for HIV-infected individuals. We examine the impact of care utilization in a comprehensive, interdisciplinary HIV clinic on survival from AIDS- and non-AIDS-related mortality.

Methods: Medical history, clinical laboratory and mortality data were collected for subjects age ≥ 19 years old enrolled between 01-Jan-2004 and 31-Dec-2015 in a specialized HIV clinic located at St. Paul's hospital, an acute care, teaching and research hospital located in downtown Vancouver, British Columbia. Patients were classified as active (i.e. utilizing care) if they had at least 2 visits, more than 60 days apart, at any point during the study period. Cox proportional hazard ratios (HRs) were used to determine the risk of AIDS- and non-AIDS-related mortality.

Results: Of 2244 HIV-positive patients enrolled in the clinic, 1947(87%) were classified as active and 297 (13%) as inactive. Inactive patients had higher rates of AIDS-related mortality than active patients (26.19 vs. 4.28 per 1000 person-years [PY]; p<0.001), as well as of non-AIDS-related mortality (40.74 vs. 13.49 per 1000 PY; p<0.001).After adjusting for age at time of first visit, baseline CD4 count and plasma viral load and whether patients had been on antiretroviral therapy at any point during the study period, inactive patients had a higher risk of AIDS-related mortality compared to active patients (HR, 4.24; 95% confidence interval [CI], 2.50-7.19). Inactive patients also had a higher risk of non-AIDS-related mortality compared to active patients (HR, 2.95; 95% CI, 2.09-4.16) when adjusting for age at first visit and baseline CD4 count.

Conclusion: We observed increased survival rates from AIDS- and non-AIDS-related mortality for a cohort of patients utilizing care in a comprehensive interdisciplinary HIV clinic. These findings suggest that comprehensive HIV care interventions are important for sustaining patient engagement in care and treatment leading to improved health outcomes.

HIV prevention for key populations

La prévention du VIH dans les populations clés

EPHP4.01

HIV-associated vulnerabilities at first sex among adolescent and young women in Mombasa, Kenya: a cross-sectional study

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Background: Young women in Sub-Saharan Africa experience high rates of HIV following sexual debut. However, HIV-associated vulnerabilities at first sex are not well understood. We sought to explore the prevalence of these vulnerabilities among young women in Mombasa, Kenya, and examine the context of first sex in association with current sexual partnerships.

Methods: We conducted a cross-sectional survey in 2015 of 1,299 women aged 14-24 years who frequented venues traditionally associated with sex work solicitation. We examined the association between biological, behavioural and structural vulnerabilities at first sex and current engagement in self reported sex work (FSW); transactional sex (TS); or casual sex (CS). TS was defined as sex when there was an expectation of money/goods in return but the price was not negotiated upfront.

Results: The mean age of first sex was 16 years. 10.6% of women had a first sex partner who was >10 years older. 41.3% of women felt coerced into their first sex and 12.5% of first sex was forced. 45.9% of 548 women who experienced a coerced or forced first sex now identify as FSW (p<0.001). All first sex was condomless and 39.7% included anal sex, of these 60.6% of women went on to engage in casual sex partnerships (p<0.001). 566 women (43.6%) reported the exchange of money or gifts at first sex, of whom 32.5% went on to sex work and 18.4% TS (p<0.001).

Discussion: A vulnerable first sex event was common among young women irrespective of trajectories across a spectrum of current sexual partnerships. This suggests that HIV prevention programs need to reach women early in their sexual lifecourse.

EPHP4.02

The CMIS Cohort (1988-2015): progress in the prevention of mother to child transmission in a resource-rich setting

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Background: The principal barriers to the prevention of mother-child transmission of HIV (PMTCT) are availability of combination antiretroviral therapy (cART) for women and health infrastructure challenges in resource-limited settings. We report our experience of >20 years of PMTCT in a resource-rich setting to describe some of the remaining barriers to effective PMTCT.

Methods: The Centre Maternel et Infantile sur le SIDA (CMIS) cohort was established in 1988 to prospectively follow HIV-infected pregnant women, their newborns, and all new HIV diagnoses in children. CMIS, based at CHU Sainte-Justine, is a multidisciplinary team that includes obstetricians-gynaecologists, paediatricians, immunologists, pharmacists, nurses and social workers.

Results: Among 977 pregnancies followed at CMIS, the perinatal transmission rate decreased from 29.4% (1988-1990, pre-treatment era) to 7.7% (1990-1993, AZT only during pregnancy), to 3.3% (1994-1997, AZT three phases as per PACTG-076 protocol), to 0.76% (1998-2015, triple cART and neonatal prophylaxis). Of the 5 perinatal transmission cases that occurred between 1998 and 2015, 2 were related to maternal refusal of treatment, and 2 to late seroconversions in pregnancy. One case of transmission occurred despite PMTCT measures (delayed initiation of cART at 29 weeks, but >8 weeks of cART prior to delivery, detectable viral load until 20 days before delivery, neonatal cART).

Conclusion: Since cART became available for mothers and infants under a well-structured multidisciplinary setting, the risk of mother-to-child HIV transmission has been 0.76% at our centre, with no cases transmission in the past 10 years. These results reinforce the notion that adherence to treatment is the overwhelming challenge and determinant of success in perinatal HIV care in resource-rich settings.

EPHP4.03

Online Health Information-Seeking Behaviours of East and South-East Asian MSM

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Background: There is a lack of knowledge regarding the health information needs of racialized gay, bisexual, and other men who have sex with men (MSM). We sought to describe sexual health information accessed online by East and South-East (E/SE) Asian MSM.

Methods: MSM in Ontario (aged >15 years) were recruited via Internet sites, mobile apps and community-based organizations to complete an anonymous online survey from 12/2013 to 1/2014. Chi-square analyses and eight multivariable logistic regression analyses (outcomes: various health information topics sought online) explored the differences among E/SE Asian MSM compared with all other self-identified ethnicities ('Other'). Regression models controlled for HIV status, age, geographic location, education, and sexual orientation.

Results: Of 1830 participants, 122 (6.7%) self-identified as E/SE Asian. Compared with 'other' ethnicities, E/SE Asian MSM reported no difference in HIV status (p=0.26), were younger (p<0.001), more highly educated (p<0.001), more likely to identify as gay (p=0.03), more likely to live in Toronto (p<0.001), more likely to have used condoms during their last sexual encounter (74%-vs-60%, x^2:p=0.004) and more likely to look up sexual health information online whenever they experienced symptoms/concerns about STIs (39%-vs-28%, x^2:p=0.03). E/SE Asian MSM were more likely to look up information online regarding HIV/STI prevention, dating and relationships, and connecting with other gay men (Table).

Unadjusted and adjusted association between looking online for health information (outcomes) and ethnicity (E/SE Asian versus 'Other')

Outcomes: Looked online for... (yes/no)	OR (95% CI)	Adjusted OR* (95% CI)
Signs and symptoms of STIs	1.43 (0.98-2.08)	0.87 (0.58-1.30)
HIV and STI testing services	2.02 (1.39-2.92)	1.17 (0.78-1.75)
HIV and STI prevention	2.17(1.48-3.17)	1.16 (1.12-2.64)
HIV and STI treatment and care	1.91(1.25-2.94)	1.52 (0.96-2.42)
How to use condoms	1.21 (0.54-2.67)	1.26 (0.54-2.91
Dating and Relationships	2.85 (1.96-4.15)	2.43 (1.61-3.66)
Coming out / sexual identity	1.91 (1.16-3.13)	1.56 (0.92-2.67)
How to connect with other gay men in my community	1.61 (1.06-2.45)	1.71 (1.09-2.68)

OR: odds ratio; 95% CI: 95% confidence interval; STI: sexually transmitted infection
*Adjusted for HIV status, age, geographic location, education, and sexual orientation.

Conclusion: E/SE Asian MSM were more likely to report condom use, but also an interest in HIV prevention information, even after controlling for demographic differences; this indicates a need for accessible online resources competent to the experiences of this community.

EPHP4.04

HIV-negative partners in serodiscordant relationships: A missing link in the HIV cascade of care?

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Background. An estimated 23% of the 71,000 people living with HIV in Canada are in serodiscordant relationships. Yet little is known regarding the clinical and social challenges faced by these couples.

Objective: HIV-negative partners in serodiscordant relationships may have two distinct roles to play in the cascade of care: 1) HIV prevention (testing and use of PrEP), and 2) engagement in partners' treatment and health. This paper examines the role of the HIV-negative partner along the continuum of the cascade of care.

Methods: *Positive Plus One* is an ongoing national survey of serodiscordant couples recruited from clinics/ASOs/NGOs across Canada. We have conducted preliminary (descriptive and multivariate logistic regression) analyses using the first 310 quantitative survey participants.

Results: Among HIV-negative partners (n=128), 72% disclosed their serodiscordant relationship to a physician, 70% had HIV-tested in the past year, and 11% had used PrEP during their relationship. Controlling for sociodemographic characteristics, those with a physician who was aware of their serodiscordant relationship had greater odds of testing within the past year, compared to those whose physician was unaware (OR: 4.99, 95%CI=1.7-14.66). Of those who had not used PrEP, 60% would consider using it. Among HIV-positive partners (n=182), 92% currently used ART; of whom, 74% reported at least 95% adherence over the past month. Adherence increased with partnership duration per year (OR: 2.44, 95%CI=1.13-5.29) and with the HIV-positive partner's report of better relationship quality (OR: 1.51, 95%CI=1.04-2.19).

Discussion: Open discussions with health providers appear to have a positive impact on testing behaviours and possibly the uptake of PrEP, thereby strengthening prevention and care outcomes. Longer and stronger relationships may have positive effects on adherence to treatment for the HIV-positive partner, thereby strengthening treatment outcomes. These findings encourage more active engagement of HIV-negative partners at two important ends of HIV care cascade.

EPHP4.05

Scaling Up Supervised Consumption Services in Canada: Navigating a New Legal Environment

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There is an urgent need to expand supervised consumption services (SCS) to communities where drug use is prevalent in order to reduce overdose deaths and behaviours that lead to HIV and HCV transmission, and to increase safety. Yet, in Canada, despite a dramatic rise in overdose deaths, unjustifiable barriers to launching and operating SCS remain.

The introduction in December 2016 of Bill C-37 signals an important shift in Canada's drug policy, emphasizing evidence, public health and human rights above fear, stigma and misinformation. The government has chosen to repeal the 26 onerous conditions for obtaining federal ministerial exemptions enabling new SCS to operate without risk of criminal prosecution for drug offences – conditions that are currently imposed by the the *Respect for Communities Act* enacted in 2015 in the previous Parliament. While the many provisions of Bill C-37 (including those having nothing to do with SCS) are studied and debated in Parliament, some health services providers are contemplating how to move forward without delay in implementing these essential services.

This presentation will examine the evolving legal reality that has emerged in Canada following the government's announcement that it would introduce a series of legislative changes that will speed up the process for opening SCS. It will examine how, while these developments may remove unnecessary requirements from legislation, it is critical to ensure that Health Canada not continue to apply them in departmental policy or practice when reviewing SCS applications. CAHR 2017 offers a timely opportunity to convene service-providers, researchers, community members, health policy makers and advocates to discuss the future of SCS, with a view to scaling up this key health intervention for people who use drugs.

EPHP4.06

Incomplete diffusion of "Treatment as Prevention" in key groups highlights the need for more inclusive health promotion

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Background: Despite the clinical efficacy of Treatment as Prevention (TasP), HIV incidence remains elevated among gay and bisexual men (GBM). We evaluated the diffusion of TasP awareness, attitudes, and behaviours within this population.

Methods: We recruited sexually active GBM, aged ≥16 years, between 2012-2015 using respondent-driven sampling. At six-month intervals, participants completed a computer-administered questionnaire and nursing visit. Repeated measures latent class analysis (RMLCA), stratified by self-reported serostatus, identified patterns of TasP endorsement by considering one item assessing TasP awareness, four items assessing attitudes towards viral load undetectability, and one item assessing viral-load sorting. Univariate interaction with visit number identified factors associated with longitudinal changes in class membership.

Results: Across a maximum of 7 visits, 556 HIV-negative/unknown men provided 1,845 observations and 218 HIV-positive men provided 745 observations. Representing a continuum of increasing TasP endorsement, RMLCA identified three classes: "Unaware," "Skeptical," and "Believing." Among HIV-negative/unknown men, 64.2% were "Unaware" and only 6.1% were "Believing." Comparatively, 29.2% of HIV-positive men were "Unaware" and 47.7% were "Believing."Over time, class membership was stable among HIV-positive men, but shifted towards greater TasP endorsement among HIV-negative/unknown men ($p < .001$). Among HIV-positive men, increasing TasP endorsement were predicted by starting treatment in the past year (OR=1.45, 95%CI:[1.09,1.94]), being white (vs. Asian/other, OR=0.72, 95%CI:[0.57,0.90]), being older (OR=2.13, 95%CI:[1.13,3.99]), being partnered (OR=1.14, 95%CI:[1.03,1.26]), and always using condoms (OR=1.24, 95%CI:[1.09,1.40]). For HIV-negative/unknown men, the same was predicted by greater education (OR=1.16, 95%CI:[1.01,1.34]), being employed (OR=1.13, 95%CI:[1.01,1.26]), and being partnered (OR=1.14, 95%CI:[1.03,1.26]). Conversely, TasP endorsement was hindered among HIV-negative/unknown men reporting recent STI diagnoses (OR=0.67, 95%CI:[0.50,0.89]) and serodiscordant/unknown CAS (OR=0.86, 95%CI:[0.76,0.98]); and, among HIV-positive men reporting substance use (e.g., poppers, OR=0.86, 95%CI:[0.76,0.97]).

Conclusion: Hindered TasP endorsement among HIV-negative men, those engaging in high risk sex, substance users, and other marginalized GBM highlights the need for inclusive TasP promotion.

EPHP4.07

The Cedar Project: Understanding the lifetime vulnerabilities associated with syphilis positivity among Indigenous women who use drugs and live in Vancouver, BC

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Introduction: Outbreak investigation and national surveillance data demonstrate that Indigenous people are disproportionately at risk of contracting STIs. Ulcerative STIs, such as syphilis, increase susceptibility to HIV acquisition. Despite recent surges in syphilis infections in Western Canada, there is a dearth of information pertaining to vulnerability to syphilis among Indigenous communities.

Methods: The Cedar Project is an Indigenous led initiative addressing the health of Indigenous young people who use drugs in British Columbia. During routine follow-up HIV and Hepatitis C testing, we sought informed consent from participants to collect additional samples to test for syphilis antibodies. Point estimates of syphilis seroprevalence and 95% confidence intervals were established, and bivariate analyses explored differences in demographic characteristics, drug use patterns, and sexual vulnerabilities among individuals who tested seropositive. As 95% of seropositive individuals were women living in Vancouver, statistical analyses were restricted by gender (women) and location (Vancouver).

Results: A history of syphilis was found among 21 of the 250 participants who were tested (8% [5%-11%]). A history of syphilis was significantly associated with having a mother who attended residential school (69% vs. 36%; p=0.05), experiencing violence in the past six months (43% vs. 4%; p<0.01), experiencing recent sexual abuse (14% vs. 0%; p=0.04), binging on non-injection drugs in the past six months (82% vs. 31%; <0.01), smoking crack in the past six months (100% vs. 80%, p=0.05), smoking heroin in the past six months (46% vs. 10%; p=0.03), injecting drugs in the past six months (75% vs. 18%; p<0.01) and being in a methadone treatment program (100% vs. 53%; p<0.01).

Conclusion: Sexual health programming that is culturally safe, trauma-informed and gender specific must be coupled with harm reduction programs to intervene in the pathways of risk factors for STIs that reduce quality of life and increase risk for contracting HIV.

EPHP4.08

Trauma-informed care: addressing the risks of HIV in a Domestic Violence Service

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No matter the primary mission of an organization delivering primary care, the organization needs to be committed to providing services that are welcoming and appropriate to the complexities of individuals affected by trauma (Harris & Fallot, 2001). A trauma-informed service must recognize the impact of not only current trauma an individual has endured, but also previous trauma and violence (Motivational Interviewing and Intimate Partner Violence Workgroup, 2010). Women living with HIV experience intimate partner violence at a rate of 55.3%, more than five times the national average, 68% reported a history of sexual assault, 66% reported a history of childhood physical, or sexual abuse, and 25% reported a history of abuse by a partner as an adult (Brezing, Ferrara, & Freudenreich, 2015).

How do trauma-informed systems take into account both HIV and violence? This presentation will describe an ongoing project with The AIDS Committee of York Region and the York Region Centre for Community Safety (YRCCS), a wrap-around service encompassing over 30 partner agencies. This project aims to ensure YRCCS is providing trauma-competent care, by doing an organizational self-assessment with all trauma related questions pertaining to a client's experience at YRCCS, the intake questions asked at YRCCS and the service that are provided. These questions specifically looked at previous trauma including: domestic violence, sexual assault and sexual health. This presentation will draw on best practices in developing trauma-competent approaches to care, and will specifically examine the relationship between previous trauma and HIV risk to improve the sexual health outcomes of women. The agencies will emphasise a community-based process and develop training modules for both community members and service-users of YRCCS. This presentation will offer the opportunity for reflection regarding needs when working with traumatized individuals at heightened risk of contracting HIV.

EPHP4.09

Structural factors increase inconsistent condom use by sex workers' one-time and regular clients in Northern Uganda

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Background: While sex workers (SWs) in Uganda bear the brunt of the HIV epidemic, research on the structural drivers of HIV prevention among SWs, including client condom use remains scant. This study examined the individual, interpersonal and structural correlates of inconsistent condom use by SWs' one-time and regular clients.

Methods: Data were drawn from the Gulu Sexual Health Study, a cross-sectional study of young (14+ years) women SWs, conducted in partnership with The AIDS Support Organization (TASO). Bivariate and multivariable logistic regression were used to examine the correlates of inconsistent condom use by one-time and regular clients.

Results: Of the total 400 SWs, 84.5% reported inconsistent condom use by regular clients and 76.8% reported inconsistent condom use by one-time clients in the 6 months. In multivariable analysis, physical/sexual violence by clients (AOR=5.39; 95%CI 3.05-9.49), low sexual relationship power (AOR=2.86; 95%CI 1.47-5.58), alcohol/drug use while working (AOR=1.98; 95%CI 1.17-3.35) and migration to Gulu for sex work (AOR=1.73; 95%CI 0.95-3.14) were positively correlated with inconsistent condom use by one-time clients. Correlates of inconsistent condom use by regular clients included:low sexual relationship power (AOR= 4.63; 95%CI 2.32-9.23), physical/sexual violence by clients (AOR=3.48; 95%CI 1.85-6.53), police harassment (AOR=2.57; 95%CI 1.17-5.65) and being a single mother (AOR=2.07; 95%CI 1.09-3.93).

Conclusions: Structural factors, including gender-based violence, poverty, migration and police harassment contribute to the low rates of client condom use with SWs in Gulu, Uganda. These results underscore the need for peer-led structural interventions that promote SW organization/collectivization as a conduit to improving access to occupational health and safety standards (e.g., venue-based violence prevention and alcohol/drug harm reduction programs/policies, HIV prevention services and supplies). Policy shifts away from the current punitive approaches towards SWs is integral to the success of such interventions, as they fuel stigma and violence towards SWs and undermine HIV prevention efforts.

EPHP4.10

HIV prevalence and incidence among men who have sex with men (MSM) in Benin, West Africa

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Background: Like in most countries of the sub-region, homosexuality is highly stigmatized in Benin. Most MSM are obliged to hide and practice their homosexuality clan-

destinely. We carried out an HIV prevalence study among MSM in Benin in 2012, followed by a prospective study of HIV incidence about those identified as HIV-negative at baseline.

Methods: 291 MSM were enrolled in the study using a respondent-driven sampling method. Eligible MSM were 18 years old and above, reporting having had at least one oral or anal sex with another man in the past 12 months. Those found to be HIV negative were enrolled in a prospective cohort study with 3 follow-up visits every six months.

Results: Among the subjects enrolled, 39% reported bing homosexual and 61% bisexual. 58% had preference for insertive sex, 29% for receptive sex and 13% had no preference. 34% of MSM reported using condoms systematically during anal sex. 27.6% informed their circle about their sexual orientation. 17% reported having been victims of a physical and/or verbal aggression because of their status. 92% knew at least (03) modes of HIV transmission and 87% had an exact knowledge of the means of HIV prevention, 71% rejected misconceptions about HIV. HIV prevalence among MSM was 12%. The prevalence ratios for homosexual vs. bisexual orientation and for being aged 25+ vs younger were 7.0 (p < 0,031) and 2.5 (p < 0,050), respectively In 196.1 person-years of follow-up, there were 11 seroconversions for an incidence rate of 5.6 per 100 person-years (95% Confidence interval: 3.2-10.0).

Conclusions: Despite high levels of knowledge about HIV infection, MSM in Benin have not largely adopted safe sex practices so far. Comprehensive combination programs, including access to pre-exposure prophylaxis, should be quickly implemented to reverse the tide of the HIV epidemic among MSM in Benin.

EPHP4.11

Voluntary HIV testing among gay and bisexual men who have experienced childhood maltreatment

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Background: Childhood maltreatment is a known factor for HIV risk behaviors: condomless anal sex with a sero-discordant (HIV-positive/HIV-unknown) casual male partner (SDCAS) among gay and bisexual men (GBM). Routine HIV testing remains the sole method to detect HIV infection early and initiate treatment. We explored the association between childhood maltreatment and voluntary (not work/immigration mandated) HIV testing in a sample of HIV-negative Toronto GBM.

Method: Three time points (baseline, 3-month and 6-month) data (n=470) were used. Latent class analysis was used to identify classes of childhood victimization from five types of maltreatment –emotional abuse, emotional neglect, physical abuse, physical neglect and sexual abuse. Treating number of HIV tests in the past 9 months as count, we fit a Poisson regression model with the identified classes as the independent variable adjusting for personal (age, race/ethnicity, relationship status), psychosocial (depression, openness) and enabling (income, social support) factors.

Results: Most participants (mean age =35±12yrs) were white (59%) and gay-identified (86%). Fit indices suggested a four class solution. Around 65% of the GBM classified in no/minimal maltreatment subclass, 17% in emotional, 11% in sexual, and 7% in poly (multiple) maltreatment class. Regarding HIV testing, 9% of the sample reported never testing, 58% once, 24% twice, and 10% three times in the past 9 months. GBM with multiple forms of abuse or neglect were twice (RR=2.53;95%CI:1.16-5.51; p=0.02) as likely to report SDCAS compared to GBM with no/minimal abuse or neglect, however, in terms of HIV testing uptake, there was no difference between the two sets of GBM (p=0.16).

Conclusions: Almost half (44%) of the GBM with multiple forms of abuse or neglect reported multiple testing. Results highlight the importance of addressing systematic barriers to increase testing uptake. Gay-friendly health services and home-testing in addition to current services may further improve HIV testing among high-risk GBM.

EPHP4.12

No Evidence of Increasing Condomless Anal Intercourse among GBMSM seeking Community-based HIV Testing in Montreal, 2009-2016

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Have trends in condomless anal intercourse (CLAI) among GBMSM in Montreal changed as we enter an era of preventive approaches that combine sexual practices, partner sorting, and pre- and post-exposure prophylaxis (PEP and PrEP)? We collected data at up to three timepoints over 9 months from GBMSM in Montreal who received community-based HIV testing along with intensive HIV risk-reduction peer counseling (the SPOT project). We constructed a panel dataset comprising 2,879 GBMSM, allowing for trends analysis from 2009 to 2016. We analysed trends in calendar time (quarterly) and key variables for two outcomes: (a) overall CLAI (regardless of partners' serostatus or viral load), and (b) at-risk CLAI with partners of unknown serostatus or HIV-positive partners with unknown or detectable viral load. From 2009 to 2016, the outcomes mean rates were 48.9% for overall CLAI and 26.6% for at-risk CLAI. To test for trends, we removed data on participants' first visits, as they were likely triggered by CLAI, and analyzed only follow-up visits since they were dependent solely on the study calendar. Trends in both overall CLAI and at-risk CLAI revealed a steady but generally non-significant decrease over the years, with only a few quarters being sig-

nificantly lower than baseline. Non-gay/bisexual-identified MSM were consistently less likely to report overall CLAI, while those born in Canada (vs elsewhere) and who had been tested in the previous year (vs never been tested) were consistently more likely to report at-risk CLAI. We found no evidence of increased CLAI over 7 years among study participants. Enrollment in regular HIV testing with intensive counselling on HIV risk reduction strategies may have contributed to these results. However, given recent increases in access to PrEP for GBMSM in Montreal, it will be important to monitor whether PrEP is being used as substitute for or in combination with condoms.

EPHP4.13

Syringe sharing among people who inject drugs in London, Ontario

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Background: London, Ontario has recently experienced an outbreak of HIV among people who inject drugs (PWID). However, little is known about HIV transmission risks in this setting. Therefore, we sought to characterize syringe sharing among PWID in this mid-sized city in southwestern Ontario.

Methods: Peer research associates electronically administered a cross-sectional quantitative survey to PWID at three sites in London between March and April 2016. Bivariable and multivariable logistic regression models estimated associations of socio-demographic characteristics, drug use behaviours, and service access with syringe sharing (defined as borrowing and/or lending) in the previous six months.

Results: Of 198 PWID (median age=39; 38% female; 9% HIV-positive), 44 (22%) reported syringe sharing in the past 6 months. In multivariable analyses, older age was negatively associated with syringe sharing (adjusted odds ratio [AOR] per 5-year increase=0.81; 95% CI=0.66 – 0.99). Selling drugs (AOR=4.37; 95% CI=1.79 – 10.69), number of daily injections (AOR per 5 injection increase=1.20; 95% CI=1.01 – 1.44), daily crystal methamphetamine injection (AOR=3.52; 95% CI=1.50 – 8.25), and self-reported HIV-positive status (AOR= 10.21, 95% CI= 2.96 – 35.23) were positively associated with reporting syringe sharing. In a subanalysis to further explore the association between HIV serostatus and sharing we found that self-reported HIV-positive respondents were more likely to report syringe borrowing (56% versus 13%, p<0.001), but not lending (24% versus 13%, p=0.27).

Conclusion: We observed a high rate of syringe sharing among PWID in London, with sharing being associated with high-intensity injection, particularly of crystal methamphetamine, as well as with involvement in drug sales. Considering the 2015 HIV outbreak among London PWID, efforts to increase syringe access are urgently needed. Potential interventions include expanded geographical coverage and hours for needle and syringe programs and street outreach, greater engagement of people who sell drugs in harm reduction programs, and supervised injection services.

EPHP4.14

HIV Acquisition among Federal Offenders in Canada

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Background: The prevalence of HIV is known to be several times higher among incarcerated populations compared to the general Canadian population. While the burden of prevalent infections is recognized to have been acquired prior to incarceration, there is still a risk of in-prison HIV transmission.

Methods: Offenders in CSC are offered routine screening for HIV on admission and throughout incarceration. Enhanced surveillance data between 2005 and 2012 were examined for repeat HIV serology testing. HIV seroconversion was defined as a negative HIV antibody test result followed by a positive serology result. Data were extracted June 2016.

Results: A total of 7,166 offenders had repeat HIV serology testing and 17 were identified as HIV seroconverters. The mean time between seroconversion was 3.3 years (range 73 days to 7.0 years). Based on the total number of days under observation in this open cohort, the incidence rate for newly acquired HIV among offenders at risk was 1 case per 1,000 per year. The estimated relative risk of HIV acquisition associated with risk behaviours were non-significant due to small numbers: injection drug use (RR 1.2, 95%CI 0.4-5.0); tattooing (RR 0.7, 95%CI 0.2-2.2); and sex with an IDU (RR 2.0, 95% CI 0.4-9.7). Preliminary investigation into the 17 HIV seroconverters indicated that 9 had spent some time in the community, ranging from 2% to 90% of the time interval under observation.

Conclusion: Among offenders at risk the rate of newly acquired HIV infection was estimated at 1 case per 1,000 per year. Not all offenders are at risk. These findings can help inform HIV prevention programs. Offenders may reengage in risk behaviours in the community and could be at risk for HIV via both community and in-prison exposures. Understanding the role of in-community and in-prison risk behaviours in viral acquisition requires more study.

EPHP4.15

HIV prevalence and sexual partnerships among clients of female sex workers in Sub-Saharan Africa: a systematic review and meta-analysis

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Background: Clients of female sex workers (FSW) may represent important connections – and thus, an unmet need - in the complex sexual networks that lead to HIV transmission among FSW, their sex partners, and the wider population in Sub-Saharan Africa (SSA). We sought to estimate the burden of HIV and characterize the sexual partnerships of clients of FSW in SSA.

Methods: We performed a systematic review of electronic databases and grey literature to identify studies published between January 1, 2004 to June 6, 2016 which reported on the following outcomes among clients of FSW: HIV prevalence; number of FSW visits, non-FSW female or male sex partners; proportion condom use by partnership type and number of sex acts by partnership type. We pooled outcomes using random-effects meta-analyses. Clients were defined as men who paid for sex with an FSW in the last year (current clients), or ever in their lifetime ('ever' clients). N reflects the number of studies.

Results: We identified 80 cross-sectional studies of 31,189 clients in East (N=20), West/Central (N=42), and Southern Africa (N=18). Most (N=72) studies were household surveys using face-to-face interviews. The pooled HIV prevalence among current and 'ever' clients was 8.2% (95% CI:4.0-10.2; I^2 =96.6%) and 13.6% (95% CI:7.3-21.5, I^2=95.3%), respectively. Three studies of current clients reported on number of FSW visits per month (median 5, range 1-11), proportion with non-paying female sex partners (pooled proportion 54.7%,95% CI: 36.4-67.5, I^2=90.2%, N=6). The proportion of current clients who used condoms at last paid sex was 68.7% (95% CI: 45.8-78.1%, I^2=90.2%, N=59). No studies reported on the number of sex acts.

Conclusions: In SSA, clients of FSW experience a high burden of HIV and most also have non-paid sexual partnerships. Preventing HIV in clients may help reduce HIV transmission across their FSW and non-FSW partnerships.

HIV Program Science

La science dans l'élaboration des programmes sur le VIH

EPHP5.01

A Pharmacy-led Interdisciplinary Teaching Model in Specialized Pharmacotherapy: an HIV Pharmacy Rotation for Medical Residents.

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Background: The medical training model has traditionally been physician-to-physician, contrasting the current interdisciplinary health-care practice environment. Pharmacists with specialized drug knowledge are well-positioned to provide expert training in complex antiretroviral therapy. We developed a collaborative teaching model incorporating a pharmacist-led rotation for medical residents to learn specialized HIV pharmacotherapy**.**

Description: Since 2010, the Ontario HIV Treatment Network (OHTN), partnering with the University of Toronto Department of Family & Community Medicine has been offering a postgraduate residency program focused on the delivery of HIV care. The provision of HIV care, however, is multifaceted and drug treatment can be complex. Thus, in 2013, a specialized HIV pharmacy rotation was created at St. Michael's Positive Care Clinic with the primary goal to augment HIV drug knowledge and better equip family physicians to provide exemplary HIV care. The concept was for the medical trainee to "become the pharmacist", learning to recognize and manage common drug-therapy issues in HIV-infected persons.

Action: A formalized curriculum was developed, including rotation goals to foster key competencies in family medicine while addressing gaps in pharmacology training and HIV care. The rotation could be tailored to the resident but generally consists of a core set of one-on-one teaching, case-based learning, and application of pharmacotherapeutics in a busy specialized ambulatory HIV clinic.

Evaluation: A pre- and post-rotation survey was developed to assess whether the pharmacy rotation improved the resident's confidence in their knowledge of HIV pharmacotherapy. This survey also gathered feedback and recommendations to enhance future rotations. Thus far, 4 residents have completed the OHTN residency with the elective pharmacy rotation and have strongly endorsed the rotation as valuable to their future practice.

Implications: This collaborative teaching model appears to be extremely valuable to enhance physician knowledge and should be considered at other major academic centers training physicians in HIV care.

EPHP5.02

Talk on the front lines: Challenges and effective strategies for communicating about HIV risk for outreach workers in Ontario.

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Background: Effective communication about HIV risk is critically important to encourage health decisions that prevent HIV transmission. However, to take preventive action, individuals must first understand their risk. There is a crucial need for accessible information about risk as well as the health literacy skills to assess risk – particularly with the current focus on biomedical and combination prevention. The project goal was to explore how the health literacy needs of those living with or at risk of HIV are being assessed and met, and how outreach/prevention services can improve risk communication.

Methods: Literature reviews were conducted examining effective interventions for improving client health literacy and strategies for communicating about HIV. Focus groups were also conducted with outreach workers ($N = 18$) who work with at-risk populations across Ontario, including: men who have sex with men; street involved people; African, Caribbean, and black populations; and women. Audio recordings of these focus groups were transcribed and a thematic analysis was conducted using NVivo.

Results: The literature reviews highlight the importance of providing information that contextualizes HIV risk. Emergent focus group themes included: stigma as a barrier for effective HIV risk communication and the use of tailored approaches to meet clients' unique needs and goals. Although outreach workers are not receiving formal training to identify the health literacy levels of their clientele, they use subtle cues (e.g., language used, specificity of questions asked, facial expressions, etc.) to intuit this information and deliver HIV risk information suited to individual needs and abilities.

Conclusion: The results of these analyses provide unique insight into the process of HIV risk communication conducted by outreach workers in Ontario; the challenges, the successes, and the opportunities for improvements. These findings will help inform policy, program planning, and evaluation of resources needed to support people at risk for HIV.

Interdisciplinary Epidemiology (Biological, Behavioural and Social) or Biopsychosocial Research

Épidémiologie interdisciplinaire (biologique, comportementale et sociale) ou recherche biospychosociale

EPHP6.01

Beyond Undetectable: The Concerns of People Living with HIV in Canada

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Background: Treatment advances have drastically altered the experience of living with HIV. We explored the perspectives and concerns of people living with HIV (PLWH) in Canada in an era where treatment has rendered many HIV counts undetectable.

Methods: In this mixed method study, we collected open-ended personal narratives of 19 PLWH in Canada. The themes expressed in the qualitative interviews were explored in a quantitative questionnaire distributed to 150 PLWH in Canada.

Results: In the qualitative study, we interviewed men (63%, 12/19) and women with a mean age of 47 across Ontario (42%), Quebec (32%), and British Colombia (26%). Three themes emerged: 1) Most participants reported at least one other chronic comorbidity. 2) Concerns about these conditions were often more salient to them than HIV. HIV was not something PLWH thought about frequently except when taking their medication. 3) PLWH perceived their doctors to be focused on HIV counts and wished for broader discussions on their other conditions and the long-term effects of treatment.

In the quantitative study, we surveyed men (66%, 99/150) and women with a mean age of 47 across Ontario (49%), Quebec (24%), and British Colombia (27%). 74% reported living with at least one additional chronic condition (111/150) and 76.6% were on at least one additional medication besides HAART (115/150). When thinking about the next visit with their HIV specialist, patients primarily hoped for more time to discuss their long-term health (70%, 105/150), their other chronic conditions (62%, 93/150), and the long-term side effects of their medication (46%, 69/150). In logistic regression models, frequency of visits and time spent with the doctor did not temper expressed desire for greater discussion on long-term health and other conditions.

Conclusion: Our findings indicate that many PLWH wish to have a broader dialogue with their HIV specialist about their whole health.

EPHP6.02

Changes in Cigarette Smoking Over Time Among HIV-Positive and HIV-Negative Gay, Bisexual, and Other Men Who Have Sex with Men in Vancouver

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Background: Cigarette smoking is common among gay, bisexual, and other men who have sex with men (GBMSM) and most of the mortality gap between HIV-positive and HIV-negative individuals is attributable to smoking.

Methods: We recruited sexually active, HIV-positive and HIV-negative GBMSM age ≥16 years using respondent driven sampling in Vancouver. Study visits occurred every six months and included a computer-assisted self-interview and clinical assessment. We conducted bivariate analyses to compare factors associated with "never", "former", "daily", or "non-daily" smoking at baseline and longitudinal mixed effects models to examine factors associated with cessation and (re)initiation.

Results: 774 participants completed a baseline visit and 525 completed at least one follow-up visit. The median age was 34 years and 31.5% were daily smokers. In follow-up (median=2.5 years), 116 smokers (41%) quit at least once and 101 (87%) remained former smokers at their last visit. Factors associated with smoking cessation and increasing to or resuming daily smoking are reported in Table 1. HIV-positive GBMSM were more likely to have a family doctor than HIV-negative participants (96.4% vs. 51.2%) but were also more likely to smoke (p=.004) and no more likely to quit.

Conclusions: Polysubstance use and having a partner who smokes were contributing factors to increased and sustained smoking. Despite being highly engaged in care, HIV-positive GBMSM were no more likely to stop smoking in follow-up. More targeted and culturally relevant smoking cessation resources are needed, especially for HIV-positive GBMSM given increased morbidity and mortality risks. Engaging couples in cessation interventions may be useful.

Table 1. Multivariable analyses of smoking cessation and (re)initiation.

		Cessation		(Re) Initiation	
		aRR	**95% CI**	**aRR**	**95% CI**
Annual Income	< 30k	Ref		Not selected	
	30-59,999	0.97	0.64, 1.47		
	≥ 60k	**1.80**	**1.06, 3.07**		
Self-Reported HIV Status (univariable)	Negative	Ref		Ref	
	Positive	1.20	0.82, 1.75	**2.57**	**1.53, 4.30**
	Unknown	1.96	0.47, 8.13	1.72	0.21, 13.95
Current Health	Excellent	Ref		Not selected	
	Very good	**0.46**	**0.28, 0.76**		
	Good	**0.52**	0.32, 0.84		
	Fair	**0.40**	**0.21, 0.76**		
	Poor	0.24	0.03, 1.78		
Partner Tobacco Use	No current partner	Ref		Ref	
	No tobacco use	1.29	0.87, 1.92	**0.34**	**0.16, 0.72**
	Yes, but not daily or almost daily	1.16	0.61, 2.21	1.28	0.53, 3.06
	Daily or almost daily	**0.47**	**0.23, 0.95**	**2.12**	**1.03, 4.36**
Participant Drinker Type	Non-drinker	Ref		Ref	
	Social	**0.38**	**0.22, 0.67**	**0.45**	**0.22, 0.92**
	Binge	**0.48**	**0.30, 0.76**	**0.39**	**0.20, 0.77**
	Heavy binge	**0.40**	**0.17, 0.93**	**0.17**	**0.05, 0.67**
	Non-binge Frequent	0.58	0.26, 1.29	0.18	0.02, 1.41
Ecstasy Use	No	Ref		Not selected	
	Yes	**0.63**	**0.40, 1.00**		
Cannabis Use, past 3 months	< Monthly	Not selected		Ref	
	None			0.83	0.34, 2.03
	Monthly			1.32	0.44, 3.94
	Weekly			**3.27**	**1.17, 9.20**
	> Weekly			**2.97**	**1.00, 8.79**
	Daily or Almost Daily			1.67	0.62, 4.50
GHB Use, past 6 months	No	Not selected		Ref	
	Yes			**2.03**	**1.01, 4.06**
Crystal Use, past 6 months	No	Not selected		Ref	
	Yes			**2.26**	**1.13, 4.50**

EPHP6.03

Correlates of HIV infection among women who inject drugs and report sex work in the SurvUDI network

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Objective: The objective was to examine the correlates of HIV infection among women who inject and report sex work in the SurvUDI network.

Methods: Participants (having injected in the past six months) were recruited through harm reduction programs across the Province of Quebec and Ottawa. They completed an interviewer-administered questionnaire and provided saliva samples for anti-HIV antibody testing. Questions about behaviours referred to the past 6 months. Female participants reporting client sex partners between 03/01/2004 and 03/31/2015 were selected. Analyses were conducted with generalized estimating equations (GEE) taking into account multiple participations. Variables with univariate p-value ≤0.3 were included in the multivariate analysis. Significant variables (p-value <0.05) and confounders were retained.

Results: Data from 570 women (972 visits) with a mean age of 33.5 years were included. Baseline HIV seroprevalence was 12.9% [95% Confidence intervals (95% CI):10.2-15.9%]. HIV prevalence was independently associated with age ≥25 years (adjusted prevalence ratio (aPR)=4.6 [95% CI: 1.7-12.7]), recruitement in an urban region (aPR=2.7 [95% CI: 1.3-5.8]), high school not completed (aPR=1.6 [95% CI: 1.0-2.3]), recent incarceration (aPR=1.6 [95% CI: 1.1-2.3]), injection with a syringe used by someone else (aPR=2.0 [95% CI: 1.3-2.9]), not having lent used syringes to others (aPR=1.8 [95% CI: 1.2-2.9]), always injecting alone (aPR=1.7 [95% CI: 1.0-2.8]), cocaine as the most often injected drug (aPR= 1.6 [95% CI: 1.1-2.3]), and consistent condom use for vaginal or anal sex (aPR=1.6 [95% CI: 1.1-2.2]), adjusting for time since first injection, injection with strangers and using material other than syringes used by someone else obtained mainly from strangers.

Conclusion: Correlates of HIV prevalence in women who inject and report sex work are similar to those observed in all SurvUDI participants. These data should be interpreted with caution since these are prevalent cases, and behaviors may have occurred before or after the time of infection.

EPHP6.04

Online Health-Seeking Behaviour and HIV Serodiscordant Condomless Sex among Gay, Bisexual and Other Men Who Have Sex with Men in Ontario

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Background: Given gay, bisexual and other MSM (GBM)'s increased use of the Internet for seeking sex and health information, we sought to determine if socio-sexual or online sexual health-seeking behaviour was different between HIV statuses (HIV-positive detectable/undetectable, and HIV-negative/HIV-unsure) and associated with HIV risk.

Method: GBM aged>15, were recruited across Ontario from 12/2013-1/2014 via websites, mobile-apps, and ASO's to complete an anonymous online questionnaire. Pearson's Chi-square tests were used to explore differences in socio-sexual demographic and online health-seeking behaviour. HIV-positive status was dichotomized as undetectable viral load/VL≤200 copies/ml (UVL) versus detectable/unsure/VL>200 copies/ml (DVL). Logistic regressions modeled factors associated with 'HIV risk' at last anal sex event among 1) HIV-negative GBM: HIV risk defined as condomless anal sex with an HIV-positive/unknown partner, and 2) HIV-unsure GBM: HIV risk defined as any condomless anal sex.

Results: Among HIV-positive GBM, 124/143 (86.1%) reported UVL and 19/143 (13.3%) reported DVL. Non-condom use with HIV status serodiscordant partners did not differ by UVL/DVL status (47.7%-vs-66.7%;p=0.374). DVL men were more likely to have searched online for 'alcohol/drug use before/during sex' (47.4%-vs-9.7%;p<0.001) and 'HIV/STI testing services' (42.1%-vs-20%;p=0.035). 7.5% (86/1,144) of HIV-negative GBM reported HIV risk and 49.7% (86/173) of HIV-unsure GBM reported HIV risk. Table 1 presents the multivariable analyses results describing the socio-sexual and online health-seeking behaviours associated with HIV risk by HIV status.

Conclusions: Online sexual health-seeking differentially predicted risk among HIV-negative and HIV-unsure GBM. Differences between HIV statuses are important factors when developing online tools for sexual health online outreach for GBM.

Table 1: Multivariable Logistic Regression Analyses

Outcome: HIV Risk at Last Anal Sex Event among 1) HIV-Negative GBM and 2) HIV-Unsure GBM					
		HIV-Negative Risk		HIV-Unsure Risk	
		Adjusted Odds Ratio	95% CI	Adjusted Odds Ratio	95% CI
Age (years)	<26 (ref)	1.00		1.00	
	26-35	1.10	0.46-2.67	0.56	0.21-1.51
	36-45	1.57	0.60-4.11	1.59	0.43-5.87
	46-55	5.55	2.12-14.52	0.19	0.05-0.71
	55+	4.59	1.36-15.50	0.42	0.08-2.27
Alcohol/Illicit drug use before/during sex					
	None (ref)	1.00		1.00	
	One partner yes	1.99	0.88-4.52	2.32	0.86-6.27
	Both partners	2.99	1.39-6.43	1.57	0.51-4.81
How know partner's HIV status					
	Read on online profile (ref)	1.00		1.00	
	Asked or told	0.07	0.01-0.49	0.09	0.01-1.38
	Mixed	0.31	0.05-1.82	0.11	0.01-2.41
	Other	0.18	0.01-2.29	0.33	0.01-20.01
	Didn't know	7.44	1.58-39.92	0.11	0.01-1.55
Type of sex					
	Receptive (ref)	1.00		1.00	
	Both	2.16	0.97-4.80	0.77	0.21-2.78
	Insertive	2.25	1.15-4.43	1.91	0.73-5.02
Met Partner Online					
	No (ref)	1.00		1.00	
	Yes	0.75	0.38-1.50	0.62	0.24-1.58
Look Online for…					
	...Signs/Symptoms of STI				
	No (ref)	1.00		1.00	
	Yes	0.77	0.40-1.46	3.82	1.50-9.77
	…STI/HIV testing				
	No (ref)	1.00		1.00	
	Yes	1.99	1.03-3.85	1.08	0.47-2.51
	…STI/HIV prevention				
	No (ref)	1.00		1.00	
	Yes	0.64	0.32-1.30	0.23	0.07-0.79
	…How to use condoms				
	No (ref)	1.00		1.00	
	Yes	0.38	0.07-2.07	0.12	0.01-1.27
STI testing or treatment, previous 12 months					
	Not treated nor tested (ref)	1.00		1.00	
	Tested and negative	1.59	0.77-3.30	1.08	0.35-3.27
	Tested and treated or treated due to partner notification or STI-related symptoms	1.63	0.61-4.37	0.28	0.07-1.08

EPHP6.05

High Prevalence of Gender-based Violence and its Socio-demographic, Clinical and Psychosocial Correlates Among Women Living With HIV in Canada

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Background: Gender-based violence (GBV) is a global epidemic that disproportionately impacts women living with HIV (WLWH). We aimed to assess factors associated with experiencing GBV among WLWH enrolled in a Canadian cohort.

Methods: Baseline survey data were analyzed for WLWH (≥16 years) enrolled in a community-based research cohort study in British Columbia (BC), Ontario (ON), and Québec (QC). GBV was assessed through self-reported experiences of control, physical, sexual, or verbal abuse in adulthood (>16 years). Multivariable logistic regression was used to identify socio-demographic, clinical and psychosocial factors associated with having experienced any adulthood GBV, and each type of violence separately.

Results: Of 1322 participants, the median age was 43 (IQR=36-51) years and 22% identified as Indigenous, 28% African, Caribbean or Black (ACB), 42%white/Caucasian, and 8% other. Most (80%) participants reported ever experiencing any adulthood violence, including physical (62%), sexual (45%), verbal (74%), and control (46%). In adjusted multivariable analyses (n=1004), factors associated with experiencing violence included *socio-demographic* (age, incarceration history, food insecurity, living in one's residence < 1year, living in B.C. vs. Ontario), *clinical* (lower anti-retroviral adherence, Hepatitis C, cancer, delayed access to HIV medical care after diagnosis) and *psychosocial* (current cigarette use, recent and former cannabis use, recreational drug use in past 3 months, PTSD, racial discrimination) factors. Socio-demographic, clinical and psychosocial correlates varied for each type of violence. For example, sexual violence was associated with lower income, depression, Hepatitis B, and gender discrimination. Physical violence was higher among Indigenous women, and participants who had lived in a group home.

Recommendations: Most (80%) women living with HIV in Canada experienced violence in adulthood. Violence was associated with social marginalization and poorer clinical and psychosocial outcomes, demonstrating the importance of syndemics approaches to understanding wellbeing among women with HIV. GBV needs to be addressed and screened for in HIV care.

EPHP6.06

Prevalence and pattern of chemsex in patients attending Montreal urban clinic

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Introduction: Chemsex is a growing phenomenon in Europe where individuals take a variety of synthetic drugs in a sexual context. Higher sexual risk-taking behaviour had been reported in Europe and USA among «chemsexers». Lack of data describing the extent of chemsex in Montreal motivates us to study its prevalence and assess the risk factor associate with crystal use in Montreal.

Methods: We conducted a survey at Clinique médicale Quartier Latin, a Montreal's urban center specialized in sexual health. Data on socio-demographics, previous/current drug use, sexual practices & health were collected by auto-administered questionnaire completed by patients while waiting to see a clinician. Proportions were compared by X^2 and Odds Ratios were obtained by logistic regression using SPSS-20.

Results: Between Oct & Nov 2016, 504 patients participated to the study. 72% were male, median age was 49y (IQR 36-60), 53% were MSM, 35% heterosexual and 12% had relation with both sex. 22% never used drug, while lifetime use of recreational drug was 75% cannabis, 44% cocaine, 36% speed, 33% ecstasy, 24% GHB, 19% ketamine, 14% crystal and only 2 patients reported use of mephedrone, meaning a lifetime and recent prevalence of chemsex of 56% and 19% respectively. The 68 crystal-users of our sample were mostly MSM (75%), polydrug users (6.6 drugs vs 2.9 among non-crystal-users;p<0.001), who had tried injection at least once (OR=5.05,p=0.006), take drug for new sexual experience (OR=4.86;p=0.003), use sauna (OR=3.88;p=0.013) and apps to find partners (OR=2.96,p<0.001), had higher number of partners since last 12months (51 vs. 15; p<0,001) and were more frequently diagnosed for recent STI and HIV (OR=2,87 and 3.17 respectively, p<0.001).

Conclusion: Chemsex in Montreal is now a reality and it constitute a core of highly at risk individual for HIV and STI. It is urgent to develop targeted intervention for harm reduction in «chemsexers».

EPHP6.07

Differences in food insecurity in HIV-HCV co-infected individuals in British Columbia, Ontario, and Quebec

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Background: The Food Security & HIV-HCV Study (CTN264) of the Canadian Co-infection Cohort is a multi-province study of food insecurity (FI) in individuals living with HIV-HCV co-infection. This analysis describes the prevalence of FI and some of its potential determinants in British Columbia (BC), Ontario (ON), and Quebec (QC).

Methods: We used longitudinal data from 665 participants in 13 clinics across 3 provinces (November 2012-May 2015). FI (past 6 months) was measured using Health Canada's Household Food Security Survey Module. Descriptive statistics were stratified by province of enrolment and generalized estimating equations were used to estimate unadjusted risk ratios (RR) for the association between province and FI.

Results: Among participants at baseline, the prevalence of FI was: 72% (BC, N=244), 59% (ON, N=128), 63% (QC, N=293). The average median monthly incomes (Q1-Q3) over the past 6 months were: $1100 ($1000-$1400), $1317 ($1100-$2000), and $920 ($908-$1077) in BC, ON, and QC, respectively. Unstable housing (past 6 months) was experienced by 10% (BC), 6% (ON), and 7% (QC) of participants. The prevalence of injection drug use (past 6 months) [44% (BC), 18% (ON), 33% (QC)] and depressive symptoms (past week) [56% (BC), 51% (ON), 54% (QC)] also differed across provinces. Using BC as the referent group, the unadjusted associations between province and FI were: RR[ON]=0.79 (95% CI=0.68-0.92) and RR[QC]=0.81 (95% CI=0.73-0.90).

Conclusions: Compared to BC, the unadjusted risk of FI is approximately 20% lower for participants enrolled in ON or QC. This analysis also describes differences in the distributions of socioeconomic, sociodemographic, behavioural, and clinical determinants of FI in these provinces. Therefore, these descriptive findings highlight the potential need for province-specific strategies to reduce FI and motivate future regression-based decompositions to examine to what extent these or other determinants (e.g., food assistance) contribute to the observed differences in FI in this population.

EPHP6.08

How are People Talking about their Serodiscordant Relationships? Preliminary findings from the Positive Plus One Study

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Importance: Although practices involved in disclosing one's HIV-status to sexual partners are well studied, much less is known about disclosure of serodiscordant relationships by both partners within personal and healthcare networks. As many as 23% of people living with HIV in Canada may be in a serodiscordant relationship. Lack of relationship disclosure could negatively affect access support from personal and healthcare provider networks.

Objectives: We investigated the impact of HIV-status on relationship disclosure within personal (i.e., family/friends) and healthcare provider (i.e., doctors/nurses) networks. We hypothesized that HIV-positive partners would be more likely to disclose their relationship to healthcare providers with whom they have already consulted regarding their HIV-status.

Methods: We used data from a national sample of people self-reporting current engagement in an HIV-serodiscordant relationship in an online survey. We employed bivariable and multivariable analyses using generalized estimating equations with a logistic link function to account for non-independence of the data within dyads.

Results: At time of writing, the study had recruited N=310 participants (128 HIV-negative; 182 HIV-positive; 79 dyads), all in current relationships. Compared with HIV-positive partners, fewer HIV-negative partners disclosed their relationship to any healthcare provider (72% v. 82%; $p<0.05$) or within personal networks (74% v. 85%; $p<0.02$). HIV-positive partners were more likely to disclose to family (AOR=3.0; $p<0.001$), friends (AOR=2.6; $p<0.01$) and their healthcare provider(s) (AOR=2.6; $p<0.05$). HIV-positive partners diagnosed during a relationship were less likely to disclose within any network, including to their healthcare provider(s), compared with those diagnosed prior to a relationship (AOR=0.04; $p<0.001$).

Discussion: Disclosure of a relationship's serodiscordant status may facilitate engagement with social and healthcare support. HIV-negative and HIV-positive persons diagnosed during a serodiscordant relationship may be less likely to access these supports. Future work should consider the reasons for (non)disclosure, and impacts on relationship quality and HIV prevention.

EPHP6.09

Phylogenetic Analysis of HIV Transmission Networks among People who Inject Drugs in Pakistan

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Background: Pakistan is currently facing a concentrated epidemic among people who inject drugs (PWID). Well-defined transmission networks, based on molecular epidemiology, have the potential to assist in the development of targeted screening and prevention strategies as well as identify hidden epidemic drivers. Here we present molecular transmission networks re-constructed from HIV-1 pol sequences collected from PWID located in major urban centres in Pakistan.

Methods: Dried blood spots (DBS) were collected from PWID in Karachi, Larkana, Peshawar, Quetta and Hyderabad (n = 1,500). Sampling locations were identified through a mapping approach developed by the HIV/AIDS Surveillance Project. Briefly, the mapping approach involved identifying and validating locations where high-risk activities take place through interviews and data triangulation. Protease and part of the reverse transcriptase genes were amplified and sequenced using an in-house HIV genotyping assay. Transmission networks were characterised by HIV subtyping tools, patristic distance based analysis and BEAST v1.8.3.

Results: Phylogenetic analysis revealed that a large proportion of infections (75%) are genetically related which supports the idea that local injection practices are playing a major role in the spread of HIV among PWID. A large transmission cluster made up of a genetically distinct A1 subtype was identified in Peshawar. Also, subtypes CRF 02_AG and CRF 35_AG have been introduced into the PWID community. Together, this suggest that the introduction of foreign subtypes has occurred and that the current epidemic is not simply an onward transmission of a limited number of A1 subtype founder viruses as suspected previously.

Conclusions: Re-construction of transmission networks based on sequencing-based approaches has the potential to expand our understanding of the HIV epidemic currently taking place in Pakistan especially if used in combination with epidemiological data. Particular attention maybe warranted for Karachi since transmission linkages were observed with all the other cities included in this study.

Methodological Advances in Epidemiology, Public Health and Mathematical Modelling

Progrès méthodologiques en épidémiologie, santé publique et modélisation mathématique

EPHP7.01

Modulating effects of epidemic conditions on projected HIV vaccination efficiency in South Africa

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HIV vaccination models for South Africa show that re-vaccinations boosting the immune response to a partially effective vaccine could help stem the HIV epidemic. The ongoing HVTN 702 phase 2b/3 trial tests a 5-dose regimen which will likely require periodic boosting. Our goal is to determine how uncertainty around epidemic conditions and booster efficacy affect vaccine impact projections.

We modified a HIV transmission model calibrated to 2012 epidemiological data from South Africa to simulate a vaccination program starting in 2027 based on the HVTN 702 regimen. We assume 50% average vaccine efficacy over 2 years, periodic boosters every 2 years (20% attrition between revaccinations), and recruitment of adults to maintain 50% coverage. We explore 30% and 60% booster efficacy (BE) with no efficacy after missed boosters. We identified two epidemic settings differing in ART coverage and adherence and resulting in low (0.33%) and high (1.56%) HIVIHIV incidence in 2027. Under CD4<500 cells/mm^3 ART eligibility, we measured effectiveness (cumulative fraction of infections prevented, CFP) and efficiency (infections prevented per 1000 vaccinations, IPV).

CFP is 42-57% higher with 60% BE and 9-17% higher under low incidence. IPV is 41-54% higher with 60% BE and 230%-380% higher under high incidence. Efficiency improves over 30 years under high incidence while it worsens under low incidence (Table). Booster efficacy and epidemic conditions may greatly influence the benefits from future vaccination programs. Although vaccination is slightly more effective in low incidence settings, it is substantially more efficient in high incidence settings which will impact its cost-effectiveness.

HIV vaccine impact statistics (adult population)

Scenario	Vaccination effectiveness (CFP) / efficiency (IPV)			
Booster Efficacy (BE)	2027 HIV Incidence	After 10 years	After 20 years	After 30 years
60%	Low	32.4% / 5.5	39.8% / 5.4	45.4% / 5.0
60%	High	29.4% / 18.9	35.8% / 21.8	41.5% / 24.0
30%	Low	22.8% / 3.9	27.0% / 3.7	30.8% / 3.4
30%	High	20.0% / 12.9	23.0% / 14.2	26.4% / 15.6

EPHP7.02

Classifying HIV Diagnoses by Non-Mutually Exclusive Priority Populations to Enhance Program Planning in Ontario

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Background: HIV surveillance in Canada typically uses a mutually exclusive, hierarchical approach to classify new HIV diagnoses by their most probable route of HIV transmission (or exposure categories (ECs)). As individuals diagnosed with HIV may relate to multiple ECs, this approach limits usefulness of surveillance data for program planning (e.g., prevents understanding overlap among populations). A non-mutually exclusive approach was developed to better describe HIV epidemiology by population in Ontario.

Methods: Public Health Ontario Labratory collects data on new HIV diagnoses in the province. Case definitions for five non-mutually exclusive priority populations (PP) prioritized in Ontario's HIV strategy were created using risk factors, ethnicity and/or country of birth. Diagnoses by PP and overlap among PP were explored.

Results: Between 2009–2015 there were 6,278 HIV diagnoses, of which PP could not be determined for 34% due to missing data. Overall (where PP known), 60% were gay, bisexual and other men who have sex with men (GBMSM), 26% were African, Caribbean or Black (ACB), 11% were people who inject drugs (PWID), 3% were Indigenous, and 19% were at-risk women – with 26% of diagnoses belonging to more than one population.

Conclusions: Large overlap among PP highlight the importance of a non-mutually exclusive approach for classifying HIV diagnoses to better understand local HIV epidemiology. This approach generated new insights that could inform policy and program planning, implementation, evaluation and community engagement strategies. Missing data remains a limitation and future efforts are

needed to reduce missingness through improved data collection or data imputation.

Table 1: Overlap among priority populations in newly HIV diagnosed individuals, Ontario, 2009-2015.

	Priority population (PP)					
		At-risk women	ACB	GBMSM	PWID	Indigenous
Percent of PP that are…	At-risk women	100%	45%	0%	25%	35%
	ACB	60%	100%	11%	6%	0%
	GBMSM	0%	27%	100%	32%	28%
	PWID	14%	2%	6%	100%	49%
	Indigenous	5%	0%	1%	11%	100%

Policy Evaluations

Évaluations des politiques

EPHP8.01

Eli Lilly v. Canada: Potential Implications of Investor-State Arbitration for Access to Medicines

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Canada is facing an unprecedented lawsuit by Eli Lilly under an international trade regime that poses serious threats to human rights and access to medicines. The multinational pharmaceutical corporation is accusing Canada of breaching its obligations to foreign investors under the North American Free Trade Agreement (NAFTA) by allowing its courts to invalidate patents for two of its drugs. It is seeking damages in excess of half a billion dollars.

Eli Lilly's NAFTA investor-state challenge marks the first attempt by a patent-holding pharmaceutical corporation to use the extraordinary investor privileges provided by trade agreements as a tool to push for greater monopoly patent protections, which increase the cost of medicines for consumers and governments. The allegation that Canada interfered with Eli Lilly's expectation of monopoly profits is particularly troublesome given that it may have a chilling effect on the willingness of courts and lawmakers to regulate the pharmaceutical industry. The outcome of the case is critical for those seeking to safeguard countries' ability to determine their own patent standards, a prerogative that is essential for preventing patent "evergreening" and protecting access to medicines.

As the Eli Lilly case advances, similar "investor-state" provisions in other trade agreements (e.g., as in the proposed Trans-Pacific Partnership (TPP)), threaten to not just replicate, but expand, the prospects for such challenges to countries' legitimate patent policies. This presentation will examine how such trade deal provisions can undermine the protection and promotion of a range of human rights, and how the benefits of expanded trade relationships — obtained by granting foreign investors expansive rights under investment treaties — must be balanced with the need for effective policy autonomy so that countries can regulate in accordance with human rights standards and safeguard access to essential medicines.

EPHP8.02

Community Voices in the PrEP Regulatory Process

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Although pre-exposure prophylaxis (PrEP) is a promising tool for HIV prevention, access to PrEP in Canada remains limited. This is in part due to the regulatory pathway for new medications in Canada that requires separate reviews of a drug's efficacy, suitability for public listing and negotiations on pricing before a medication makes its way onto public drug plan formularies that roughly 10 million Canadians use to access prescription drugs. Rather than sitting on the sidelines, service providers and community groups have played an active role submitting their input in these processes in an effort to expedite approval and ensure appropriate access to PrEP for communities most impacted by HIV. Drawing on outputs of regulatory bodies and submissions by community groups, this poster outlines how regulatory decisions and community feedback are shaping the future of PrEP access in Canada.

EPHP8.03

(En)Gendering Prevention: An Exploration of HIV and HCV prevention policies and the needs of women who inject drugs in Nova Scotia, Canada

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Objective: HIV and HCV continue to represent serious public health concerns in Canada, particularly among priority populations such as injection drug users (IDUs). Given this, HIV/HCV prevention and related harm reduction policies are needed to support and guide ongoing public health and disease prevention efforts for IDUs. The key objective of this study was to explore the history and current state of HIV and HCV prevention policies in Nova Scotia, Canada with particular reference to how they were developed, how they have influenced programming, and how they address the needs of women IDUs.

Methods: The Walt and Gilson's policy framework (which analyzes the context, actors and processes involved in determining policy content) and gender-based analysis (GBA) was used to frame our study. This qualitative case study utilized both a policy document review and a key informant interview methodology to explore the research

questions. Study participants included government and non-government policy decision-makers, and service providers who have engaged in provincial HIV and/or HCV policy development. All relevant provincial HIV and HCV prevention policies with a focus on harm reduction and blood borne pathogens were analyzed.

Results: Our study found that HIV/HCV prevention policies in Nova Scotia do not take into consideration the gender-based aspects of IDU in general and do not address the needs of women who inject drugs specifically. As such, attention and resources are not going to this population and the existing policies are not addressing their HIV/HCV risk and prevention contexts.

Conclusions: This study demonstrates the importance of examining the differential impact prevention policies can have on men and women who inject drugs. Additional GBA attention is required to help ensure current and future HIV and HCV prevention policy and programing directions consider more fully their utility for priority populations such as women who use injection drugs.

Process Advances and Lessons Learned in Complex or Community-based Public Health Research

Progrès des processus et leçons tirées dans les recherches complexes ou communautaires en santé physique

EPHP9.01

Documenting best practices for the implementation of supportive housing programs for people living with HIV

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Background: McLaren Housing Society of British Columbia (BC) provides secure, affordable housing and support services for individuals affected by HIV throughout BC. In 2013, McLaren opened the Howe Street Residence, a 110-unit supportive housing complex. As no mechanisms were initially incorporated for rigorous evaluation of this intervention, the documentation of best practices will serve as a descriptive tool for future implementation of similar programs.

Description: The *At Home At Howe* study is a collaborative research project between the BC Centre for Excellence in HIV/AIDS and McLaren Housing Society aiming to monitor the impact of a supportive housing intervention among a prospective cohort of people living with HIV (PLHIV) at-risk of homelessness. Peer Research Associates (PRAs) (PLHIV with common experiences to the client population) were hired to design and implement the survey tool.

At baseline and 12-month follow-up, 69 participants were asked to complete a 1-hour peer-administered survey, including questions concerning the impact of the housing intervention on health and well-being. Survey data will be contextualised by semi-structured qualitative interviews. Preliminary data was reviewed with PRAs and McLaren and a literature review was conducted to outline best practices from similar programs. Knowledge translation will be conducted in the form of workshops with Howe Street staff to flag concerns and implement suggested changes.

Best Practices: The research team worked with McLaren to identify best practices for successful supportive housing and areas for improvement at Howe Street, including building policy and service provision. The peer-based model has helped garner trust amongst participants, which may enhance the validity of self-reported information.

Recommendations: Our experience underscores the importance of establishing open lines of communication between the housing provider and research team, allocating sufficient time and resources to grounding the research in the affected community, and cultivating a culture of collaboration and transparency within the evaluation.

EPHP9.02

Translating Research to Realities: lessons learnt in scaling up anti-HIV stigma interventions in ethno-racial communities

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Background: HIV stigma has been a key driver in undermining HIV prevention and support initiatives. The Committee for Accessible AIDS Treatment formed a multi-disciplinary team to undertake community based HIV stigma reduction intervention in 2011-2015 amongst African Caribbean, Asian and Latino Canadian communities in the Greater Toronto Area. The CHAMP project: Community HIV Advocate Mobilization Project, demonstrated successful results in reducing stigma and increasing community mobilization and engagement in HIV related work amongst both its HIV positive participants and HIV negative community stakeholder groups. Since 2015, the team has been working on multi-pronged strategies to translate the research intervention into frontline programming.

Methods: The CHAMP research team comprised of community-campus partnership made up of researchers, service providers, community based organization representatives and people living with HIV/AIDS. Working together since the inception of the project, the team

has explored different strategies to translate the CHAMP interventions into practice, including applying for further knowledge to action research grants, new program funding, and integration of intervention elements into existing program practices.

Results: In 2016, the team has successfully applied and received approval for community alliance funding to scale up the CHAMP intervention amongst 5 community partner organizations in Toronto. As we worked together to translate the research intervention into real-life program practices using a collective empowerment grounded, community succession train-the-trainer model, we learnt valuable and important lessons about processes that are needed to foster buy-in and common understanding on mechanisms needed to ensure capacity building and intervention integrity; and resources needed to ensure feasibility and sustainability. As different partners within the alliance faced resource cutbacks, the team also learnt to innovate in finding options and synergies to address emerging challenges.

Conclusion: Collaborative partnerships to translate research interventions to real-life programming can provide important framework for similar inititaives in HIV prevention and stigma reduction.

EPHP9.03

Integration of Clinic-Based, Opt-Out Testing for HCV Into an Existing HIV testing Framework at a community health center in Chicago

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Howard Brown Health, one of the nation's largest LGBTQ healthcare organizations, was awarded funding in 2015 to create best practices around the expansion of routine opt-out HIV testing and integration of Hepatitis C virus (HCV) screening into this framework.

After modification of the Electronic Medical Record to prompt for HIV testing, testing was routinized by training Medical Assistants (MAs) to offer testing using a script during vitals. HIV testing was rapid. HCV testing was routinized by adding labs to order-sets for a variety of visits. Education emphasized the importance of HCV screening for people born 1945-1965, the HIV-positive, and/or those with drug use risk. Finally, the HCV Ab test was changed to auto-reflex a viral load test if positive to avoid extra visits in determining active HCV.

The number and percentage of visits where HIV and/or HCV testing were offered and conducted, the number of new HIV and HCV positives identified through opt-out testing, and the number of new positives linked to care were quantified monthly. Patient test refusal reasons and MA-perceived barriers were documented and addressed continuously. Meetings were held with providers at all levels to discuss how the project fit into their workflow and to assess their buy-in.

EMR prompts, standardized scripts during patient interactions, and documentation of barriers are important. Ongoing education and progress presentations sustain provider buy-in. Skills trainings were conducted with MAs to address refusal reasons. HCV testing importance was discussed in Clinical Quality Meetings to obtain agency buy-in to continue the high-cost testing. Providers and patients were allowed flexibility in selecting testing types to improve workflow and acceptance. This project contributed to 51% of eligible patients being tested for HCV at least once, and an increase in offers of HIV testing at eligible visits (88% to 99%) while maintaining a testing rate of 90%.

EPHP9.04

Inuit Community Readiness: Adapting the Community Readiness Model with Inuit Communities for HIV Prevention

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With the highest rates of STIs in Canada, high mobility between North and South and a lack of adequate screening for STBBIs, it is possible that Inuit communities could face an HIV epidemic. If no action is taken to scale up prevention efforts, an epidemic in Inuit communities in the North could soon be a reality. Therefore, gauging an Inuit community's level of readiness to develop and participate in community-based HIV prevention, education, screening, and ensuring approaches are culturally relevant is imperative.

This current research project builds directly on priorities outlined by Inuit stakeholders, and is facilitated through strong partnerships between the three communities (Kugluktuk, Arviat, and Clyde River Nunavut), Pauktuutit Inuit Women of Canada, the Canadian Aboriginal AIDS Network, and Dalhousie University. The goal of this research project is to engage Inuit communities and organizations in adapting, piloting and using the Community Readiness Model (CRM) to improve readiness to engage in HIV-modalities at the community level. This presentation will outline the community engagement and integrated knowledge translation processes, progress to date, and next steps for this community-based research project.

This project has adopted *Inuit Qaujimajatuqangit (IQ)* as a framework, which supports personal wellness through a collective cultural sense of health. Consultations with the project advisory committee (Canadian Inuit HIV/AIDS Network (CIHAN)), Community Health Representatives from

three respective Nunavut communities and the research team were held November 2015. We are working collaboratively to: 1) adapt the CRM; 2) ensure it is Inuit-specific; 3) pilot the adapted tool; and 4) determine the applicability of this tool. Representatives from Nunatsiavut, Nunavik and Inuvialuit will also be mentored on how to use the adapted CRM. By engaging knowledge users and communities, this project will address HIV prevention in Inuit communities by identifying factors that impact readiness for HIV interventions.

Social epidemiology of HIV infection (structural, social and individual determinants)

Épidémiologie sociale de l'infection au VIH (déterminants structurels, sociaux et individuels)

EPHP10.01

Gender-Based Violence Impacts Food Insecurity Amongst Marginalized Women Living with or Affected by HIV in Metro Vancouver, British Columbia

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Background: Limited research has documented the impact of gender-based violence on food insecurity among marginalized women sex workers (SWs) living with and affected by HIV, despite evidence substantiating this association in the general population. The present study examines the impact of gender-based violence on moderate-to-severe food insecurity among SWs living with or affected by HIV in Metro Vancouver.

Methods: Data were drawn from AESHA, a prospective community-based cohort of women SWs (2010-2014) enrolled through street and off-street outreach by a diverse and experiential team. The primary outcome was moderate-to-severe food insecurity, measured using a modified food security scale. The variable of interest was lifetime gender-based violence (physical and/or sexual). Bivariate and multivariable logistic regression using GEE was used to analyze the independent effect of gender-based violence on food insecurity.

Results: Of 761 SWs enrolled in the study, 64.9% (n=494) were food insecure at baseline and 79.0% (n=601) had experienced gender-based violence (lifetime). Over a third of SWs (35.2%; n=268) were Indigenous and 25.6% (n=195) identified as a gender/sexual minority. Within the 11.0% (n=84) of women living with HIV, 96.4% (n=81) were food insecure at some point during the follow-up period. In multivariable GEE analysis, experiencing lifetime physical and/or sexual violence remained independently correlated with moderate-to-severe food insecurity (AOR 4.62 [95% CI: 2.99, 7.14]).

Conclusion: Gender-based violence was associated with a 4.5-fold increase in being food insecure, with the highest rates of food insecurity among women living with HIV. These intersecting gendered risks highlight the potential for interventions that address structural violence (e.g. removal of criminal sex work laws and gendered housing and HIV care supports to reduce food insecurity) to have crosscutting impacts on both gender-based violence and HIV prevention, treatment, and care.

EPHP10.02

Substance Use Trends in Gay, Bisexual and Other Men Who Have Sex with Men seeking HIV testing in Montreal (Quebec, Canada), 2009-2016

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Substance use before or during sex is an important driver of the HIV epidemic in gay, bisexual, and other men who have sex with men (GBMSM), being strongly associated with condomless anal intercourse (CLAI). We collected data at up to three timepoints over 9 months from GBMSM in Montreal who received community-based HIV testing along with intensive HIV risk-reduction peer counseling (the SPOT project). We constructed a panel dataset comprising 2,879 GBMSM, allowing for trends analysis from 2009 to 2016. We first performed random-effects (RE) panel data analyses of substance use before or during sex by calendar time (quarterly). Compared to the 2009 baseline, we observed a decline for alcohol from 2010; for alkyl nitrites, sildenafil, speed and ecstasy from 2011; for GHB from 2012; and for cocaine and ketamine from 2013. Because first visits to the testing site are more likely triggered by at-risk behaviours, which could potentially include substance use, we then excluded data from participants' first visits and analyzed only follow-up visits since they were dependent solely on the study calendar. We then observed significant declines only in sildenafil and alkyl nitrites use. Trends for alcohol, marijuana, GHB, cocaine, heroin, LSD, methamphetamine, ketamine, crack, ecstasy, and speed decreased slightly but were not significantly different from baseline. Use of club drugs (GHB, ketamine, methamphetamine, cocaine) and sexual-enhancement drugs (alkyl nitrites and sildenafil) before or during sex was consistently higher among participants reporting CLAI with partners of unknown serostatus or HIV-positive partners with unknown or detectable viral load (at-risk CLAI). Enrolling GBMSM in regular HIV testing with intensive counselling on HIV risk reduction strategies is associated with a decline in the use of club and sexual-enhancement drugs, both of which are well-known risk factors for at-risk CLAI and HIV infection.

EPHP10.03

Changes in substance use patterns amongst people living in an HIV-specific supportive housing facility in Vancouver, Canada

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Background: Housing stability has been shown to decrease substance use and improve health outcomes for people living with HIV (PLHIV) who use drugs. However, little is known about how HIV-specific housing impacts substance use. We examined changes in drug use for PLHIV after entry into an HIV-supportive housing facility in Vancouver, Canada.

Methods: Surveys were conducted with participants at baseline (after admission to housing facility) and 12-18 month follow-up from March 2015 to October 2016. The biviariate analysis compared socio-demographic and drug use differences between those with reported decrease in drug use versus those without decrease in drug use at follow-up. Fisher's exact test was used for categorical values and Wilcoxon rank sum test for continuous variables.

Results: Among the 69 participants who completed both interviews, 27 (39.1%) reported a decrease in drug use at follow-up, 25 (36.2%) reported either an increase in drug use or no change in drug use since moving, and 16 responded not applicable. Comparatively, those reporting a decrease in drug use at follow-up (n=27) were more likely to be living at the housing facility for fewer months (median 33 vs. 35, p=0.019) and lived alone before entry into the facility (77.8% vs. 40.0%, p=0.010). Feeling emotionally supported (56.0% vs. 20.0%, p=0.034), having a better sense of community (81.5% vs. 40.0%, p=0.004), and having no depressive symptoms (66.7% vs. 24.0%, p=0.003) were also more likely among those reporting decrease in drug use at follow-up.

Conclusion: Despite nearly 40% of our sample reporting a decrease in drug use after entry into supportive housing, a large proportion reported an increase or no impact at all. This suggests that supportive housing facilities must consider social, as well as physical, aspects of housing as determinants of health, and work to address the complex and interrelated challenges faced by this population.

EPHP10.04

HIV Diagnosis on First Test and Infection Stage Among HIV+ Visible Minority MSM in BC

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Little is known about the burden of HIV on visible minority MSM in British Columbia. Currently, more than half of new HIV diagnoses are among MSM and increasingly, among MSM who identify as visible minorities (VM - i.e. persons other than Indigenous peoples who are non Caucasian). STOP HIV/AIDS is a provincial program aimed at increasing reach and engagement in HIV prevention, testing, linkage to care and treatment. HIV positive diagnosis on a client's first test and infection stage at time of diagnosis can help evaluate the STOP program.

We linked individuals with new HIV diagnoses during 2003-2015 with their previous HIV testing data from the provincial health laboratory. Clients were categorized as VM or nonVM based on self-identified ethnicity. We used logistic regressions to examine associations between VM status and HIV positive diagnosis on first test, late infection stage and acute infection stage. To examine trends between last negative and first positive test (inter-test intervals), Poisson regressions were calculated with VM status, age group and years.

1963 MSM were diagnosed with HIV during the study period. A quarter identified as VM (n=472) with a median age was 38 years (IQR: 30-46) and 686 MSM were diagnosed on their first test. The median ITI was 17 months (IQR: 7-47). VM-MSM were more likely to be diagnosed on the first HIV test (aOR=1.8, 95%CI=1.42.2) and more likely to be diagnosed in late stage (aOR=1.4, 95%CI=1.0, 2.0) after adjusting for age and whether the diagnosis year was during STOP program. No difference on VM status on acute stage or ITI was found.

The findings suggest that strengthening relationships with VM-MSM communities are needed to encourage engagement in HIV testing to ensure early diagnosis and linkage to care. However, once engaged with HIV testing, inter-test intervals show no differences between these groups.

EPHP10.05

Pathways From HIV-related Stigma to Sub-optimal Antiretroviral Therapy Adherence and Delayed Initiation Among Women Living With HIV in Canada

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Introduction: Antiretroviral therapy (ART) adherence is vital to viral suppression and health of women living with HIV (WLWH). HIV-related stigma may be a barrier to ART initiation and adherence, yet the mechanisms through which HIV-related stigma may influence initiation and adherence are underexplored. This study tested a conceptual model of pathways between HIV-related stigma and ART initiation and adherence.

Methods: We conducted a national community-based cohort study with WLWH in Ontario, BC and Quebec. We hypothesized that HIV-related stigma (including personalized stigma, disclosure, negative self-image, public attitudes) would be associated with lower likelihood of ART initiation and sub-optimal adherence (self-report of <90% of pills taken in previous month), and that social support, resilience, and depression would mediate the associations between HIV-related stigma and ART initiation/adherence. We conducted structural equation modeling using maximum likelihood estimation to test the model.

Results: Of 1425 participants (mean age: 42.8 [SD=10.6]) 12.2% (n=174) had never initiated ART. Of those on ART, 17.3% (n=216) self-reported <90% adherence. HIV-related stigma scores were significantly higher among participants who never initiated ART (mean=64.0, SD=20.2) vs. initiated ART (mean=56.2, SD=19.8) and those reporting <90% (mean=59.6, SD=19.6) vs. ≥90% (mean=55.4, SD=19.8) adherence. In independent models, HIV-related stigma was associated with lower resilience, social support, ART initiation, adherence, and increased depression. In the simultaneous model controlling for socio-demographic factors, HIV-related stigma had significant direct effects on reduced likelihood of initiating ART and sub-optimal ART adherence. Social support, resilience and depression partially mediated the associations between HIV-related stigma and ART initiation and adherence. The model fit the data well (CFI=0.91, TLI=0.90, RMSEA=0.031).

Conclusions: Findings that HIV-related stigma was associated with delayed ART initiation and sub-optimal adherence underscore the salience of multi-level HIV-related stigma reduction interventions. Strategies to improve ART initiation/adherence should address stigma and improve social support, resilience and mental health among WLWH.

EPHP10.06

Design and operational preferences of supervised injection services among people who inject drugs in London, Ontario

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Supervised injection services (SIS) are associated with reduced drug-related harms for people who inject drugs (PWID). While SIS feasibility research has been conducted in large urban centres, little is known about acceptability and operational preferences in mid-sized cities. We describe SIS design and operational preferences among PWID willing to use SIS in London, Ontario. Between March and April 2016, peer research associates administered a cross-sectional survey to PWID in London. Participants were recruited through city-wide outreach strategies, with interviews conducted at three sites to reach a diversity of PWID. Chi-square tests were used to compare characteristics and preferences by expected frequency of SIS use. Among 197 PWID, 170 (86%) reported willingness to use SIS (Median age: 39; 67% male). Of these, 106 (63%) would use SIS always/usually while 62 (37%) would use sometimes/occasionally. A higher proportion of PWID living in unstable housing, and reporting daily public injecting, crystal meth injecting and opioid injecting in the past 6 months reported that they would use SIS always/usually (all $p<0.05$). Approximately 82% preferred a private cubicle layout and 71% preferred daytime operating hours. Eighty (49%) believed PWID should be involved in SIS operations - primarily greeting clients (74%), working at the entrance (70%), registering clients (68%) or in the chill-out room (68%). The most important amenities for SIS reported included distribution of injection equipment (98%), preventing and responding to overdoses (98%), needle distribution (97%), HIV/HCV testing (96%), washrooms (94%) and nursing staff and supervised injection teaching (94%). There were no significant differences in preferences by expected frequency of use. The majority of PWID who would use SIS expressed that they would use it frequently. In order to maximize uptake of SIS, particularly among high risk users, program planners and policy makers should consider the views of PWID regarding SIS design and operational preferences.

EPHP10.07

Engagement in HIV care among women living with HIV: Results from the Ontario HIV Treatment Network Cohort Study (OCS)

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HIV engagement is often described for men versus women. However, comparisons in care engagement among women living with HIV remain unexplored. We investigated factors associated with engagement in HIV care among women in a clinical cohort in Ontario, Canada. Data was collected at 10 HIV specialty clinics participating in the Ontario HIV Treatment Network Cohort Study (OCS) in 2008-2013 using medical chart abstractions, annual interviews, and linkage with Public Health Ontario Laboratory for viral load tests. Among women, we investigated the prevalence of receiving ART and the prevalence of being virally suppressed if on ART, using generalized estimating equations with Poisson distribution and log-link function. A total of 888 women were included. In 2013, the mean age was 43.7 years (95% CI:42.8-44.6), 49% were African-Caribbean-Black, 36% were White, 9% were Indigenous, and 67% were born in Canada. In 2013, 83% were on ART, and among them 90% were virally suppressed. A greater prevalence of being on ART (Table) was associated with older age, being an immigrant, living longer with HIV, and receiving disability benefits. A greater prevalence of being virally suppressed was demonstrated in women on ART who were older and former smokers. We observed that there are sub-groups of women living with HIV who have a greater prevalence of being on ART or/and virally suppressed. Although the differences are small and the OCS represents the best case scenario of HIV care in Ontario, there is room for improvement in order to achieve the 90-90-90 UNAIDS targets in this setting.

Factors associated with being on ART and suppressed viral load among women 2008-2013

		On ART		Viral Suppression	
Factor	Categories	Unadjusted* PR (95% CI)	Adjusted** PR (95% CI)	Unadjusted* PR (95% CI)	Adjusted*** PR (95% CI)
Age (every 10 years)		1.07 (1.05-1.10)	1.04 (1.02-1.06)	1.06 (1.04-1.07)	1.05 (1.03-1.07)
Immigration Status (Immigrant vs. Being Born in Canada		1.08 (1.02-1.14)	1.12 (1.02-1.22)	1.08 (1.02-1.14)	NS
Years living with HIV (every 5 years)		1.10 1.08-1.13)	1.05 (1.03-1.06)	1.02 (1.01-1.04)	-
Employment Status (Ref: Unemployed)	On Disability	1.04 (1.01-1.08)	1.04 (1.00-1.08)	0.98 (0.93-1.04)	NS
	Employed	1.01 (0.97-1.05)	NS	1.02 (0.97-1.08)	NS
Smoking History (Ref: Never Smoked)	Current Smoker	0.97 (0.92-1.02)	-	0.92 (0.87-0.96)	NS
	Former Smoker	1.05 (1.00-1.10)	-	1.03 (1.00-1.06)	1.04 (1.01-1.07)
*adjusted for time					
**adjusted for time, history of injection drug use, race/ethnicity, income, marital status					
***adjusted for time, history of injection drug use, race/ethnicity, income, marital status, time on ART					
PR=Prevalence Ratio; NS=Non Significant					

EPHP10.08

Psychosocial health and HIV risk behaviour associations with bisexuality among men who have sex with men in Vancouver, Canada

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Background: Poor psychosocial health is an important driver of HIV risk for bisexual men. This study examined psychosocial factors and HIV risk behaviours associated with bisexuality in a mixed serostatus sample of men who have sex with men in Vancouver, Canada.

Methods: Using respondent-driven sampling, men aged ≥16 years reporting sex with another man within the past six months were enrolled into a bio-behavioural cross-sectional study between 2012-2015 and completed a computer-assisted self-interview. Multivariable logistic regression identified associations for bisexual compared to gay men. Sexual orientation was classified based on an attraction measure with a past 2-year recall period.

Results: Of the 774 participants, 80.4% identified as gay, 14.7% as bisexual, and 4.9% as other sexual identities. 33.4% reported any bisexual attraction and 22.7% reported any bisexual sexual activity. Median age was 34 years (Q1,Q3:26,47). Most were White (68.5%), had

some post-secondary education (67.4%), and earned <CAD$30,000/year (72.9%). At the multivariable level (p<0.05), bisexuality was positively associated with sexual sensation seeking (AOR=1.11,95%CI:1.06,1.16), cognitive escape (AOR=1.05,95%CI:1.02,1.08), collective self-esteem (AOR=1.16,95%CI:1.06,1.28), 'good' (AOR=2.71,95%CI:1.53,4.80), 'fair' (AOR=2.65,95%CI:1.33,5.32), or 'poor' (AOR=5.50,95%CI:1.68,17.98) compared to 'excellent' self-rated health, always using condoms for anal sex (AOR=1.97,95%CI:1.33,2.93) and avoiding anal sex (AOR=1.95,95%CI:1.36,2.81) as safer sex strategies, and cocaine/crack (AOR=1.63,95%CI:1.10,2.41) and heroin (AOR=3.15,95%CI:1.27,7.78) use in the past six months. Bisexuality was associated with lower social support (AOR=0.92,95%CI:0.87,0.97), lower odds of attending gay-specific groups (AOR=0.52,95%CI:0.32,0.83) or using apps to seek sex (AOR=0.43,95%CI:0.29,0.64) in the past month, any STI testing in the past six months (AOR=0.57,95%CI:0.39,0.84), and "poppers" use in the past six months (AOR=0.47,95%CI:0.31,0.70).

Conclusions: Differences in psychosocial health and HIV risk behaviours for bisexual versus gay men in this study highlight the need to distinguish between these groups in public health planning and policy-making, and point toward potential areas for targeted prevention and health promotion initiatives.

EPHP10.09

Examining HIV related vulnerabilities and sex work involvement among young Indigenous men and women who use drugs in Vancouver and Prince George, BC

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Objective: To examine HIV related vulnerabilities associated with sex work involvement among young Indigenous men and women in BC.

Methods: The Cedar Project is an ongoing cohort study involving young Indigenous people who use illicit drugs in Vancouver & Prince George, BC. This study included data collected between 2008-2015. Sex work involvement was defined as exchanging sex for money, drugs, food or shelter in the previous six months (p6m). HIV related vulnerabilities were organized in the following subsets: sociodemographic; historical and ongoing trauma; drug and alcohol vulnerability; sexual vulnerability; mental and physical health outcomes; and access to services and treatment. Generalized estimating equation models examined relationships between sex work and vulnerabilities in each subset. Models were adjusted for known confounders. Variables significant at p<0.10 level within each model were included in a final multivariable model. Unadjusted and adjusted odds ratios (UOR/AOR) and 95% confidence intervals (CI) were calculated.

Results: Among 515 participants, 47% had a parent in residential school and 70% had been in foster care. 9% of men and 55% of women reported sex work involvement in p6m at baseline. In adjusted analysis, those involved in sex work were more likely to be women (AOR: 8.76, 95%CI: 5.09-15.05), identify as LGBTQ (AOR: 3.58, 95%CI: 2.05-6.23), to have experienced childhood sexual abuse (AOR: 1.57, 95%CI: 1.00-2.49), to report homelessness (AOR: 1.41, 95%CI: 1.04-1.91), to have been sexually assaulted in p6m (AOR: 2.72, 95%CI:1.55-4.75), to smoke crack daily in p6m (AOR: 3.81, 95%CI: 2.60-5.59), to use injection drugs in p6m (AOR: 2.27, 95%CI: 1.64-3.13) and were unable to access alcohol and drug treatment in p6m (AOR 1.50, 95%CI: 1.24-1.81).

Conclusion: Culturally safe, community driven interventions that address intergenerational impacts of trauma, sexual violence and limited access to addiction treatment services, particularly for Indigenous women involved in sex work are urgently needed.

EPHP10.10

Using individual-level variables to investigate HIV transmission among people who inject drugs in Pakistan, 2014

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Background: The HIV prevalence among people who inject drugs (PWID) in Pakistan is high and varies by city, suggesting that contextual, behavioural, or network factors may shape local HIV subepidemics. In this analysis we tested the characteristics and behaviours of PWID in five cities for associations with HIV infection.

Methods: Descriptive analyses of behavioural data from surveys conducted among 1,453 PWID in five cities across Pakistan in 2014 were performed using STATA 11.2. Adjusted odds ratios and p-values for the association between demographic and behavioural variables and HIV positivity were calculated using logistic regression analysis

for the overall sample and Fisher's Exact tests were used for individual cities.

Results: Overall, 25% of participants were HIV-positive, and this ranged from 8% in Quetta to 45% in Karachi. In the overall sample, HIV positivity was associated with HCV positivity (OR=39.7), and having injected for five or more years (OR=0.6) or having recently received help injecting (OR=0.7) were protective against HIV infection. Upon adjusting for city of residence, HCV positivity continued to be associated with HIV but only residing in Larkana was protective against HIV (OR=0.5). In bivariate analyses stratified by city, having received help injecting was significant only in Larkana, where 8% of those who had received help were infected compared to 16% of those who had not.

Conclusions: There is some indication that receiving help with injection may be protective in Larkana, warranting some exploration into the practices of people who help with injection in Larkana and their possible connection to HIV prevention programs, which could offer an approach to reducing transmission applicable in other cities. Otherwise, individual demographic and behavioural characteristics offered few insights into what is driving HIV transmission. A subsequent analysis will assess the possible role of injection network factors in driving HIV transmission among PWID in Pakistan.

Epidemiology and Public Health: Other

Épidémiologie et santé publique : Autre

EPHP11.01

Size Estimate of Key Populations who are at Risk of Acquiring HIV and HCV in British Columbia

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Background: We designed a project to ascertain reliable and reproducible population size estimates (PSE) of key populations for use by program managers at the health authority level across BC.

Methods: We conducted a narrative literature review to identify published journal articles and grey literature containing information on PSE for men who have sex with men (MSM), people who inject drugs (PWID) and sex workers (SW) in BC. We prioritized available data sources which could potentially be updated over time to provide estimates at the health authority level. We then disseminated estimates and conducted interviews with key informants from health authorities and community-based organizations to ascertain the validity and utility of this first set of estimates.

Results: We found 82 reports from scientific journals, unpublished articles and grey literature. Of these reports, 21 contained information relevant to our objectives. For MSM, analyses of self-reported gay/bisexual identities in the 2013-2014 Canadian Community Health Survey provided estimates for each health authority (adjusted for 30% underestimate) (see Table). Data from the BC Hepatitis Testers Cohort Study, that includes data on HIV / HCV testing and surveillance linked with administrative healthcare datasets, provided PSE for PWID in each health authority (adjusted for 10% under-testing). We were unable to develop reliable PSE for SWs. Estimates were presented to 42 key informants who provided validation.

Conclusion: We developed reproducible PSEs of PWID and MSM for health authorities across BC. These estimates will fill a crucial data gap for HIV/HCV programing in BC and should be routinely updated.

Geographic Area	2015 Total Population Size (≥ 15 years)			Estimated Population Size of:			
				PWID			MSM
	Total	Male	Female	Total	Male	Female	
British Columbia	4,000,845	1,972,170	2,028,675	42,200	25,200	17,000	50,900
Vancouver Coastal HA	1,013,719	494,171	519,548	12,900	8,300	4,600	26,100
Vancouver	-	-	-	-	-	-	20,700
Fraser HA	1,455,534	719,930	735,604	13,300	8,200	5,100	11,800
Vancouver Island HA	666,343	325,016	341,327	6,800	3,800	3,000	5,500
Interior HA	636,297	314,677	321,620	5,600	3,000	2,600	5,300
Northern HA	228,952	118,376	110,576	3,300	1,700	1,600	2,200

EPHP11.02

Fracture Prediction using FRAX with and without BMD in Older HIV-Infected subjects followed-up at the Clinique Médicale du Quartier Latin (CMQL) in Montreal

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Background: FRAX is a World Health Organization fracture risk assessment algorithm for estimating the 10-year risk of major osteoporotic fracture and hip fracture. FRAX calculation could be done with or without bone mineral density (BMD) measured by a dexa scan. There is not clear evidence about the incremental benefit by including BMD in FRAX calculation.

Methods: From HIV_infected patients followed at *Clinique* Médicale *du Quartier Latin*, we included patients with age

≥50 years screened with BMD. FRAX calculation was done with and without BMD. Frax-Mean score and proportion of patients were compared using a paired t-test and paired Mc Nemar's Test, respectively. The number of patients needed to treat (NNT) was also estimated using FRAX with BMD compared to FRAX without BDM to identify one additional subject at risk of fracture in 10 following years.

Results: 532 patients with BMD measurements were included. For hip, the FRAX mean score with BMD vs without BMD was different (1.00±1.43 vs 0.81±1.28, p value=0.007). For major osteoporotic, the FRAX mean score with BMD vs without BMD was different (5.13±2.95 vs 4.92±2.75, p value=0.0190).The proportion of subject at risk of hip fracture (score > 3% in following 10 years) was different when FRAX was calculated with BMD vs without BMD (8.27% vs 4.51%, p value=0.003). The proportion of subject at risk of for major osteoporotic facture (score > 20% in following 10 years) was not significantly different between FRAX with BMD vs FRAX without BMD (0.58% vs 0.39%, p value=0.317).By comparing FRAX with BMD vs without BMD, the NNT for hip femoral was 27 subjects The NNT for major osteoporotic was 527 subjects

Conclusions For hip fracture prediction, the benefit of using BMD in FRAX score calculation seems incremental. But this incremental benefit seems low for other major osteoporotic fractures prediction.

EPHP11.03

National Practice Guidelines in Peer health Navigation for People Living with HIV

Logan Broeckaert[1], Laurel Challacombe[1], Christine Johnston[1], Erica Lee[1], Jason Altenberg[2], Glen Bradford[3], Vijaya Chikermane[4], Miranda Compton[5], Clarence Frenchman[6], Holly Gauvin[7], Scott Harrison[8], Kira Haug[9], Shazia Islam[4], Murray Jose-Boerbridge[10], Marvelous Muchenje[11], Susanne Nasewich[12], Mary Petty[8], Sudin Sherchan[4], Carol Strike[13]

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Background: For a person living with HIV to achieve optimal health outcomes, they need access to a continuum of services: HIV testing and diagnosis, linkage to appropriate medical care and other health services, support while in care, access to ART if and when they are ready, and support while on treatment. Estimates from around the world and several Canadian provinces demonstrate that people living with HIV are not optimally engaged across the HIV continuum of care. Evidence shows that peer health navigators—people living with HIV who have been trained to guide, connect, refer, educate and accompany people through systems of care--can have a significant, positive impact on the health and wellness of people living with HIV. Currently, a number of Canadian regions have established navigation programs and there is interest in others. However, there are currently no Canadian guidelines on how to deliver effective peer health navigation programs.

Methods: CATIE conducted an extensive peer-reviewed and grey literature review. We also convened a 15-member national expert working group of researchers, clinicians, public health practitioners, program planners, frontline service providers, and people living with HIV. The working group informed and developed research-based and practice-based guidelines on peer health navigation for people living with HIV. The guidelines are intended to provide direction to agencies considering the development, implementation or strengthening of peer health navigation programs.

Results: The working group has developed guidance for new and existing peer health navigation programs in HIV. Evidence-based and practice-based recommendations are available on assessing peer and agency readiness; integrating navigators into the host agency, and with community and healthcare partners; recruiting, selecting, training and supervising navigators; navigator roles and responsibilities; and related ethical and policy considerations. NEXT STEPS: The *Practice Guidelines in Peer Health Navigation for People Living with HIV* will be published in 2017.

EPHP11.04

Reaching the HIV Undiagnosed: Scaling up effective programming approaches to HIV Testing and Linkage to Prevention and Care

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CATIE, Toronto, ON

Background: There is an urgent need to improve diagnosis of HIV in Canada. Of the estimated 75,500 people who live with HIV in Canada, 21% are unaware of their status. Engagement in HIV care/treatment can only begin with a diagnosis of HIV. Early diagnosis and engagement is crucial for optimal health; it is also an effective means of preventing transmission. An enhanced effort to reach the undiagnosed includes the uptake of programmatic approaches based on new knowledge in HIV testing and the scale-up of evidence-informed approaches. We needed an opportunity to share knowledge of effective testing and linkage practice to help improve efforts to reduce HIV transmissions and improve health.

Objectives:

- To reveal priority issues in HIV testing programming
- To articulate program approaches that need to be considered to drive down the epidemic
- To discuss practice/policy shifts associated with effective approaches

- To foster multi-region, cross-sector collaboration and knowledge-sharing.

Methods: We convened a national deliberative dialogue with a group of 50 national HIV testing/linkage experts (public health policy makers, clinicians, social service providers, and people living with HIV) to discuss research and practice-based knowledge about effective strategies within and across regions and populations.

Results: This dialogue articulated priority issues to consider in improving HIV testing/linkage in jurisdictionally-relevant and population-specific ways. The priority issues that were revealed at this dialogue reflect gaps that exist in evidence on effective interventions; for example, establishing the most effective mix of testing interventions for a specific jurisdiction/context; employing the right tester for the right population/setting (i.e., physician, nurse, peer); integrating self-directed HIV testing approaches into a public health response; and establishing effective mechanisms for ensuring linkage to HIV treatment. These outcomes will inform future intervention and health system research focused on HIV testing and linkage initiatives.

Social Sciences

Sciences sociales

Aboriginal Health

Santé des Autochtones

SSP1.01

Creating an Identity: 'Who' is the AHA Centre?

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Background: The CIHR Aboriginal HIV and AIDS Community-Based Research Collaborative Centre (AHA Centre) was funded in 2012 and formally launched in 2013. This Canadian Aboriginal AIDS Network (CAAN)-led Centre unites a team of 55 Knowledge Users, Investigators and Collaborators in a 'network of networks' that strategically contributes to an effective response to HIV and AIDS-related issues relevant to Aboriginal Peoples in Canada and international Indigenous populations. The AHA Centre is guided by CBR principles and grounded in Indigenous and decolonizing methodologies as well as rights, strengths and action-based inquiry.

Issue: The AHA Centre is an integral initiative of CAAN, an organization also engaged in research. The staff and governing body of the AHA Centre have had to wrestle with creating an identity for an independent Centre that is attached to an already well-established and instantly recognizable organization. As more Centres are established to drive research innovation and development, learning how to create a stand-alone identity will become increasingly important.

Discussion: The process of answering the question "where does CAAN end and the AHA Centre begin?" has become a journey. Over 5 years, the Centre has supported and led research affecting and involving APHAs; contributed to capacity building; created and sustained partnerships and developed KT initiatives. Activities to celebrate include: recognition of Aboriginal HIV and AIDS CBR leadership, 22 grants supported and two highly evaluated Wise Practices Gatherings.

Lessons Learned: Identity creation takes time. Logo development involved more than 6 months of debate and attention to minor details that carry major cultural implications. Building an identity begins internally and rests upon a foundation that clarifies roles and responsibilities for staff and team members. Furthermore, understanding the operations linked to the Centre that could not occur without dedicated funding is useful. Finally, learning to self-promote effectively is essential to creating an identity.

SSP1.02

Experiences Of The HIV Cascade Of Care Among Indigenous People: A Systematic Review

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Introduction: The HIV cascade of care has emerged as a key framework to understand "success" with respect to HIV treatment. Yet, Indigenous leaders remain concerned that systemic oppression and culturally unsafe care impede Indigenous people living with HIV from accessing health services that make up the HIV care cascade. This review assesses evidence related to experiences of the HIV cascade of care among Indigenous people in Australia, Canada, New Zealand, and United States.

Methods: Medline, Embase, CINAHL, and Web of Science searches were conducted in March 2016 and combined keywords from three categories: (1) HIV/AIDS; (2) Indigenous peoples in Australia, Canada, New Zealand and United States; (3) HIV cascade of care. Articles published since 1996 were included if they reported primary data on cascade of care outcomes, involved Indigenous participants, and included findings disaggregated by Indigenous status.

Eligibility screening was completed by two independent reviewers. Data were extracted using a structured form by one author and verified through spot checks.

Results: Results from initial searches are presented here. A total of 4827 articles were identified, of which 82 (62 quantitative, 13 qualitative, 7 mixed methods) met inclusion criteria. Twelve involved data from Australia, 41 from Canada, 3 from New Zealand and 26 from United States. While the majority dealt with HIV testing/diagnosis (46), relatively few addressed post-diagnosis experiences: linkage to care (7); retention in care (10); ART initiation (14); ART adherence (18); and viral suppression (18).

Conclusions: With the HIV cascade of care framework increasingly the focus of global, national, and local HIV agendas, it is critical that culturally safe care for Indigenous people with HIV is available at all stages of the cascade. At present, considerable research exists related to HIV testing and diagnosis, however much less is known about experiences post-diagnosis, particularly linkage to and retention in care.

SSP1.03

Service Profile for Indigenous Women Living with HIV in Manitoba: An Environmental Scan (CHIWOS–Canadian HIV Women's Sexual and Reproductive Health Cohort Study)

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In Manitoba approximately 35% of people living with HIV are women, which is significantly greater than the national average of 22%. Of the women living with HIV in Manitoba the majority are indigenous (First Nations, Metis or Inuit). Given the demographic profile, there is a need to develop women-centered services with a particular emphasis on indigenous women. Indigenous (Ka Ni Kanichihk) and allied partners in Manitoba have come together to understand and address care needs of Manitoba First Nations, Metis and Inuit women living with HIV as part of the national CHIWOS study. An environmental scan was completed between May and August, 2016 to assess the "landscape" of services available to Indigenous women living with HIV in Manitoba. Twelve interviews were conducted:10 organizations in Winnipeg and two in northern Manitoba. All 12 organizations provide services for Indigenous women of all ages; some services are "group" specific (e.g., women who use drugs, are street involved, involved in the sex trade, and GLBTTQ). Three organizations provide services specifically for people living with HIV. All organizations referred to social determinants of health in their overall purpose or mission. While some organizations offered services in a traditional format (health care professional as expert), some organizations work from a philosophy that is rooted in peer engagement. These organizations explicitly identified the harm of disconnection as a factor in HIV etiology and consider reconnection as a solution to addressing poor health status and upstream factors that structure health outcomes. These organizations use the term "decolonize" to describe their philosophy and approach to care: "We work to decolonize ourselves and our relationships with the community". This presentation will summarize these key findings, offer reflections on what it means for organizations to use decolonizing approaches, and describe the next steps in the study.

SSP1.04

Sharing Circles with Aboriginal Women – Understanding perceptions of HIV, health, and wellbeing in Quebec

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Background: Aboriginal women are greatly over-represented in HIV cases in Canada. However, available data suggest that the HIV-epidemic is not currently as widespread in Quebec, prompting the need to better understand Aboriginal women's perceptions of HIV and experiences of health, wellbeing, and care seeking to build appropriate prevention and care strategies.

Methods: This research is imbedded within the Canadian HIV Women's Sexual and Reproductive Health Cohort Study – Prioritizing the Health Needs of Positive Aboriginal Women (CHIWOS-PAW). In Quebec, the purpose is to understand Aboriginal women's perspectives regarding HIV and overall health. In December 2015, a two-day research retreat was conducted with 14 Aboriginal women, led by Aboriginal researchers drawing on Indigenous Methodologies. Sharing circle discussions were collaboratively analyzed and validated in an interactive workshop.

Findings: Fourteen diverse Aboriginal women participated; they ranged from 24-74 years of age; Inuit, Métis and First Nations were represented from 12 different communities; and seven distinct languages were spoken. HIV-status varied from HIV-positive, HIV-negative, and HIV-status unknown. In the sharing circles, emphasis was placed on root causes of HIV, including gendered violence, unequal relationships, and intergenerational trauma. Recommendations for improving the care and prevention response included ensuring safe spaces for women to meet, share, and learn from one another. Programming must also be peer and youth led to be effective. Strategies to ensure confidentiality within health care settings, and when seeking risk reduction services should be improved. Education and awareness regarding HIV must also be revived to communicate the risks of transmission and to dispel persisting HIV misconceptions, stigma and discrimination.

Women also exchanged stories of self-care and building self-esteem as part of overall health.

Conclusion: Aboriginal women identified key strategies for improving prevention and care including increasing awareness and education, creating safe spaces, fostering peer led efforts, and addressing root causes of HIV.

SSP1.05

Results of the Environmental Scan in Saskatchewan

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Background: There are increasing rates of Indigenous women becoming infected with HIV in Canada (PAW). This fact combined with the complex historical context along with emotional, social and economic environments has resulted in concerning reports of healthcare under-utilization by PAW. The CHIWOS-PAW study is a sub-project of the Canadian HIV Women's Sexual and Reproductive Health Cohort Study (CHIWOS) and will allow for regional epidemiologic, clinical and access to care differences to be assessed across Canada. The current analysis presents the results of the environmental scan that was completed in Saskatchewan.

Methods: In line with the review completed by METRAC and The Star, we conducted an environmental scan of 37 community organizations in Regina, Saskatoon and Prince Albert and surrounding areas. The environmental scan was completed from the months January 2016 to August 2016. The scan was designed to: 1) Assess the "landscape" of services available to Indigenous women living with HIV in Saskatchewan; and, 2) Better understand where women get Clinical assistance met. We scanned websites for information and followed up with phone calls and asked specific questions to ensure we had the most up to date and robust information.

Results: Under the guidance of an Elder, started with ceremony to launch the scan and took guidance from our Provincial Steering Committee. Our presentation will provide an overview of the organizations and services that are available for Indigenous Women's population living with HIV/AIDS in the three major Saskatchewan cities and surrounding areas. A brief overview of each of these cities will highlight the successes and areas of improvement that are needed in each community.

Conclusions: We will also provide recommendations for next steps and moving forward in the project. We will emphasize the importance of acknowledging resiliency and strengths of Indigenous women that was revealed through the environmental scan.

Combining Prevention Strategies: Social Scientific Perspectives

Combinaison des stratégies de prévention : perspectives des sciences sociales

SSP2.01

Testing for HIV, HCV and other Bloodborne Infections (STBBIs) Among Young People: A Public Health Priority?

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Background: Current epidemiological evidence indicates youth aged 16-30 are particularly vulnerable to STBBIs, and represent the highest proportion globally, including HIV and HCV. Testing is therefore an intervention, however, access to testing remains variable and certain priority populations experience significant challenges in access to, and uptake of, testing. These challenges are particularly relevant to key youth populations including those who are: street-involved; injection drug users; MSM; and resident in rural and remote locations. This project- based on qualitative data from two HIV and HCV prevention studies in Canada and Scotland - explored issues around testing, with the aim of better understanding the needs of youth at enhanced risk for infection.

Methods: Combined analysis of qualitative data that emerged from individual and focus group interviews with youth, and stakeholders with knowledge, or experience, of accessing HIV, HCV and STI prevention services. Data were analysed thematically, with a focus on identifying key themes around access to, and normative dimensions of, testing.

Results: Three overarching themes were: peer and community norms as a factor in informing access to testing; geographical location as a factor in testing uptake; and the need for 'community relevant' HIV, HCV and STI prevention and testing information. Access to testing was particularly difficult for youth in rural/remote locations; and intersected with, and enhanced, concerns around anonymity and confidentiality. Youth identified the need for more community relevant information to support them in identifying risk factors and accessing testing services.

Conclusions: Future sexual health promotion interventions must align with the global push to reduce rates of STBBIs among youth, recognizing local community contexts of risk in relation to testing stigma; norms and attitudes towards testing; and access to testing services. In line with the UNAIDS '90-90-90' targets, access to a variety of methods of testing must underpin integrated prevention approaches.

SSP2.02

Wireless Physical Activity Monitor Use Among Adults Living with HIV: A Scoping Review Protocol

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Background: Physical activity is a self-management strategy with the potential to address health-related challenges and enhance health outcomes for people living with HIV (PLWH). Wireless physical activity monitors (WPAM) are becoming increasingly popular as an objective tool to measure physical activity. However, little is known about the use of WPAM and their measurement properties among PLWH.

Purpose: To characterize the literature pertaining to wireless physical activity monitor use among PLWH.

Methods: We will conduct a scoping review using the Arksey and O'Malley Framework to answer the question: What is the nature and extent of evidence pertaining to WPAM use among PLWH? We will search databases including: MEDLINE, EMBASE, CINAHL, PsycINFO, PubMed, Cochrane, reports, and websites from January 1980-January 2017 for literature pertaining to WPAM use among PLWH. We will independently screen abstracts to include peer-reviewed and grey literature evidence pertaining to WPAM use among PLWH with any study design, and published in English. We will extract data from included studies including: authors, study location, year published, study design, purpose, population, outcomes of interest (and measures), intervention (if applicable), type of WPAM use, context for WPAM use, results, and overall conclusions. We will describe the characteristics of the literature using frequencies (percent) and medians (interquartile ranges) for categorical and continuous variables, respectively. We will synthesize data pertaining to results and conclusions using content analytical techniques. Where applicable, we will specifically report on: a) the measurement properties of WPAM and b) their use as an intervention to enhance physical activity among PLWH.

Results and Conclusions: To our knowledge this will be the first scoping review to characterize the evidence on WPAM among PLWH. Results will help to characterize the emerging evidence about what is known and not known regarding the WPAM as a tool to measure and enhance physical activity for PLWH.

SSP2.03

Acceptability of New Prevention Technologies among Key Populations in South African Townships: Integrating Social and Biomedical Approaches

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Background: To support a Fast-Track approach to HIV, we explored location-population-specific acceptability of new biomedical prevention technologies (NPTs) in townships near Cape Town, South Africa, with the world's largest HIV epidemic.

Methods: From October 2013-March 2014, community outreach staff recruited Xhosa-speaking adolescents (15-17 years-old), heterosexual adults, and adult men who have sex with men (MSM) in two underdeveloped, informal townships. We conducted 6 focus groups (FG)(2/population; n=36), 12 in-depth interviews (IDI)(4/population), and 8 IDIs with healthcare providers (N=56). FGs and IDIs explored acceptability, and perceived risks and benefits of pre-exposure prophylaxis (PrEP), future HIV vaccines, rectal microbicides and vaginal rings. FGs/IDIs were transcribed, translated and coded thematically using framework analysis.

Results: Initial overwhelming acceptability of NPTs revealed, on further exploration, concerns about pervasive challenges in integrating NPTs into everyday life. Adolescent and adult women preferred vaginal rings and HIV vaccines, with concerns about male partner/husband reactions and violence amidst economic dependence, partners' inconsistent condom use, and ubiquitous rape. Male adolescents preferred HIV vaccines given longer duration of protection, and stigma and costs of procuring PrEP. Heterosexual adult men preferred PrEP given familiarity with pills and mistrust of HIV vaccines. Adult MSM preferred gel-based rectal microbicides, perceived as familiar and user-friendly, with concerns about dosing frequency given unplanned sexual encounters, stigma, and frequent rape. All groups expressed antipathy towards healthcare venues, described as geographically inaccessible, overburdened and stigmatizing, as sites for accessing NPTs. Healthcare workers highlighted pervasive social-structural (poverty, unemployment, alcoholism) and behavioral challenges (risk compensation) for NPT implementation.

Conclusions: Despite high NPT acceptability, biomedical technologies are unlikely to circumvent enduring contexts of poverty, racism and gender- and sexuality-based violence underlying HIV epidemiology in South Africa, which may impede translation of NPTs into daily life. Tailored combination prevention strategies integrating social and

biomedical approaches may support NPT effectiveness in controlling HIV.

Critical Approaches to Community-Based Research

Approches critiques à la recherché communautaire

SSP3.01

Outcomes of a 2016 community-based consultation on HIV/AIDS research priorities for Quebec

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Background: In the landscape of HIV/AIDS research in Quebec, community-university partnerships have a long-standing and fruitful history. In 2013, a forum brought provincial stakeholders in community-based research together for the first time. In 2016, the 2nd "Rencontre de recherche communautaire VIH/sida" was organized in Montreal to revisit research priorities and promote community leadership in research. An online consultation preceded the face-to-face meeting.

Method: The project was guided by the principles of community-based research and implemented the following method: 1) establishment of a working committee comprising representatives of community-based organizations and academic researchers; 2) implementation of a DELPHI consultation survey in order to identify research priorities; 3) organization of an in-person meeting in Montreal to disseminate the results of the consultation and facilitate the development of new research projects; 4) process evaluation and evaluation of the meeting.

Results: A total of 77 participants (stage 1) and 46 participants (stage 2) from across Quebec answered the DELPHI survey. They ranked research priorities in terms of relevance, then listed concerns related to the following four top-ranked priorities that were retained as the focus for the meeting : 1) Access to health care and services, 2) Stigma, discrimination, criminalization, 3) HIV Prevention; 4) Aging, comorbidities, cognition. Seventy participants took part in the two-day meeting in Montreal and brainstormed research questions. Potential research projects were identified to address key gaps in current community-based research. The evaluation of the consultation process and of the meeting itself shed light on the challenges of providing meaningful *capacity-bridging* opportunities and engaging various stakeholders, in particular those outside Montreal, in the development of research projects.

Next steps: Results of the consultation will be widely disseminated. Next steps include further development of the proposed projects to secure funding. Key priorities will be revisited again in 2019.

SSP3.02

Perceptions and Experiences of Health Service Delivery for Women Living with HIV in the Maritime Provinces, Canada

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Community-based organizations play an important role in providing services to people living with HIV worldwide. Changes to the HIV service paradigm, including the broadening mandate to address sexually transmitted and blood-borne infections and the shift towards service integration, will affect people living with HIV. Denied project funding by the Public Health Agency of Canada to historically funded HIV organizations has caused significant changes to be made to these agencies. For example, some essential disease-specific programming that people living with HIV have come to rely on, including transportation or support groups, are no longer available. Prevention efforts for a wider range of conditions of public health importance are in place instead. The effect of these changes can already be felt in communities. Even a simple name change by HIV organizations can act as a barrier to service access or lead to feelings of abandonment for people living with HIV.

I have used interviews and geographical information software (GIS) to document women's experiences accessing health and social services in the Maritime Provinces. GIS visualizes the availability of services to better understand the challenges faced by women in communities, especially mapping the navigation of social service and referral systems by women. Taking place in the Maritime Provinces from 2014 to 2015, the purpose of the project was two-fold: (a) assess the quality of HIV services currently being offered in the Maritime Provinces, and; (b) consider the future direction of HIV treatment and care for women, especially those in remote communities. Findings indicate that women living with HIV, by and large, want a woman-centered approach to care to better address their needs, including emotional support, re-entry programming, and food vouchers. Online networks and mobile outreach services will also help to meet the needs of women.

SSP3.03

Lessons learned: employing Indigenous Methodologies to understand Aboriginal Women's perceptions of HIV prevention and care in Quebec

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Background: Approaches to HIV-research with Aboriginal communities in Canada must focus on both strengths and challenges. For Aboriginal women, vulnerability to HIV is structured by gender inequities, colonization, racialization and social immobility (poverty, education). Importantly, these vulnerabilities coexist with resilience, cultural continuity and strength. A history of exploitative and misrepresentative research encounters also creates the necessity for employing Indigenous methodologies in research. This abstract details lessons learned in conducting four full-day workshops with Aboriginal women in Quebec, drawing from Indigenous methodologies.

Methods: The research is imbedded within the Canadian HIV Women's Sexual and Reproductive Health Cohort Study – Prioritizing the Health Needs of Positive Aboriginal Women (CHIWOS-PAW). In Quebec, the purpose was to understand Aboriginal women's perspectives and strategies regarding HIV prevention, care and overall health. Between December 2015 and December 2016, under the direction of Aboriginal leaders, two research retreats, a community analysis workshop, and a celebration event were conducted with 14 Aboriginal women.

Findings: Our research process allowed us to draw the following recommendations. Strengths included: 1) incorporating culturally-adapted sharing circles, arts, and ceremony encouraged participation, safety and comfort during the research; 2) conducting numerous workshops with the same women was valuable to participants and researchers; 3) validating findings with participants was an essential step to ensuring that the knowledge, experience, and priorities of Aboriginal women were respected. Facilitators to our process included: 1) existing networks with Elders, art-therapists, musicians; 2) a strength-based, neutral space to conduct the research (e.g. Aboriginal Art Gallery); 3) experienced Aboriginal researchers with facilitation skills; and 4) sufficient funds and coordination support to plan and carry out multiple events.

Conclusion: Adopting a strength-based, culturally-adapted, peer-lead approach is essential to conduct effective and ethical research with Aboriginal women. Further work, *by, with*, and *for* Aboriginal women is needed to address HIV in Canada.

SSP3.04

A Critical Examination Of Housing Services For People Living With HIV And Recommendations For Action

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Background: *Positive Living, Positive Homes* (PLPH) is a community-based study exploring the interactions between health and housing for adults living with HIV in three case study sites in BC (Prince George, Kamloops, and Greater Vancouver). In this paper we describe the benefits and challenges of accessing and using housing services described by participants and preliminary recommendations for action.

Methods: Ninety-nine adults living with HIV along with 50 service providers and policy makers participated in qualitative, in-depth interviews as part of PLPH. In keeping with the tenets of CBR, responses to questions about provision, accessibility, use, and experience of housing services were analyzed in a participatory manner with community advisory groups in each site. Community members are also participating in generating action recommendations.

Results: Although responses varied according to services accessed, some key themes emerged. In addition to support in obtaining housing, participants highlighted the need for more variety and continuity in housing-related supports (e.g., with budgeting and other skills that help maintain stable housing; with confronting discriminatory practices in the rental market, etc.). Many participants also experienced frustration and confusion when applying for subsidized housing, given the number of different housing providers and their varying application processes. Participatory analysis and knowledge translation activities are leading our team to produce change tools, including a guidebook for service providers on supporting HIV-positive clients with housing needs over time, and a comprehensive list of subsidized housing providers and their application processes for each site community.

Conclusions: Participant responses illuminated what works and what is challenging about housing services and revealed the need for advocacy on a number of fronts. The participatory approach to analysis and knowledge translation is allowing our team to address that need by developing user-friendly, relevant resources to improve housing for people living with HIV.

Critical Social Theory: Applications and Advancements in Understanding the HIV Epidemic

Théorie sociale : Applications et progrès dans la compréhension de l'épidémie de VIH

SSP4.02

Nothing was the same: The role of HIV in shaping infectious disease physician advocacy in Canada

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Background: The field of infectious diseases (ID) has long been a fertile ground for advocates. ID practitioners have historically and contemporaneously advocated for a change in the poor social conditions that accompany so many communicable diseases. This project aims to interrogate how advocacy has been conceptualized in the field of ID and what factors shape the way Canadian ID practitioners conceive of themselves as advocates.

Methods: Discourse analysis was used to explore and understand the intersections of ID and advocacy, drawing from Foucauldian analytic approaches. The textual archive included formal curricula and standards, including Royal College of Physicians and Surgeons of Canada objectives and training requirements for Adult Infectious Diseases from 1982 to the present. The broader scholarly literature, namely the table of contents, editorials, and seminal articles from the journal *Clinical Infectious Diseases,* were analyzed to link trends in curricular and professional objectives to broader conversations taking place in the field of ID.

Results: Since the inception of the field of ID in Canada, the dominant discourse of *impending threat* is evident. HIV largely shaped the ways in which ID specialists positioned themselves within the healthcare setting, and determined how they conceived of themselves as advocates. The threat of HIV made possible certain things, connecting the field and its practitioners to a broader social movement that included access to treatment and prevention, and an emphasis on broader social determinants of health like housing, drug use, and stigma.

Discussion: As HIV has largely morphed into a chronic condition in North America, it is essential for ID practitioners to reflect on the types of advocacy and activism made possible by the HIV movement. Such reflection is key to continuing the fight for equitable access for all individuals, and to ensuring that the lessons learned from the movement are not forgotten.

Engaging (with) Communities in HIV Research

Participation des collectivités à la recherche sur le VIH

SSP5.01

The Positive Plus One study: Enrollment and comparison of the survey sample to the distribution of people living with HIV across Canada

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Importance: *Positive Plus One* is a national mixed-methods study of HIV-serodiscordant couples that aims to include people from various backgrounds and regions of Canada. Approximately one-quarter of people living with HIV in Canada are in serodiscordant relationships, this study helps to illuminate who these couples are.

Objective: This paper describes: the HIV-positive people in the sample recruited to date; compares their distribution to 1985-2015 PHAC surveillance figures; and examines recruitment of their HIV-negative partners.

Methods: People were recruited to participate in online/telephone surveys with the assistance of 142 clinics and ASOs/NGOs across Canada, and via social media. First, the sample distribution of people living with HIV was compared to PHAC surveillance data on sex, age at diagnosis, ethno-racial identity, and region. Second, participation of HIV-negative partners was examined across groups and regions. Chi-squared tests were used for all analyses.

Results: To date, 361 people have participated (210 HIV-positive, and 151 HIV-negative partners). Relative to the PHAC data, the sample underrepresents HIV-positive people who were over age 29 at diagnosis, are men, people who identify as Indigenous or Black, and those who are from Quebec and British Columbia ($p<0.0001$ for all comparisons). Of the HIV-positive people in current relationships enrolled in the study, 43% also have their HIV-negative partner enrolled. HIV-negative partners of Indigenous People, Latin Americans ($p=0.03$), and heterosexual men ($p=0.006$) were less likely to be recruited.

Discussion: *Positive Plus One* is the most comprehensive survey of serodiscordant couples in Canada to date. While selection may confound our estimates, the study continues to pursue outreach among underrepresented groups. However, findings may also reflect genuine population-level differences from PHAC surveillance data. If so, these data suggest that people diagnosed later in life, Indigenous and Black people, and those from specific regions of Canada may be less likely to form serodiscordant relationships.

SSP5.02

Portraits Against Stigma

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Background: Science for treatment of HIV has progressed significantly over the last 30 years, leading to HIV becoming a chronic manageable disease. However, **stigma associated with HIV is reported by many to be worse than the disease**.

As part of a World AIDS Day 2016 projects, the Oak Tree Clinic (OTC) in BC Women's Hospital, Vancouver worked with HIV+ women (WLWH) on a portrait series to highlight their experiences of - and to mitigate - stigma.

Methods: Two practicum students and two clinical staff created the concept. Invitations to participate were circulated to 4 local HIV women/youth peer support groups. Over two months, the 2 students took photos and recorded the words of the women who chose to take part in the project during their support groups. Participants were asked for 3 words that they associated with stigma, and then one "power word" which properly represents them. Women also spoke about themselves and their lives. Their words were transcribed verbatim. The portraits were developed individually, and also combined in booklet form, with the women's life stories.

Results: Across the 4 support groups, 25 women and youth chose to participate. **Those who participated felt empowered** and welcomed the opportunity to educate the public to their personal experience of stigma. **Some women spoke out for the first time.** Portraits were displayed on World AIDS Day in BCWH, and the booklets were distributed to various HIV ASOs and key individuals.

Additionally, on World AIDS Day, the CBC interviewed one of the participants in the project along with the lead staff.

The images are displayed on several websites, Twitter and Facebook.

Conclusions: Involving WLWH in this project was empowering to them; increased resilience; and promoted dialogue within the groups and the public.

The responsibility to stand up against Stigma belongs to all of us.

SSP5.03

Prévention du VIH et culpabilité associée aux prises de risque chez les hommes gais. La participation à l'étude IPERGAY est-elle un facteur d'empowerment ?

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L'essai IPERGAY, mené en France et au Québec de 2012 à 2016, a démontré l'efficacité de l'utilisation intermittente de la prophylaxie pré-exposition. Outre la mise à disposition de médicament, l'étude offrait des dépistages réguliers, un counselling et l'accès à des préservatifs. Les questions de recherche en sciences sociales ont avant tout porté sur les risques de désinhibition préventive. La présente sous-étude propose d'explorer, à partir des données qualitatives collectées dans IPERGAY au Québec, la manière dont la participation à cet essai est un facteur d'empowerment et de meilleure confiance en soi. Ce travail s'appuie sur une analyse en profondeur des entrevues qualitatives menées auprès d'un échantillon de 13 participants d'IPERGAY. Ces hommes séronégatifs ont pris part à trois entretiens au cours de l'essai (inclusion, 6 mois et 18 mois).

Les résultats démontrent que la participation à IPERGAY ne produit pas des effets homogènes sur les attitudes et les représentations vis-à-vis du risque pour le VIH. Pour une majorité de participants, l'essai a permis un travail de conscientisation du risque. Cette prise de conscience produit des effets divers : pour certains, elle s'accompagne d'une relativisation du risque VIH, qui contribue à diminuer le sentiment de culpabilité ; pour d'autres, la participation à l'essai redéfinit la frontière morale entre « bons » et « mauvais » sujets de la prévention. IPERGAY apparaît alors comme une manière d'affirmer un comportement sexuel responsable. Dans les deux cas, le soutien apporté par l'équipe de l'essai (counseling, suivi médical) contribue à déculpabiliser leur propre rapport au risque.

Ces analyses soulignent l'importance d'envisager les essais de prévention comme un levier potentiel d'empowerment individuel. Dans un contexte communautaire marqué par la réprobation morale des pratiques sexuelles à risque, l'étude IPERGAY a transformé la capacité d'agir des participants, sans pour autant leur faire abandonner le souci de prévention.

SSP5.04

HIV-Related Stigma: A Qualitative Analysis of the Lived Experiences of Current and Former HIV-Positive Male Federal Inmates

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Background: The HIV prevalence rate inside Canadian Federal Penitentiaries is estimated to be 7 times higher than the rate in the general Canadian population. Additionally, a survey of Correctional Services of Canada (CSC) HIV-positive inmates showed that over half were worried about HIV-related stigma while incarcerated. This study of HIV-positive current and former inmates, the first Canadian study of its kind, investigated participants' lived experiences in and out of prison. Topics included experiences of stigma and disclosure of HIV status.

Methods: This study consisted of semi-structured, in-person interviews. A total of 9 interviews were conducted with 3 currently incarcerated and 6 recently released HIV-positive males. Currently incarcerated participants were recruited through the Ontario Region of CSC. Formerly incarcerated participants were recruited from social service organizations in Kingston, Ontario, that focus on working with formerly incarcerated individuals.

Findings: Participants reported experiencing or witnessing enacted, perceived and internalized stigma in and out of the prison environment. Experiences of enacted stigma ranged from verbal insults to being ostracized, threats of violence, and actual violent attacks. Variations in experiences of enacted stigma were explained by non- or limited disclosure based on fears of discrimination, as well as perceived standing in the prison hierarchy. Additionally, the majority of participants reported having experienced a variety of childhood traumas and feelings of poor self-worth and suicidal ideation.

Conclusion: HIV-related stigma is a common experience of HIV-positive current and former inmates. Although there are HIV prevention programs including testing, bleach kits, condom distribution, and HIV treatment within CSC prisons, there are no reported programs that specifically target the reduction of HIV-related stigma. As a result, future research is needed to develop and evaluate possible avenues for intervention to prevent experiences of stigma, both within and outside of the prison environment.

SSP5.05

Community engagement critical to rapid PrEP implementation - experiences from New South Wales, Australia

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Across the globe, as the efficacy of PrEP has been established, communities affected by HIV have been mobilising to increase access to this essential HIV prevention tool. In New South Wales (NSW), the most populous state in Australia, community based organisations such as ACON have been at the forefront of community education and engagement on PrEP access and uptake.

A strong partnership between community-based organisations, clinicians, researchers and government has underpinned the HIV response in Australia. This partnership was leveraged to develop and implement PrEP implementation trials.This presentation will focus on the work ACON has led to increase community awareness about PrEP, advocacy to improve PrEP access and its work on research studies to ensure community awareness and acceptability. A brief evaluation of ACON's PrEP campaign work will also be presented.

ACON's PrEP campaign reached 154,509 people online over Facebook and 27, 397 people over Instagram. In a random online survey of gay community in NSW, 63% of respondents reported having seen the PrEP campaign. Over half of all respondents who had seen the advertisements took some further action.

Over 2016 ACON has engaged in community outreach both physical and online, a range of community forums on PrEP across NSW and has developed resources to assist gay and bisexual men to engage in personal importation of PrEP. The PrEP implementation trial in NSW, on which ACON has led with communications, has enrolled over 4000 participants over the March to December 2016 period and remains open to enrolments.

The role of community based organisations like ACON remains central to effective engagement with affected communities around innovate HIV prevention tools such as PrEP. Community driven health promotion campaigns, peer-led education about HIV prevention tools and intersectoral partnerships have proven successful in the rapid scale up of PrEP in NSW Australia.

SSP5.06

Community engagement prior to study onset improves the research question and study outcomes

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Background: Community engagement is paramount in creating a well-designed research study involving human participants. In 2010, we engaged the community from Sunshine House, a community-based health promotion organization working with street-involved individuals, majority of whom are indigenous, through a series of dinners and meetings. The research team and Sunshine House community members met and exchanged experiences regarding: health concerns, research studies and knowledge translation activities. Overall, the community was very open to the research and satisfied with the proposed study methods. With this relationship established, we were ready to address our research question: if the immune response is modified by solvent uptake and how this affects HIV.

Hypothesis: Community engagement prior to study onset will improve the research question and create an important relationship between the community members and the research team resulting in better quality research.

Methods: Before onset of the research study, several meetings with the Sunshine House community occurred to establish new relationships. Following these meetings, interested community members were invited to visit Dr. Fowke's lab. The group participated in a discussion about the immune system, visited the lab, received a demonstration of how the samples will be processed and analyzed and given the chance to partake in some science experiments.

Results: The community engagement and knowledge translation period prior to study onset created trust between the community and the researchers, outlined which questions were important for the community and where their interest in health research laid. Community members who attended the lab tour returned to Sunshine House enthusiastic about the study and became informal research ambassadors which, greatly facilitated study enrollment.

Significance: The use of community engagement and knowledge translation is an instrumental part of study design. It helps refining the research questions assisting in study enrolment, and increasing study relevance, thereby improving the study's quality.

SSP5.07

HPV Literacy: Engaging with Positive Women to Understand Cancer Risks, Screening Procedures and Prevention Options

Joanne D. Lindsay

CANOC Community Investigator, Toronto, ON

Overview: The value of HIV research became apparent to Joanne after a Community Forum on anal cancer led her to discover screening was only available through a lab established with a research grant. Concerned about the health of Positive Women, she became a Community Investigator with CANOC (Canadian HIV Observational Cohort Collaboration), seeking to explore links between HIV, HPV and cancer risks. The presentation reflects on her learning process with an HIV clinical/epidemiology research community, as she transitions from community member to researcher to community educator.

Approach: Literature and data review led to an overview of clinical practices for screening and treatment options. With support of epidemiologists, biostatisticians and research scientists, Joanne's community role became that of an HPV literacy tutor, presenting data analysis and research findings to HIV+ women's groups in Toronto and to Positive Women's Network - USA at SPEAK UP! 2016.

Lessons Learned: Presentations identified for community learners the screening gaps for some HPV related cancers amongst HIV+ women, despite their increased risk for cancer, as people with both HIV and HPV. Through HPV literacy sessions with HIV+ women, researcher and community members share stories of their collective experiences with prevention, screening and treatment options available to them. Together, they identify deficiencies and gaps in access to health care and cancer prevention for women with HPV.

Conclusions: Exploring how HIV+ community members, specifically HIV+ women, should find ways to involve themselves in cancer research, so as to improve their health care and clinical outcomes, can lead to advocacy for improving access to prevention, care and treatment for all in the HIV+ community. The community investigation has led to shared learning about strategies HIV+ women can take to ensure access to prevention, screening and treatment of HPV related cancers, and strategies to increase research participation by HIV+ women.

SSP5.08

GIPA in the Family Matters Research Project: Community Engagement from Conception to Completion

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Background: The Canadian Aboriginal AIDS Network (CAAN) membership has consistently identified the importance of understanding the effect of HIV on Aboriginal families, and implications for providing culturally adequate and appropriate supports and services in this context, the CBR approach taken by the *Family Matters* research team has led to rich data on the complex realities of living with HIV as an Aboriginal family and family-oriented care, treatment and support service needs.

Objectives: The objectives of this research project were to:

1. Identify HIV-related supports, services, policies, and programs for APHAs and their families;
2. Explore the impact of HIV on the family from different perspectives; and
3. With Aboriginal families affected by HIV identify priorities for Aboriginal culturally informed, family-based intervention program options.

Methods: We began by hosting a pre-grant focus group that informed our direction. Within a CBR framework the research team applied Indigenous and two-eyed seeing approaches to engage with family members across Canada. An online survey gathered details regarding programs and policy; story telling circles gathered data from family members and APHAs; collaborative team analysis prepared coding for a National gathering to fully review and reflect on the data.

Discussion: Research process can be just as important as research findings. The Family Matters team embraced the Greater Involvement of People Living with HIV (GIPA) and the Meaningful Engagement of People Living with HIV (MEPA) principles throughout the project with spectacular results. This presentation will: highlight how the team included APHAs and their families in all areas of the research project to ensure: scientifically rigorous Indigenous research, responding to community identified needs, operationalizing GIPA in an indigenous research setting, and embracing culture and the inclusion of ceremony in research to create a safe environment for research participants and to enhance the richness of data.

SSP5.09

Social Changes from the Ground Up

Haleh Raissadat

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HIV and AIDS epidemic remains to be one of the challenges of the era with over 35 million infected individuals around the world. There have been countless local, national and international efforts to prevent, treat and educate people on HIV and AIDS. Today, we know that in order for the HIV and AIDS education to be effective, it needs to be culturally sensitive, gender specific and age appropriate. Youth have particular educational requirements that need to be addressed properly. Youth need to be involved in the solution and advise policy makers of their needs. Furthermore, in order for the solutions to be sustainable, youth have to become the advocates for the solution.

One of the effective methods in involving youth to produce sustainable social change around the issue of HIV and AIDS, especially among marginalized population, is use of participatory arts-based research method. This is a community based research method that uses arts to creatively inquire knowledge, and involves participants in producing knowledge. Photovoice is a participatory arts-based method that is getting attention especially in Sub Saharan Africa and among First Nation in Canada. Photovoice is a process by which people can identify, reflect and represent on the critical issues in their personal lives or their community through captioned or not captioned photography. Using photovoice, marginalized people are educated and empowered to voice their concerns, especially about issues that are taboo or controversial, to policymakers and service providers. Through photovoice youth can participate in developing a sustainable solution that allows them to explore issues that policy makers would not know about otherwise.

The focus of this paper is to explore how photovoice could be a sustainable method in addressing HIV and AIDS education in communities where HIV and AIDS are considered cultural taboo.

SSP5.10

Closing the Gap on HIV Issues in Manitoba Through Collective Impact

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The Manitoba HIV Collective Impact Research-Evaluation-Action Network was launched in March 2016 and for the

first time has brought together previously siloed partners including researchers, community-based organizations, regional health authorities, policymakers, indigenous organizations, peers and others in Manitoba to work together on common HIV goals.

We understand HIV issues in Manitoba as "complex" and requiring a systems approach to understanding and making change. This is why we have adopted a collective impact approach. There is an increasing rise of collective impact networks in North America, Europe and Australia as it is being recognized that "no single organization has the ability to solve any major social problem at scale by itself. Collective impact is a powerful new approach to cross-sector collaboration that is achieving measurable effects on major social issues".[1]

Since March 2016 we have been able to secure funding for coaching (Innoweave McConnell Foundation) to develop the collective impact network and funding for key activities including research projects on Stigma (CIHR) and Community Readiness(REACH 2.0) in the North. We have held two significant events and are developing our operating structure, including a shared leadership model and evaluation framework.

In this presentation we will discuss our on-going journey and process to build the network, our early wins, challenges and lessons learned as we discuss our early days for the Network and for collective impact. We will discuss how we think this collective impact approach will make a difference to HIV issues in Manitoba and also engage the audience in discussion on this approach.

[1] Kania J., Kramer M. (2011). Collective Impact. Stanford Social Innovation Review.

Everyday Actualities of Living with HIV

Vivre avec le VIH au quotidien

SSP6.01

Living with HIV: The need for publicly-funded rehabilitation vs availability in Canada

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HIV is now considered to be a chronic health condition, and is often complicated by multiple comorbidities related to ageing, exposure to medication, and the effects of the virus. More than 30% of people living with HIV (PLWHIV) in Ontario were found to be living with at least one other physical condition (Kendall, 2014). Physiotherapy, and other rehabilitation services, are well placed to assist people living with chronic health conditions manage symptoms and functional impairments (CPA, 2012). Poor health is a predictor of decreased income resulting partly from decreased labour force participation (Conference Board of Canada, 2013). Therefore, when people living with chronic health conditions, including HIV, look to access rehabilitation services, they may not have the capacity to pay out-of-pocket.

An environmental scan of the publicly-funded rehabilitation services across Canada was conducted in 2016. Three cities (or towns) each were selected from a cross-section of Canadian provinces and territories ensuring geographical representation from across the country. Web-based searches were conducted for each area chosen looking at the publicly-funded out-patient/community-based physiotherapy, occupational therapy, speech language pathology services for adults aged 18-64.

The scan found that, although publicly-funded rehabilitation is available in each area looked at, there are not enough spaces for all people living with chronic health conditions to participate, and services are disproportionately located in urban centres (Camp et al 2015, Realize, 2016). Realize is aware of only one community-based HIV organization in Canada which offers rehabilitation services, specifically occupational therapy, for PLWHIV. Another is planning to offer physiotherapy and occupational therapy in late 2017. This presentation will delve into the findings of the environmental scan of publicly-funded rehabilitation services across Canada and offer creative examples that are being used or could be used to improve access to rehabilitation services for people living with HIV and chronic health conditions.

SSP6.02

The Impact of In-clinic Support Groups for Adolescents Living with HIV

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Background: Children living with HIV can exhibit increased symptoms of stress/anxiety, depression and low self-esteem. They can also face issues related to stigma, discrimination and disclosure and sometimes struggle with transitioning to adult care. We describe a mutual-aid support group for adolescents living with HIV at SickKids hospital facilitated by The Teresa Group social work staff. Following a 3-month pilot, the program was incorporated into regular clinic days twice a week.

Methods: The Teresa Group staff facilitated groups that ran during regular clinic hours twice a week (9.30am to 11.30am). Attendance was voluntary. SickKids staff discussed the option of attending the group with all adolescent clinic patients. Returning group members were encouraged to invite their peers to attend.

Results: Over an 8 month period, 40 group sessions were held with up to 8 attendees at each (mean=4). 65 individuals attended at least one session; 50% attended multiple sessions. 68% were male. Eight youth who had not previously participated in other The Teresa Group programs

became more engaged in programming, such as external support groups, school tutoring and summer camp. Topics discussed included HIV disclosure, dating, life goals, treatment adherence and transitioning to adult care. Group members expressed their interest in having more practical scenarios, more discussion around HIV and intimacy and more support around family dynamics. They also asked for more music/arts-based programming. An objective assessment will be conducted in 2017.

Conclusions: In-clinic support group interventions are effective in addressing the numerous issues and challenges faced by adolescents living with HIV. The groups led youth to feel less alone, to be more hopeful and more self-confident about their HIV status and encouraged them to attend clinic appointments and other community-based programs outside the hospital.

SSP6.03

Understanding Women's Experiences of HIV Treatment Side Effects Using Body Mapping

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Women living with HIV (WLWH) are not only more likely to experience side effects than men, but they also experience different and more severe side effects. Women have a higher risk than men to develop side effects and higher prevalence of side effects. Reasons why their experiences of side effects is different than men include: exposure to gendered expectations (e.g, body, sexuality, femininity, and roles), interactions with physicians and other providers (e.g., paternalism, pathologization, and blaming), feelings (e.g., isolation, anger, despair, and shame) and individual situations with respect to side effects, and heightened risk for low adherence and poor clinical outcomes because of structural and gender-related barriers. Body mapping is an arts-based participatory method that can be used for self-reflective, therapeutic, and/or research purposes. It is particularly useful when trying to gain a deeper understanding of complex and meaningful experiences such as being sick, taking medications, living with side effects, and going through a major life event. Body mapping takes the real-life size drawing of the body as its starting point and allows participants to tell their own story. We conducted two body mapping workshops with WLWH in Ottawa and Toronto (n = 25). In this presentation, we will discuss what we learned from using body mapping to understand women's experiences of side effects. More specifically, we will describe the methodological and practical implications of using body mapping. We will also provide an overview of the analysis, the findings and the 'Side Effects Survival Kit' developed in partnership with International Community of Women Living with HIV/AIDS (ICW). In conclusion, we will explain the significance of body mapping and its research, policy, and practice implications.

SSP6.04

HPV Health Literacy, Risk Perception, and the Clinical Encounter: HIV-Positive gbMSM Understandings of HPV and Anal Cancer

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Background: Human papillomavirus (HPV)-associated anal cancer rates disproportionately impact HIV-infected gay, bisexual, and other men who have sex with men (gbMSM), with rates about 100-fold that of the general population. Despite this, there are no established protocols for screening and treatment of anal cancer precursors. Little is known about the acceptability of HPV vaccination and anal cancer screening among HIV-positive gbMSM.

Methods: As part of the HPV-SAVE study, we are conducting mixed-methods research on HPV and anal cancer screening in Ontario and British Columbia. We recruited HIV-positive gbMSM who underwent anal cytology (Pap) screening for in-depth qualitative interviews. Utilising situational analysis, we examined the interviews of 20 participants who were screened at one of five Toronto clinics.

Results: HIV-positive gbMSM considered HPV and anal cancer to be significant health priorities and were interested in routine anal Pap testing and HPV vaccination. However, HPV health literacy levels, anal cancer risk perceptions, and motivations for accessing Pap screening and vaccination varied based on the following: (1) *the feminization of HPV* (e.g., HPV's established association with cervical cancer); (2) *healthcare barriers* (e.g., vaccine costs); (3) *physician-patient rapport*; (4) *history of anal and genital warts*; (5) *history of gastrointestinal issues* (6) *abnormal anal pap test results*; (7) *sexual practice and STI stigma*; and (8) *a patient's relationship to HIV* (e.g., effects of treatment and aging with HIV).

Discussion/Conclusion: Our examination adds to immunological, clinical, and epidemiological research. We elucidate how, in addition to the clinical encounters directly associated with HPV and anal cancer prevention, multiple components related to living with HIV significantly shaped HPV health literacy and the uptake of anal cancer prevention practices among HIV-positive gay men. Understanding the relationship between the everyday management of HIV and HPV remains crucial to the development of targeted HPV and anal cancer education and service delivery.

SSP6.05

Social capital and HIV-serodiscordance: Differences in personal and professional sources of help for HIV-positive and HIV negative partners

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Importance: Social capital is defined as resources embedded within social relationships; lower levels are associated with worse health and earlier mortality. As many as 23% of people living with HIV in Canada may be in serodiscordant relationships. HIV stigma may limit access to social capital among such couples.

Objectives: We investigated social capital among people in HIV-serodiscordant relationships. We hypothesized that HIV-positive people would have lower levels of 'personal' social capital (help from friends and family) but higher levels of 'professional' social capital (help from doctors, and other service providers), compared to negative partners, due to HIV stigma, and high rates of HIV treatment and care.

Methods: We used data from a national online and telephone survey of people in serodiscordant relationships (N=310; 128 HIV-negative, 182 HIV-positive), which included 79 dyads (matched partners). Social capital was measured using self-reported access to help from different groups. To account for the non-independence of social capital within dyads, we employed actor-partner interdependence models.

Results: HIV-positive individuals had lower levels of personal social capital (b=-0.07, p<.01) and more professional social capital (b=0.13, p<.001) compared to HIV-negative individuals. Positive and negative individuals reported similar levels of help from each other. However, HIV-negative individuals were more likely to report that they could access advice about sex from their partner (HIV-negative: 57%; HIV-positive: 41%). Heterosexual men had lower levels of personal capital than men who have sex with men (b=-0.15, p<.01), and this association did not vary by HIV status.

Discussion: People living with HIV in serodiscordant relationships may link the couple to sources of professional knowledge about HIV, thereby placing them in a position of relative expertise in the relationship, especially as regards sexual activity. This suggests additional care and/or counseling could benefit HIV negative partners, particularly if it enhances their relations with service providers.

SSP6.06

"It's Not Easy": Infant Feeding in the HIV context in a Resource-Rich Setting – Strengths, Challenges and Choices

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The dichotomy of infant feeding recommendations for women living with HIV (WLWHIV) in resource rich versus resource poor settings causes confusion and frustration for women with diverse feeding experiences. The societal 'breast is best' perception leads WLWHIV to experience personal, social and cultural pressures to breastfeed. We undertook a qualitative descriptive study to explore these experiences in greater depth.

Materials and Methods: WLWHIV were invited to participate in 2 focus groups, and were recruited from community networks by word of mouth. Participants self-identified as WLWHIV, had a child within 5 years. A semi-structured interview guide was used in the first focus group allowing for spontaneous, participant driven discussion. A structured interview guide informed by the previous session was used in follow-up. Directed content analysis was used to identify themes of importance.

Results: Eleven and four WLWHIV attended the two focus groups. Women were born in Canada (n=2), the Caribbean (2) and Africa (9). Most women had breast feeding experience from low resource countries or prior to HIV-infection. Three major themes were identified: novel stories of lived experience; potential solutions in supporting WLWHIV; research considerations for Canada. Novel experiences of infant feeding included; personal strength and resilience in the face of a difficult decision; the issues around choice, or lack thereof; and the long-term grief and trauma women face. Solutions included holistic approaches to education/care to support WLWHIV. Proposed innovative supports included home based programming, spaces for open discussion, formalized peer-support. Community-based research ideas included exploration of cultural significance of breastfeeding, and implementation science programming with home visits to support new mothers LWHIV.

Conclusions: WLWHIV have a wealth of knowledge, ideas, and experience pertaining to infant feeding, but confusion about guidelines and risks of transmission persists. Community based innovative approaches are needed to better support WLWHIV regarding infant feeding.

SSP6.07

Family Quality of Life (FQoL) in Families Affected by HIV: The Perspective of Children of HIV-Positive Mothers

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Background: The HIV-infection of a family member can impact family quality of life (FQoL) in terms of resiliency, social support, parentification, and the physical and emotional health of members (Lachman et al., 2013).

Objectives: The objectives of this study are to: 1) Describe patterns of FQoL among children of mothers living with HIV (MLWHIV); and 2) Identify key factors associated with FQoL in families affected by HIV.

Methods: A total of 71 children in 55 families were recruited in HIV-specialized clinics and community organizations. Children were aged 11 to 28 years (16 years old on average). Half were boys, two thirds were aware of their mother's positive HIV status, and a fifth was diagnosed with HIV. All HIV-positive children were aware of their status. A latent profile analysis was performed on five continuous indicators of children-reported FQoL.

Results: Three profiles were identified: low FQoL (27%), moderate FQoL (52%), and high FQoL (21%). Higher proportions of children in the low FQoL profile were attending school and were the youngest child in their family. Children in the moderate FQoL profile displayed higher scores on adult role-taking parentification. Children in the high FQoL profile displayed lower anxiety scores and higher scores on resilience and seeking social support. Lower proportions of mothers in the high FQoL profile were married or were in a common law union.

Discussion: Theses results confirmed previous analyses on FQoL with MLWHIV (Blais et al., 2014). FQoL seems to be sensitive to family structure, the role played by the child in the family, and mental health of both children and parents. FQoL profiles can be used to plan family interventions with both parents and children. Other relevant indicators must be studied (e.g. closeness and support between family members, availability and accessibility of care; father-child relationships, medical condition of the mother).

SSP6.08

Sexual and social development issues of young people living with HIV since birth: Lessons learned and next steps

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On a worldwide scale, about 3.2 million children under 15 years old live with HIV, the majority of them acquiring it through vertical transmission (ONUSIDA, 2014). On top of having to deal with developmental tasks specific to adolescence, i.e. exploring intimate relationships and sexual behaviors, these youths have to live with a chronic, sexually transmittable, socially stigmatizing and criminalized illness. According to the dominant paradigm, youths living with HIV (YLWHIV) are considered an at risk group and inadequately equipped to manage their sexuality in a secure manner (Persson & Newman, 2012). As a consequence, their individual and interpersonal developmental issues associated with their sexuality aren't very well documented.

Objectives:

1. Draw a scientific review of the findings on the sexual development of YLWHIV since birth; and
2. Reflect on lessons learned and next steps for future research and interventions.

Methods: The articles listed on PubMed and PsychInfo databases were analyzed.

Results: Four dimensions emerged from the research:

1. The key role of the family environment on HIV representations, romantic relationships and sexuality;
2. Sources by which YLWHIV obtain information about sexuality and their knowledge on this matter ;
3. The stakes raised by the HIV status disclosure in romantic and sexual contexts;
4. Sexual behaviors of YLWHIV, including transitioning towards sexually active lives, representations on sexuality and risk reduction strategies.

Discussion: The paradigm position centered on at risk behaviors overshadows adaptive strategies, resilience mechanisms and specific competences developed by YLWHIV in managing sexual risks. Further work would benefit from exploring specific competences developed by YLWHIV and serve as intervention levers in actions destined for them.

SSP6.09

A Qualitative Study Examining Successful Aging in People Living with HIV

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Introduction: As people living with HIV (PLWH) continue to live longer, the notion of what constitutes successful aging in the context of HIV is of interest. Increased understanding of individual's values and perceptions of suc-

cessful aging can assist health providers in working with PLWH to set meaningful goals as they age. The purpose of this study was to understand how PLWH define successful aging and their perceptions of contributors to successful aging.

Methods: This qualitative study was part of a longitudinal study that recruited PLWH over the age of 50 years from AIDS Service Organizations to participate in a series of four in-depth interviews over 1.5 years. Interviews explored men and women's experiences of aging with HIV over time through a disability and rehabilitation lens .At the fourth interview, participants provided their thoughts of how they would define successful aging and reflected on their perceptions of whether they considered themselves to be aging successfully. Transcribed interviews were analyzed using open-coding and conventional content analysis.

Results: Fourteen men and 10 women volunteered for the study. The mean age was 57.5 years (range 50 to 73 years) and mean time since diagnosis was 18.4 years (range 6 to 30 years). Participants' perspectives regarding successful aging may be understood in terms of six themes: accepting limitations, staying positive, maintaining social supports, taking responsibility, living a healthy lifestyle and engaging in meaningful activities. Participants focussed on components of successful aging that emphasized individual control highlighting the important role of self-management programs with PLWH.

Conclusion: From a clinical perspective this highlights the importance of working with PLWH to understand their values and aspirations, and create patient centered goals that are meaningful to the individual. From a research perspective this reinforces calls to include the subjective experiences of older adults in developing successful aging criteria.

SSP6.10

GIPA in Action – the impact of sharing lived experience to reduce stress and social isolation of pregnant women living with HIV

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Background: Since the introduction of antiretroviral therapies there have been significant reductions in perinatal HIV transmission globally, particularly in high-income, low prevalence countries such as Canada. However, women living with HIV who are pregnant can face significant fear and anxiety due to stigmatizing attitudes and discriminatory behaviours from health care providers, friends and family. For over 5 years, The Teresa Group has run pre-natal groups for HIV+ pregnant women to address the many issues related to childbirth and infant feeding faced by HIV+ women. Following the development of a GIPA/MEPA policy across the organisation, all prenatal groups over the past year have been co-led by a peer facilitator.

Methods: The Teresa Group conducted 5 prenatal groups between November 2015 and November 2016. Pregnant HIV+ Moms were invited to join the group. The group was co-facilitated by a TTG social worker and an HIV+ Mom who had recently given birth. Mom co-facilitators were oriented to the program and supported throughout the process. Group participants completed an evaluation survey at the end of each 2-hour group.

Results: Twenty women participated in the groups. Women reported feeling more at ease to discuss their fears and anxieties with the peer co-facilitator. They were more likely to trust the information given by the peer co-facilitator, particularly regarding medications and formula feeding. Group members exchanged phone numbers, developed support networks, and engaged in other programs at The Teresa Group.

Conclusions: Including HIV+ women with recent, lived experience of childbirth decreases HIV+ pregnant women's anxiety and increases their understanding, their own confidence and feelings of hope around the birth process. It also increases social connections and support, decreasing social isolation.

SSP6.11

"It was hard not to start to think that my suspicions around HIV playing into this were not coming true...": Experiences of PLHIV within the Ontario Adoption System

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Background: With over 80% of people living with HIV (PLHIV) in Canada being of reproductive age, it is unsurprising that many in the HIV community desire to expand their families. While many pursue pregnancy, some may choose to, or need to, adopt. PLHIV are *eligible* to adopt through the public domestic adoption system (PDS). We aimed to explore the lived experiences of PLHIV with the adoption system to understand potential barriers/facilitators.

Method: Inclusion criteria included 1) being 18+ years of age; 2) living in Ontario; 3) interested in, pursuing, or completed the adoption process; and, 4) aware of HIV+ status prior to initiating the adoption process. We interviewed participants using a semi-structured interview guide that was co-created with our Community and Academic Advisory Board. Interviews were analyzed using Braun and Clarke's thematic analysis.

Results: Of the 6 participants (two females, four males), two had successfully adopted through the PDS; one was matched with a child and awaiting final documentation (PDS); one was waiting to be matched with a child (PDS); and two were pursuing private, international adoptions with children they knew. The participants' reasons for

adopting varied. Five themes were identified as particularly important to their perceptions of the adoption process: Interactions with Caseworker, Competitive Waiting, Information Sharing, Beliefs about Eligibility, and Emotional Responses.

Implications: Although eligible to adopt, the participants' experiences suggest PLHIV face similar challenges within the adoption system as other marginalized groups. Further, each participant experienced fear/anxiety about their HIV status at some point throughout the adoption process, whether there were explicit barriers related to their status or not. However, each participant clearly expressed that their desire to adopt a child significantly outweighed any negative experiences/feelings they had throughout the adoption process. Suggestions for how social care providers can support PLHIV throughout the adoption process are offered.

SSP6.12

'Under a Magnifying Glass': An arts-based exploration into the experiences mothers living with HIV have when navigating social services

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Mothers living with HIV (MLWH) are uniquely impacted by the social determinants of health and often interact with a range of social service providers and health care professionals to meet their basic needs. Experiences of poverty, housing and homelessness, violence and children's aid involvement intersect with HIV-related stigma in ways that often complicate women's experiences of navigating these service sectors. Using arts-based and participatory methodologies, this project explores the experiences that mothers living with HIV (MLWH) have when navigating a web of health and social services. Through bringing five MLWH from a city in Southern Ontario together, the findings of this project portray how the participants subjectively experience social service use through the creation of a collaborative collage, which includes women's submissions of photography, poetry, written words and imagery. Over a six-week period, women came together to share their experiences, make contributions to the collage and brainstorm how to enhance experiences of social service use for MLWH. Stories emerged about women's experiences navigating Children's Aid Society involvement, emergency foodbank programs, the Ontario Disability Support Program, AIDs service organizations and women-specific services. As women contributed imagery to the collage, the central themes that were explored included a lack of control, difficulties navigating essential services, perceived HIV-related stigma and a lack of opportunities for peer-involvement and leadership in service use. Action oriented recommendations included implementing more opportunities for peer-involvement in ASO's and the creation of a community kitchen program for MLWH. The findings of this project incorporate arts-based and narrative data yielding to a more comprehensive understanding of the subjective experiences that MLWH have navigating health and social service streams in Ontario.

Gay, Bisexual and other Homosexually Active Men

Guais, bisexuels et autres hommes homosexuels actifs

SSP7.01

Resilience pathways, childhood escape routes, and mentors reported by gay and bisexual men affected by syndemic conditions

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Investigation of the social and psychological antecedents of the HIV epidemic has identified a *syndemic* of conditions associated with risk behavior and seroconversion. This study inquires into the resilient practices and developmental processes of gay and bisexual men at the nexus of syndemic conditions to understand the pathways that lead to health problems or well-being. Interviews with 40 men identified branching pathways from home environments into schools that either offer refuge or a regime of gender discipline and bullying. Some found escape routes from hostile environments in worlds of books, pop culture, or internet chat. In adolescence, one set of men identified the development of sexual relationships with older men as a life line that brought a measure of emotional growth. This study points to resilience pathways and social resources that could make a difference in the lives of those deemed to be "high risk."

SSP7.02

Where the Boys Are: Apps and Websites Used by Gay, Bisexual and Other MSM for Hook-Ups and Sexual Health Information in Ontario

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Background: Little is known about the websites and apps Canadian gay, bisexual and other MSM (GBM) use for sociosexual and health information, including: what app/sites they prefer for both health information and hook-ups? How reliable was the health information found? Do responses differ by HIV status?

Methods: Using mobile-app ads and community-based agencies for recruitment, an online anonymous question-

naire collected data from GBM aged>15 across Ontario between 12/2013-1/2014. Detailed questions asked about preferences for online vs in-person hookups, time spent and places searched for health information, and satisfaction with health information found. Differences by HIV status (HIV-positive/negative/unsure) were explored using Pearson's Chi-square and ANOVA tests.

Results: Of 1830 recruited, 146 (8.0%) were HIV-positive, 1,439 (78.6%) HIV-negative, 217 (11.9%) HIV-unsure. HIV-positive men were more likely to report in-person venues (e.g., gay bars/cafes, bathhouses, or private sex parties) for hook-ups (all $p<0.05$), while HIV-negative and HIV-unsure men were more likely to have used online dating/hook-up websites ($p=0.027$). For hook-ups, HIV-positive guys were more likely to use barebackRT ($p<0.001$) and Scruff ($p=0.028$), whereas HIV-negative/unsure guys reported Craigslist ($p=0.012$) and GrindR ($p=0.025$). HIV-positive men spent more hours/week (2.1) searching for sexual health information compared to HIV-negative (1.2) and HIV-unsure (0.7; $p<0.011$) men. HIV-positive men were more likely to look up sexual health information on community websites ($p<0.001$), HIV-negative men on public health/government websites ($p=0.029$) and HIV-unsure men on search engines ($p=0.032$). More HIV-positive men found the information they were looking for ($p<0.001$). However, finding the information 'very unreliable' was more likely for HIV-positive men (12.4%) compared to HIV-negative (8.71%) and HIV-unsure men (6.9%; $p=0.02$).

Conclusion: Online cruising and sexual health information-seeking behaviours vary by HIV status among GBM. Online service providers can use these findings to tailor their outreach tools to better meet the divergent needs of GBM.

SSP7.03

Did You Find That Online? The Differences in Online Health-Seeking Practices between Younger and Older Men Who Have Sex with Men across Ontario

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Background: Gay, bisexual and other MSM (GBM) are increasingly using the Internet to access sexual health-related information. Our study sought to assess differences in online health information seeking between younger and older GBM.

Methods: Participants, aged >15, were recruited from Ontario through ASOs, mobile-apps and websites from 12/2013 to 01/2014 to complete an anonymous online questionnaire. Differences in how the Internet was accessed to cruise and find sexual health information by age group (≤ 29 vs 30+) was explored using Pearson's Chi-Squared and T-tests. Content analysis was performed to explore participants' text-based survey responses.

Results: Of 1805 participants, 617 (34%) were aged ≤ 29; 1188 (66%) were aged 30+. Older GBM were significantly more likely to be HIV-positive (10.6%-vs-3.1%), while younger GBM were more likely to not know their HIV status (16.4%-vs-9.9%; $p<0.001$). Older GBM were significantly more likely to spend time cruising online (9.5-vs-8.1 hours/week; $p=0.01$). Searching for sexual health information online (1.21-vs-1.18 hours/week; $p=0.079$) and successfully finding that information (86%-vs-85%; $p=0.448$) showed no significant differences by age. Older GBM were significantly more likely to perceive the sexual health information found online as very/somewhat unreliable when compared to their younger counterparts (19.8%-vs-11.5%; $p<0.001$). Qualitative findings showed that older GBM sought sexual health information on: (1) HIV/STI testing; (2) accurate statistics on HIV/STIs; (3) negotiating undetectable viral load, and safer sex beyond condom use. Younger GBM sought information on: (1) STIs and HIV; (2) mental health; (3) PEP, PrEP, and condom use.

Conclusion: Older and younger GBM are spending the same amount of time using the Internet to search for sexual health information. However, the information sought among older GBM is different and considered as more unreliable than younger GBM. These findings have implications on the provision of relevant, accurate and age appropriate online sexual-health information.

SSP7.04

Sex on the Menu: A Community-based Social Marketing Campaign for Men who have sex with Men in Quebec

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Background: In Quebec, the highest numbers of new HIV diagnoses are still found among men who have sex with men (MSM). For decades, the scope of prevention campaigns was limited to condom use or abstinence. A range of recent research has highlighted the benefits of combining different prevention options together ("combination prevention"). The COCQ-SIDA *hommes gais et HARSAH* committee decided to create a social marketing campaign to inform MSM about different prevention options and invite them to visit pretpourlaction.com (informational sexual health website for MSM launched in 2007).

Method: A working sub-committee composed of community workers was created to elaborate the campaign from February to June 2016. They selected six strategies based on their scientifically proved effectiveness and MSM prevention information needs (as reported by community workers): 1) PrEP 2) PEP 3) Testing 4) Condoms 5) Taking viral load into consideration 6) Negotiated safety. Promotional strategies included online and print media, and oc-

curred mostly during July 2016. Community workers used campaign material in their activities (pamphlets, aprons, kiosk, etc.).

Results: The *Sex on the Menu* campaign was launched in late June 2016. Pretpourlaction.com recorded an increase of 468.7% sessions between June and July (although further analysis needs to be conducted to determine traffic quality). Community workers integrated campaign material in their activities and social media. They reported that MSM enjoyed the campaign and the material was easy to use to reach them (1674 pamphlets distributed).

Conclusion: This community-based initiative shows how community work and campaign material can be used to reach MSM. Advertising presents specific challenges (price, efficiency, refusal by Facebook and Google AdWords) and further analysis is required to identify the best promotional channels. An evaluation framework is being developed and will be used to assess the impact the campaign had among MSM.

SSP7.05

Planned and Unplanned Barebacking Behavior among MSM: Differences in the Use of Harm Reduction Strategies

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Barebacking, or condomless anal sex in the presence of risk of contracting HIV, has developed as both a behaviour and a personal identity among men having sex with men (*MSM*) which is organized around the rejection of condoms use during anal sex. The research reviewed in this presentation includes both a synthesis of existing North American studies on barebacking among MSM, and the findings and implications of a series of ongoing and yet to be published qualitative and quantitative studies of Canadian MSM. Major findings of a series of investigations with Canadian MSM revealed engaging in barebacking behavior is not synonymous with identifying as a barebacker, and that self-reported barebacking behavior should be viewed from the perspective of the intentionality of the act. In contrast to unplanned barebacking behavior, planned barebacking behavior was associated with use of multiple effective risk reduction strategies, rather than being a vector for the transmission of HIV. Additionally, findings suggest that a primary motivation expressed by those engaging barebacking is the desire to increase relational intimacy. Insight is offered as to how HIV prevention efforts with MSM, particularly with the availability of PrEP and viral load testing, can be modified to address the different situational and psychological factors that contribute to MSM engaging in planned versus unplanned barebacking behavior and the intersections with barebacking as a core identity attribute for MSM.

SSP7.06

Barriers to Condom Use and Condomless Anal Intercourse Trajectories in Gay, Bisexual and Other Men Who Have Sex with Men Seeking HIV Testing

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How are specific barriers to condom use related, over time, to condomless anal intercourse (CLAI) at risk for HIV transmission among gay, bisexual and other men who have sex with men (GBMSM)? We used latent class regression (LCR) to identify latent segments of CLAI over six months and explore how they differ with respect to eight potential barriers to condom use (presumptions about serostatus, sexual sensation-seeking, low sexual assertiveness, low condom availability, intimacy-seeking, safer sex fatigue, interference with pleasure, HIV pessimism). We collected data at three timepoints over 6 months from 910 GBMSM who sought community-based HIV testing in Montreal (the SPOT project). We performed LCR presuming that the effect of multiple barriers to condom use may vary across segments of this sample. The optimal solution revealed two latent classes, showing that no single pattern of barriers uniformly affects CLAI among GBMSM. Over time, class 1 (78%) consistently reported lower CLAI (mean CLAI = 19%) than class 2 (22%; mean CLAI = 60%). While the two classes showed a decrease of CLAI over 6 months, each was characterized by significantly different associations with barriers to condom use. In class 1, sensation-seeking, low sexual assertiveness, and presumptions about serostatus were associated with CLAI whereas this association was only observed for sensation-seeking and safer sex fatigue in class 2. Older and less educated participants had higher odds of being in class 2. These results point to different segments of GBMSM that share little in terms of barriers to condom use. For most GBMSM, the promotion of assertiveness, better ways to cope with sensation-seeking, and less reliance on seroguessing might support condom use and HIV prevention. However, safer sex fatigue combined with sensation-seeking is a distinctive characteristic of the most at-risk GBMSM, for whom non-condom-based and biomedical risk-reduction strategies might be best suited.

SSP7.07

HIV Stigma Predicts Depression Above and Beyond HIV Status among Gay and Bisexual Men

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Background: People living with HIV have significantly higher prevalence of depression than HIV-negative

persons. Research has identified social marginalization, childhood stressors, social isolation, and HIV stigma as correlates of depression. However, no studies have examined these variables together to see if HIV status is independently associated with depression controlling for these other variables, or if experiencing HIV stigma is associated with depression above and beyond other variables.

Methods: The sample includes 304 self-identified gay and bisexual men (GBM; 152 HIV-positive) from Toronto. Depression symptoms were measured using the Center for Epidemiologic Studies-Depression Scale (score of ≥23). Multi-block regression models (Demographic Block: Age, income, race/ethnicity; Developmental Stressor Block: childhood physical, emotional and sexual victimization, verbal bullying/teasing; and Social Isolation Block: loneliness, social support from friends, family and significant others) were built to examine main effects as well as interaction effects of factors associated with depressive symptoms. A final model was fit with significant factors of preliminary models including HIV status.

Results: Most participants were White (75%), and gay-identified (90%). Around 30% of the participants reported depressive symptoms. The multivariate model identified increased experience of childhood bullying (RR=1.26;95%CI:1.09-1.45; p=0.002), support from friends (RR=0.77;95%CI:0.68-0.87; p<0.001), and HIV status (RR=1.52;95%CI:1.05-2.20; p=0.03) as associated with depression. Among HIV-positive participants, only one type of HIV stigma, embarrassment about HIV (RR=1.12;95%CI:1.02-1.24; p=0.02), was associated with depression in the multivariate model.

Conclusion: HIV status was associated with depression even controlling for demographic, abuse and bullying, and social isolation among GBM. Among GBM living with HIV, embarrassment about one's illness independently was associated with depression above and beyond each of these variables, suggesting that this form of internalized HIV stigma continues to negatively impact the mental health of GBM living with HIV. Interventions to reduce embarrassment about having HIV are needed to reduce depression among GBM living with HIV.

SSP7.08

Stigma and Resilience among HIV-positive and HIV-negative Gay, Bisexual, Two-Spirit and other MSM who 'Party-n-Play'

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Background: 'Party-n-Play' (PNP) is sex between gay, bisexual, and other men who have sex with men (MSM) that occurs under the influence of drugs. While previous studies provided important information about rates of, and factors associated with PNP among MSM, these studies often had the unintended stigmatizing effect of depicting MSM who PNP as criminals or mentally ill, and reckless vectors of HIV transmission.

Methods: 44 qualitative interviews were conducted with PNP-involved MSM in Toronto. These interviews were recorded, transcribed verbatim and were analyzed using a critical discourse methodology to identify the ways HIV-positive and HIV-negative MSM who PNP embodied and resisted stigmatizing discourses.

Results: The findings show that MSM who PNP (mean age=37; 55% HIV-positive, 43% HIV-negative; 68% gay; 82% single; 40% men of colour) faced stigma from multiple sources – from families and other MSM, within gay and other communities, from police, and in healthcare contexts. Sexual stigma and negative attitudes towards non-heterosexual behaviour, racism, and drug-related stigma, as well as stigma surrounding the transmission of blood-borne infections emerged as salient themes in the narratives of participants. HIV-related stigma presented an additional layer of complexity in the lives of HIV-positive MSM who PNP. Stigmatizing discourses also had a deleterious effect on MSM's interactions with healthcare providers and disclosure of sensitive health information regarding sexual and drug-related practices. However, some PNP-involved MSM resisted stigma by describing how they capitalize on naturally occurring strengths in their communities, and build social bonds through relations of care and support in their PNP networks.

Conclusions: These results highlight the deleterious effects of various forms of stigma from multiples sources on MSM who PNP. These findings also point out the resilience within networks of MSM who PNP, and underscore the need for initiatives that address stigma and incorporate resilience.

Intervention Based Research in the Social Sciences: Theories, Methodologies, and Outcomes

La recherche interventionniste Intervention en sciences sociales : Théories, méthodes et résultats

SSP8.01

Hand Mapping (HM) an ethnoracialized visual methodology that depics the sexual trajectories and life events with gay immigrants in Canada

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Problem: Representing the narratives of ethnoracialized gay immigrants sexual health practices has been methodologically challenging. Language barriers, lack of conducive community-based research evaluation tools, and lack of understanding on how immigration presents itself as a social/political, geographic and sexual health disruption, problematize the collection of program evaluation

data. Data is needed for program evaluations, particularly, narrative-oriented qualitative approaches. HM is a scale down Body Mapping orientation, that has the power to metaphorically and visually represent the migration of sexual bodies through the globe.

Methodology: ChicosNet a sexual health practices intervention has been conducted for the past 5 years. Over the time, HM as a new program evaluation methodology was developed from the grown up, and presented in several conferences and audiences for feedback. HM has been applied to gay Latino men (n=30), over the past three years. The use of the hand figure on a piece of paper, and drawing the lines on the hand as a metaphor of live trajectories, allows participants to vocalize their life events, sexual orientation/migration, and sexual practices.

Findings: HM has been presented in many local, national and international conferences. It has gain recognition as a community-based evaluation methodology. The HM itself visually represents an empowered journey of hope experienced by gay migrants. There are still yet many qualities and methodological aspects to be discovered and known for the potential use of HM on other communities.

Next Steps:

- HM has the potential of depicting sexual health minorities practices, therefore, further research is required.
- HM has been invited to participated in a book chapter from the Sexualities and Social Work Conference (Olten, Switzerland, August 18th, 2016), were the methodology was successfully presented.
- Further funding should be sought with the intention of properly finding qualitative community evidence-based data.

SSP8.02

Challenges and opportunities of a web-based intervention to support health behaviors: lessons learned from the online RCT LHIVE Healthy

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Background: Web-based tailored interventions are a promising way to support health-related behavior change. Online research strategies open up new avenues for data collection. A web-based tailored nursing intervention, *TAVIE en santé,* was developed to support people living with HIV (PLHIV) in the adoption of healthy behaviors. An online randomized control trial (RCT) is currently underway across Canada to evaluate the efficacy of this intervention (LHIVE Healthy - CTN288).

Objective: To discuss opportunities, challenges and issues faced during the development of a web-based tailored intervention and its evaluation through online RCT.

Methods: An Intervention Mapping (IM) framework was used to develop the intervention. All steps of a traditional RCT were transposed to an online research strategy.

Results: IM provides the framework for the development of an intervention using a systematic approach based on theory, empirical evidence, and clinical knowledge. However, it offers more guidance on the content of the intervention than on the methods of web-based format content delivery. During the evaluation phase, two major challenges arose: 1) Regarding the sample constitution, online recruitment can be advantageous as a vast audience can be reached but it generates a selection bias related to Internet accessibility. There is also less control over who registers in the study than in face-to-face recruitment. 2) Engagement and retention could be an issue. Not all participants follow the planned intervention protocol. Lifestyle behavior change is a difficult task that requires readiness and motivation: high level of engagement is needed. Attrition rates at follow-up within the online RCT can also be challenging.

Conclusion: Systematic approaches to develop interventions needs to be supplemented by frameworks to guide the web-based content delivery. Even though online RCT seem feasible, they face challenges. Considerations and ways to optimize development and evaluation will be proposed.

SSP8.03

Findings from a Systematic Review focused on the Educational Interventions for Health Science Students in Entry-to-Practice Competencies in HIV Care

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With increasing prevalence rates HIV remains, according to the Public Health Agency of Canada (2015), an "enormous challenge" (¶. 1). There continues to be growing evidence that health care providers (HCP) are not fully prepared to engage in HIV care. When HCP are uninformed about HIV care or when they engage in behaviours that are inconsistent with professional practice standards, it creates additional barriers for people living with HIV (PLWH) to access the care they need. We conducted a systematic review to identify current educational interventions focused on developing HIV competencies in higher education across all

health science disciplines. We searched multiple databases, including Web of Science, Medline, CINAHL, PsychINFO, Embase, ERIC, and Education Source for primary studies published in English or French, that were focused on interventions and included health science students; no date limit was imposed. Using PRISMA guidelines, we identified 21 distinct studies. While there was overwhelming literature that assessed knowledge, skills, and attitudes in health science students on HIV and AIDS, the dearth of intervention studies was notable. With the exception of two studies, PLWH were not included in the planning, implementation, or evaluation of the interventions; this is in contrast to well established GIPA or MEPA principles. The primary means of education was focused on delivering lectures to address HIV and AIDS knowledge for HCP, including pathophysiology and pharmacology. There was a significant lack of focus on historical, cultural and legal contexts of HIV and AIDS care; theoretical justifications of the interventions were absent. No study focused on the impact of an intervention on the care provided to PLWH after graduation. There is an urgent need to develop long term sustainable and scalable interventions that address the consistently identified lack of knowledge and skills, and stigmatizing attitudes of health care providers and students.

SSP8.04

From serodiscordant to magnetic: A pilot psychoeducational group intervention yields positive change in relationship quality

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Background: Serodiscordant or magnetic couples experience HIV-related issues that compound day-to-day stressors, such as: effects of medication and illness on social plans; anxiety about long-term outlook; HIV transmission fears; lack of support programming, particularly for the HIV-negative partner; and disclosure and privacy concerns (Beckerman, 2002; Fife et al., 2008). Couples support groups can build coping skills and increase relationship satisfaction (Palmer and Bor, 2001).

Participants: Throughout the summer of 2014, six gay male magnetic couples (n=12) collaboratively designed and participated in a 12-session psychoeducational support group hosted by a community-based HIV/AIDS organization in downtown Toronto.

Methods: Participants completed the Revised Dyadic Adjustment Scale (RDAS) (Busby et al., 1995) at three points (pre- and post-intervention and three-month follow-up). Analysis was run to determine if group participation significantly improved relationship quality and if additional factors influenced program impact on relationship quality. Seven independent categorical variables (e.g., HIV management agreement) were defined based on emerging qualitative data and by lack of significant Pearson chi-square scores.

Results: A one-way repeated-measures ANOVA found a significant time effect (Pillai's Trace = .654, F(2,10)=11.264, p=.005, multivariate = .654). Average RDAS scores at pre- and post-intervention indicate clinically distressed relationships, while follow-up average indicates non-distressed relationships. Seven mixed-design ANOVAs found that previous agreement on how to manage HIV within the relationship influenced program impact on the relationship, however the program appears to have been effective regardless of this variable. HIV management agreement: post intervention (M=43, SE=3.871); follow-up (M=52, SE=2.853). HIV management disagreement: post intervention (M=43.25, SE=2.737); follow-up (M=46.25, SE=2.017).

Conclusion: Results indicate that the quality of participant relationships significantly improved, regardless as to whether couples agreed on how to manage HIV within their relationship when the group began. The small sample size and lack of control group requires that these results be interpreted with some caution.

SSP8.05

Building Capacity, Strengthening Knowledge and Skills: Effectiveness of HIV Training for Child Protection Workers and Social Work Students in Ontario

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Background: Research with mothers living with HIV involved with Children's Aid (CAS) suggests that child protection workers have limited knowledge about HIV. Although HIV is often not the reason for child welfare involvement, for many mothers, HIV disclosure results in stigmatizing interactions. Mothers living with HIV have called for increased training for social workers; in response, the Positive Parenting Pilot Project sought to implement and evaluate an HIV training module in Ontario. This paper examines training effectiveness on participant's HIV knowledge and attitudes.

Methods: Social work students and CAS staff completed a survey before (n=116) and/or after (n=66) a 3-hour module. Statistics were compiled to understand educational backgrounds and aggregate changes in knowledge and attitudes post-training. We conducted generalized linear mixed models to understand the module's effect on HIV knowledge.

Results: Few participants (22.5%) had received HIV-specific training, often in the 1990s, compared to 80% with previous anti-oppressive practice training. Perceived HIV know-

ledge increased with 91% reporting feeling moderately to extremely knowledgeable after compared to 56% feeling not at all knowledgeable before the training. We observed a change in perceived skills to provide support (3% before and 11% after for technical knowledge; 29% before and 51% for compassionate and supportive care). There was a statistically significant increase in HIV knowledge among both students and CAS staff following the training ($p<0.01$). HIV knowledge scores were on average higher in CAS staff compared to students, however, this difference was not significant.

Conclusions: It is essential that social work programs and CAS organizations offer training to ensure social workers have the knowledge and skills to provide compassionate support to families affected by HIV. Our study reveals an increased need for partnerships between HIV and child welfare sectors, and the potential transferability of HIV-specific training to other areas of social work.

SSP8.06

Living strategies used among adults living with HIV in Canada by age group: Results from the HIV Health and Rehabilitation Survey

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Objective: To describe the type and frequency of living strategies used by adults living with HIV to address health-related challenges, and compare these across age groups.

Methods: The HIV, Health and Rehabilitation Survey is a cross-sectional web-based survey to explore disability, multi-morbidity and living strategies among adults living with HIV. The survey included a section on living strategies used to address the health challenges living with HIV: maintaining sense of control (26 items), attitudes and beliefs (8 items), blocking HIV out of the mind (7 items), and social interaction (10 items). We described the frequency of living strategy use and compared the proportion of participants who engaged in living strategies most (few times per week) or all the time (every day) versus none, a little, or some of the time across three age groups (<40 years, 40-49 years, >50 years) using chi-square tests with post hoc Bonferroni adjustment.

Results: Of the 935 participants (26% <40 years; 30% 40-49 years; 43% $\geq$50 years), the majority ($\geq$60%) engaged 'most or all of the time' in healthy lifestyle strategies related to medications, hygiene, eating, and sleep (4/6 items) and maintained a positive outlook living with HIV (3/5 items). Compared to younger participants (<40 years), a higher proportion of older adults ($\geq$50 years) engaged 'most or all the time' in strategies that involved maintaining control over health (11/24 items) and adopting positive attitudes and outlook living with HIV (6/6 items), whereas a greater proportion of younger respondents (<40 years) engaged in strategies involving social interaction (4/10 items) ($p<0.05$).

Conclusions: In this sample, a greater proportion of older participants reported engaging most or all the time for some living strategies associated with maintaining sense of control and adopting positive attitudes and beliefs, whereas a higher proportion of younger participants engaged in strategies for social interaction.

SSP8.07

Reliability and Validity of the HIV Disability Questionnaire (HDQ) with Adults Living with HIV in the United States

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Objective: The HIV Disability Questionnaire (HDQ) is a self-administered questionnaire, developed in Canada, that measures disability experienced by people living with HIV (PLWH). The HDQ has been validated for use with PLWH in Canada and Ireland. Our aim was to assess internal consistency reliability and construct validity of the HDQ with PLWH in the United States (US).

Methods: The HDQ is comprised of six domains including physical symptoms (20 items), cognitive symptoms (3 items), emotional and mental health symptoms (11 items), uncertainty (14 items), difficulties with day-to-day activities (9 items) and challenges to social inclusion (12 items). We recruited PLWH from a US clinic and administered the HDQ followed by a demographic questionnaire, and the World Health Organization Disability Assessment Schedule (WHODAS-2.0) (36 item version). We calculated HDQ disability presence, severity and episodic scores (scored 0-100). We calculated internal consistency coefficients for the disability and episodic scores and considered coefficients>0.80 acceptable. To assess construct validity, we tested 15 *a priori* hypotheses of correlations between scores on the HDQ and WHODAS-2.0. We considered

acceptance of ≥75% of hypotheses as demonstrating support for construct validity.

Results: Of the 128 participants, the majority were men (66%), mean age 50 years, taking antiretroviral therapy (93%). Highest median disability severity and presence scores were in the uncertainty domain; highest episodic scores were in the physical domain. Internal consistency coefficients ranged from 0.888-0.934 and 0.871-0.959 on the severity and episodic domains, respectively. Of the 15 construct validity hypotheses, 10(67%) were supported.

Conclusions: The HDQ demonstrates internal consistency reliability and some elements of construct validity when administered to PLWH in the United States. Reasons for lower validity (<75% hypotheses supported) may be due to cultural differences and differences in HDQ interpretation. The HDQ may be used to describe disability in countries where PLWH experience similar health-related challenges.

SSP8.08

Strengthening community action as an engagement tool in a tertiary clinic for people who inject drugs

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Issue: Marginalization of people who inject drugs (PWID) in the downtown eastside (DTES) has led to their disengagement from health care (including HIV care), especially those who are co-infected with HCV. The shift from an individual physician-based approach to a multidisciplinary, community-based intervention may be an important strategy to address this issue.

Setting: The multidisciplinary program developed at the Vancouver infectious Diseases Centre (VIDC) provides ongoing, long-term access to specialty medical care and support services in order to target the clinical, psychological, and social factors along with addiction-related needs that impact PWID, particularly the population from the DTES.

Project: Our intervention incorporates the use of community pop-up clinics (CPCs) in the DTES to test individuals for HIV and HCV. Positive test results lead to a consultation with our health care team who proactively engage patients into care and treatment. Implementation of the Ottawa Charter in our multidisciplinary program aims to strengthen community action by enabling and providing the tools to our patients to take control of their health through weekly support group meetings, which are supplemented with breakfast and lunch. This includes providing education on safe injection practices along with HIV and/or HCV-related health topics.

Outcome: From our community-based testing, 610 individuals were infected with HCV, of which 51 were co-infected with HIV. An additional 23 were infected with HIV alone. A total of 175 (28%) individuals were then productively engaged in care at VIDC. Alongside providing treatment for HIV and/or HCV, VIDC targeted social issues, such as linking patients to safer housing options, providing nutrient dense food sources, and education on safe injection drug use. Patients engaged at VIDC showed better health outcomes when programs were aimed at strengthening social supports and enabling self-help type interventions.

Organizational Strategies in the Context of Policy and Funding Shifts

Stratégies organisationnelles dans le contexte des changements dans la politique et le financement

SSP9.01

The transformative power of a peer-led leadership training program for PLHIV: An impact evaluation of the Positive Leadership Development Institute

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Introduction: The Positive Leadership Development Institute (PLDI) is a three module, leadership training program for people living with HIV (PLHIV). The success of British Columbia's (BC's) PLDI (a partnership since 2009 with the Ontario AIDS Network) includes exclusive PLHIV program leadership; completion of 20 training sessions in BC; and 167 PLDI grads. While each of the training sessions in BC were individually evaluated, no comprehensive impact evaluation of PLDI has been conducted.

Methods: Keeping with GIPA/MIPA principles and PLDI's PLHIV-led model, four peer evaluators (PEs) were hired, trained, and supported by the Pacific AIDS Network to develop a participatory, impact evaluation, including: online surveys; semi-structured, qualitative interviews; and a framework to analyze historical evaluation data. Recruitment for the evaluation is happening through PAN's 50+ member agencies; key stakeholders; PLDI graduates; and other PLHIV. Through these methods the PEs aim to get a better sense of whether the PLDI training has increased graduates' leadership capacities and communication and governance skills; whether these individual-level impacts have strengthened a broader network of PLHIV in BC; and whether the greater HIV sector has benefitted.

Results: We are currently collecting data and by April will be able to answer a number of key evaluation questions developed by the PLDI Impact Evaluation Steering Committee. The team will use the findings to: report to funders, participants and stakeholders; improve BC's PLDI program; and develop program promotional materials.

Conclusion: It is expected that BC's PLDI impact evaluation will reveal significant impacts the training has on the

lives of its graduates and the sector. PLDI has strengthened a network of PLHIV leaders in BC who have taken on active roles as change agents within their communities. Many graduates have gone on to employment and volunteer positions and participate in a diverse set of roles and functions across BC.

SSP9.02

McLaren Housing Society's Portable Subsidy Program: A Structural Intervention for People Living with HIV

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Context: Safe, affordable and adequate housing is foundational to the health of people living with HIV (PLWH) and is the mandate of The McLaren Housing Society (MHS). Assisting PLWH with securing adequate housing is particularly essential in Vancouver, where there have been unprecedented spikes in rental costs and a plunge in vacancy rates. This is extremely stressful to our low-income clients. To bridge the gap in affordability, MHS administers portable rental subsidies (PS), cash amounts, to clients so they can live independently in market housing in the community.

Program: MHS provides housing and support services to low-income individuals and families living with HIV. This program – which comprises 26% of MHS' programming – supports 74 clients including individuals, couples, and families from diverse backgrounds. The majority are men (74%), concentrated in central Vancouver (58%), single (68%), and report having an HIV specialist (80%). There are 19 families currently enrolled. This program is especially effective for people who prefer to live in the community for reasons of family size, as well as cultural or locational needs. Unlike other programs, the subsidy is portable and moves with the client. Support is also available for landlord/tenant problem solving, emotional support, and referrals. Clients are financially reviewed once per year to ascertain continued eligibility.

Implications: PS provides immediate and tangible financial relief within the Vancouver housing crisis. It also allows clients the dignity to decide where they want to live and some anonymity as they are not designated to a low-income/HIV-identified building. Indeed it facilitates the diversification of the region's neighbourhoods. PS supports people in building on or maintaining their independence, and mitigates the need for purpose-built subsidized housing. PS is a structural housing intervention that is easily administered and cost-effective.

SSP9.03

Queering the social determinants of health: Beyond HIV/AIDS

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Recent developments in the funding of HIV/AIDS services have raised concerns among community-based organizations. Will funding require these organizations to broaden their focus beyond HIV/AIDS, and what might this mean for LGBTQ-specific services? This paper examines the issue of sexual orientation, as it is understood as a social determinant of health (SDH). The SDH framework uses a structural analysis of health that goes beyond looking at lifestyle factors to recognize barriers to health in the power relations and the intersectionality of social location, class, education, geography, gender, sexual orientation, race, culture and ethnicity, and other issues of social exclusion. Furthermore, this approach articulates how social resources allocated and distributed, sometime inequitably, among various groups. Although sexual orientation is often included in the "list" of SDH, the question remains whether the broader structural and economic aspects of sexual orientation are understood and addressed in LGBTQ health policy, programs, and services. The paper provides an overview of existing LGBTQ health policy and programs, as well the literature on sexual orientation as a SDH. By developing descriptive indicators how well political, economic, and cultural factors are reflected in the literature and in policies and programs, this paper initiates a way to analyze whether the SDH framework incorporates a LGBTQ paradigm.

Pleasure, Intimacy and Romance in the HIV Era

Plaisir, intimité et amour à l'époque du VIH

SSP10.01

A critical feminist scoping review of 20 years of epidemiological research on sexual activity, sexual function, and sexual satisfaction among women living with HIV

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We conducted a scoping review of epidemiological research (1996–2016) on sexual activity, function, and satisfaction among women living with HIV (WLWH). Studies where WLWH made up all or part of the sample were included. Guided by critical feminist theory, we sought to document the diversity of women's sexual experiences positioned within social and historical contexts, and the limitations of positivist survey research. Twenty-three studies involving 6,853 WLWH were found. Forty-three percent were mixed-gendered studies that generally overlooked the different sexual realities of women and men. While samples were diverse with respect to age, ethnicity, and socio-economic status, studies provided a largely North American, heterosexual, cis-gender picture of sexuality. The vast majority researched sexual function (57%) and activity (30%), with just three (mixed-gender) studies devoted to satisfaction. They tended to approach these domains as individual experiences rather than the outcome of social context, with multiple underlying assumptions (e.g., sex-as-penetration, sex-as-mandatory). Overall, research suggests women experience declines in sexual activity, function, and satisfaction following HIV diagnosis. The extent of such declines, however, is varied, with numerous contextual forces shaping women's sexual wellbeing. Findings revealed little evidence that clinical markers, like ART use, viral load, and CD4 cell count predict sexual outcomes. Rather, women's experiences of sexuality are primarily influenced by the effects of HIV-related stigma (e.g., shame, fear) intersecting with other social, economic, and life-course factors, including relationships, violence and mental health, poverty and addiction, and aging and menopause. These factors, however, remain underresearched in favour of biological domains. Moreover, women who deviated from heteronormative expectations of 'healthy' sexuality (i.e., high levels of desire, arousal, intercourse, orgasm) were pathologized as dysfunctional and in need of fixing. This review underscores the need for feminist-based research and support concerning sexuality for WLWH that is affirming of diversity and grounded in women's sexual rights.

SSP10.02

A feminist analysis of sexual satisfaction and sexual pleasure across five relationship types among women living with HIV in Canada

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Objective: Utilizing a feminist approach to quantitative research, we compared sexual satisfaction and pleasure across relationship types among 1,335 women with HIV in the Canadian HIV Women's Sexual and Reproductive Health Cohort Study.

Methods: Through peer-designed/administered surveys, we measured women's satisfaction with their sex life ("completely" to "not at all") and pleasure from sexual experiences (solo/partnered) last month ("always" to "none"). We delineated relationship types using latent class analysis with seven indicators (relationship status, duration, exclusivity, partner HIV-serostatus, power, physical intimacy, emotional intimacy) and assessed associations with sexual outcomes using multinomial logistic regression, adjusting for confounders (age, violence, depression, physical health-related quality-of-life, HIV stigma, sex work, and drug use).

Results: Latent classes included: no relationship (46.5%), relationship without sex (8.6%), and three types of sexual relationships–short-term/casual (15.4%), long-term/unhappy (6.4%), and long-term/happy (characterized by higher levels of intimacy and shared power) (23.2%). Women in long-term/happy relationships were most likely to be "completely" sexually satisfied (48.7%), followed by women in relationships without sex (20.4%) and no relationship (12.4%)), versus short-term/casual (7.6%) and long-term/unhappy (8.2%) relationships. Fifty-two percent had recent sexual experiences, including 22% of women reporting no partnered sex (of which one-quarter reported "always" feeling pleasure). Among women having partnered sex, those in long-term/happy relationships were most likely to report "always" feeling pleasure (63%),

followed by those in short-term/casual (30.7%) and long-term/unhappy (16.2%) relationships. Some reported "no" pleasure during sex: 24.2% short-term/casual, 21.6% long-term/unhappy, and 2.8% long-term/happy. Relative to no relationship, women in long-term/happy relationships [AOR:75.92(95%CI:31.58–182.55)] and relationships without sex [AOR:2.04(95%CI:1.46–4.54)] had increased odds of being "completely" satisfied (vs. "not very/not at all"). The former group also had increased odds of "always" feeling pleasure (vs. "seldom/none") [AOR:10(95%CI:4.14–24.15)], relative to short-term/casual.

Conclusions: Sexual satisfaction and pleasure differed by relationship type. Findings underscore the relational and social bases of women's sexuality.

Sex, Sexuality and Gender: Populations across Diverse Contexts and Axes of Inequity

Sexe, sexualité et genre : Populations dans les contextes et axes divers d'inégalité

SSP11.01

One Year Evaluation of TLO: Trans Latino American Women in Ontario

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Problem: Transgender individuals have been traditionally ignored for services provided in Ontario for the past years. This situation could be explained with two arguments (1) Transphobia as a source of undermining individuals with different gender non-binary status. (2) Due to race discriminatory issues that marginalized immigrant individuals face, and who may not speak the official languages. TLO (Trans Latinas Ontario) started in November 2015, as a drop-in group to host weekly meetings for those Latino Trans women (LTW) who needed a space to talk and to relate to others experiencing similar situations.

Method: Following a drop-in program, TLO has run for the past 13 months, starting with 6 participants. Over time, the number has increased to 14.

The main goals of the group were (1) to reduce social isolation, (2) to increase empowerment, (3) to create a sustainable space as a source of support for LTW.

Results: According to qualitative evaluation narratives TLO participants shared that they were able to create meaningful relationships within the group, supporting each other trough different issues (Transition, hormone-related concerns, info sharing on condom use negotiation technics, and mental health) achieving the first outcome. Second one, TLO participants said they obtained more information and more support, and that translated into a higher sense of power/strength; and the third goal (sustainability) was achieved by the OHTN/UWW funding that was provided to support a year run of the program, and to create a visual statement of the TLO's experience.

Lessons Learned:

1. No Trans/cultural-appropriate services are available to LTW.
2. Trans people in Canada show one of the highest HIV infection rates among other groups. TLO addressed significant issues related to HIV prevention.
3. Mental health needs to be recognized as a priority in the Trans population. Groups like TLO play an important role in that matter.

SSP11.02

Sexual Self-Efficacy and Consistent Condom Use among Adolescent Men and Women Living in the HIV Hyper-Endemic Setting of Soweto, South Africa

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Background: Sexual self-efficacy (SSE), one's perceived ability to engage in HIV preventative behaviour, is thought to be an important predictor of consistent condom use (CCU). This analysis seeks to understand gender differences regarding SSE and its relation to CCU among adolescents in Soweto.

Methods: Using data from a cross-sectional, interviewer-administered questionnaire of adolescents (14-19 years) living in Soweto, South Africa, a gender-stratified analyses of SSE and lifetime CCU (defined as using a male condom at every vaginal and anal sexual act) was conducted. SSE was measured using a 6-item scale (range: 0-6, with higher scores indicating higher SSE), with 'high-SSE' assessed as ≥3 (study alpha=0.75). Gender-stratified multivariable logistic regression models assessed associations between SSE and CCU among sexually-experienced adolescents.

Results: Of 830 participants, 217 women and 200 men reported ever having sex. Among these, 189/217 (94.5%) women and 177/200 (88.5%) men had boyfriends/girlfriends in the past 6 months; almost half of men (45.3%) and 9.1% of women reported ≥2 boyfriends/girlfriends ($p<0.001$ difference by gender). Further, 5.4% of men and 32.6% of women reported being in a relationship with a partner ≥5 years older ($p<0.001$). A higher proportion of adolescent women reported high-SSE (68.7% versus 49.5%, $p<0.001$). There was no difference in CCU by gender (45.5% versus 45.8%; $p=0.943$). In adjusted models, high-SSE was not associated with CCU among adolescent women (aOR=1.43, 95%CI=0.74-2.77), controlling for age, food security, having an adult at home and depression (using the CES-D scale) however, it was significantly associ-

ated with CCU among men (aOR=3.51, 95%CI=1.86-6.64) controlling experiencing physical violence.

Conclusion: Given that young women in South Africa experience a three-fold higher risk of HIV acquisition, these findings underscore the need for gendered HIV prevention strategies that move beyond individually-focused strategies and consider how relationship dynamics, including age and gender-power inequities, influence sexual decision-making and HIV risk.

SSP11.03

Women living with HIV (WLHIV) in Quebec: an intersectional analysis of gender, violence and HIV

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Context: Women living with HIV (WLHIV) not only experience more violence than men living with HIV, they are also at greater risk of specific forms of victimisation and re-victimisation through intimate partner violence and childhood sexual abuse (Siemieniuk et al., 2010). A growing field of research raises the intersections between HIV and violence (Phillips et al., 2013). In this vein, this study's objective is to provide a better understanding of the intersection between gender, violence and HIV to guide future intervention practices.

Methods: This study was conducted as a part of the Quebec-based evaluation of the PLURIELLES empowerment program aimed at improving the emotional and sexual wellbeing of WLHIV. This community-based research project enlisted the participation of sixty WLHIV aged from 23 to 70 years old (M = 48 years). An intersectional analysis (Bilge, 2015) was performed on the transcripts of the 23 WLHIV who participated in the semi-structured interview. The theoretical framework considers five domains of power; 1) structural; 2) hegemonic; 3) disciplinary; 4) interpersonal; and 5) psychic or embedded.

Results: The experiences reported by the WLHIV, to different degrees, related to each of these power domains. In the hegemonic and structural domains, they reported experiences of stigmatization associated with HIV. In the disciplinary domain, some mentioned negative attitudes from service and care providers and employers. In the interpersonal domain, nearly half of the women reported one or more episodes of childhood sexual abuse or/and intimate partner violence. In the psychic or embedded domain, some women mentioned an internalization of stigma that affected not only their private and sexual lives but their social lives as well.

Conclusion: These results show the importance of having a more detailed understanding of the intersections of gender, HIV and violence-related issues and highlight the need to implement actions that target these intersections.

SSP11.04

Sexual Orientation Differences in Health and Wellbeing Among Women Living with HIV in Canada: Findings From a National Community-based Cohort Study

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Background: Scant research has examined wellbeing among sexual minority women (SMW) with HIV despite well-documented sexual minority health disparities. The objective was to examine sexual orientation differences in clinical, psychosocial and structural outcomes among women living with HIV (WLH) in Canada.

Methods: Cross-sectional data was analyzed from a Canadian cohort study conducted with WLH between 2013-2015. This included 1,420 participants (SMW: n=180; heterosexual: n=1240). SMW participants (median age: 38 years, IQR: 13) included bisexual (58.9%), lesbian (17.8%) and other sexualities (gay, queer, two-spirit) (23.3%). We assessed sexual orientation differences in clinical, psychosocial and structural outcomes. Multivariate logistic regression analyses were conducted to determine the adjusted risk ratio for sexual orientation.

Results: SMW were younger than heterosexual participants (median age 38 years vs. 43 years; p<.001). Caucasian was the highest reported ethnicity category for both heterosexual and SMW participants (40.4% and 46.1%, respectively); the second most frequent ethnicity was African, Caribbean or Black among heterosexuals (31.9%) and Indigenous among SMW (35.6%). Multivariate logistic regression analyses controlling for age, poverty, education, and ethnicity revealed that compared to heterosexual women, SMW reported *clinical* (<80% ARV adherence vs. 100% ARV adherence [AOR: 2.57, 95% CI: 1.45-4.56]), *psychosocial* (childhood abuse [AOR: 2.93, 95% CI: 1.83-4.70], sex work [AOR: 2.87, 95% CI: 1.71-4.81], current injection drug use [IDU] vs. never IDU [AOR: 4.54, 95% CI: 2.70-7.61], previous IDU vs. never IDU [AOR: 2.35, 95% CI: 1.51-43.65], depression [AOR: 1.06, 95% CI: 1.03-1.08], lower resilience [AOR: 0.96, 95% CI: 0.95-0.98]), and *structural* (HIV support services barriers [AOR: 1.76, 95% CI: 1.15-2.69], unstable housing [AOR: 1.72, 95% CI: 1.11-2.69], sexism [AOR: 1.04, 95% CI: 1.02-1.06], racism [AOR: 1.03, 95% CI: 1.02-1.05]) outcome differences.

Conclusions: SMW with HIV experience social and health disparities relative to heterosexual WLH. Tailored interventions are needed to promote health equity among SMW with HIV.

SSP11.05

"How am I going to Love in this Country?" Stigma, Gender, Sexuality and Disclosure Among African Women Living with HIV in Winnipeg, MB

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Racialized women in Canada are particularly affected by HIV. Current evidence indicates that HIV disproportionally impacts immigrant women from African countries. Research has also shown that stigma is one of the main factors contributing to the HIV epidemic among marginalized women living with HIV. Stereotypes in Canada about African societies, and about HIV and sexuality in these societies, contribute to the stigma experienced by people of African heritage in Canada.

Stigmatizing discourses around HIV endure and continue to reinforce prejudices and mark "otherness". Even decades into the epidemic, stigma continues to be a major concern for people living with HIV, and for those who care about them and for them.

Given its association to the morality of sexual behaviours, HIV continues to be constructed as a moral or moralizing disease. In order to better understand HIV stigma, we need to delve deeper into the understanding of human sexuality. Based on our community-based ethnographic study with women participating in a support group with African immigrant women living with HIV in Winnipeg, Manitoba, we explore the relationship between sexuality-related stigma and HIV, and public health management of HIV. In this presentation, we look at what stigma means for African immigrant women living with HIV in Winnipeg, and try to interpret their experiences of stigma. More specifically, we examine how stigma affects women's understandings of and experiences with intimate relationships and, more broadly women's sexuality. We conclude that our study sheds light on the stigma related experiences of women living with HIV. More so, it draws lessons on sexuality as a symbol of moral status in women, providing significant insights into (with implications for) broader responsive HIV prevention initiatives.

SSP11.06

Tensions and contradictions: Gendered expectations, sexual values and sexual practices of marginalized young men in Toronto

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Background: Despite decades of efforts, sex education at school continues to focus on biology (puberty and reproduction), diseases (STIs and HIV) and behavioural risks. Educational messages tend to be heteronormative and gender-biased, with emphases placed on heterosexual young women as risk-keepers. Few sexual health programs have addressed how gendered expectations have shaped the sexual practices of young men.

Methods: In the Youth Engagement Project (YEP), we studied the individual and structural factors that shaped the sexual values and sexual practices of marginalized young people aged 16 to 24 in Toronto. We used a series of two focus groups to explore the participants' growing up experiences, gender socialization and perspectives on youth-relevant sex education. This presentation reports on the perspectives and experiences of the young men in this study.

Results: Of the 47 YEP participants, 23 of them identified as men and one identified as a transman. Further, 5 identified as gay/queer and 19 identified as heterosexual. The young men's narratives reflected tensions and contradictions about their gendered socialization and sexual practices. While they all encountered similar hegemonic masculine expectations at home, school and in society, their responses varied based on their sexual and masculine identities. Study results showed that: (1) dominant discourses of ideal masculinity perpetuate homophobia; (2) lack of access to gay positive information and role models made it difficult for gay/queer young men to navigate their first sexual experience; (3) heterosexual young men faced tremendous pressure to fit within the heteronormative masculine expectations; and (4) both gay/queer and heterosexual young men expressed the desire to resist hegemonic masculine expectations.

Conclusion: Young people's sexual practices are closely linked to their everyday gendered experiences. Integrating dialogue on gender identities and gendered performances is critical to the design of effective and relevant sexual health promotion programs for young men.

Social, Structural and Systemic Drivers of HIV

Moteurs sociaux, structurels et systémiques du VIH

SSP12.01

Nuanced models of online and offline community attachments highlight differences in sexual risk among highly- and lowly-connected app-users

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Background: Previous methodologies showing a relationship between internet use and condomless anal sex with serodiscordant/unknown status partners (sdCAS) may over-simplify patterns of social interaction among gay and

bisexual men (GBM)—misrepresenting these individuals and their risks.

Methods: We recruited sexually-active GBM, aged ≥16 years, using respondent driven-sampling in Metro Vancouver. We used latent class analysis to examine patterns of social interactions including: attendance at gay venues/events (i.e., bars/clubs, community groups), social time spent with GBM, use of online social media and sex-seeking apps/websites, and consumption of gay media. Multivariable multinomial regression models identified correlates of class membership.

Results: We recruited 774 participants. Fit statistics specified a three-class solution: Class 1 "Socialites" (38.8%) were GBM who connected both online and offline. Class 2 "Online-Abstainers" (25.7%) were moderately connected GBM with no app/website use. Class 3 "Online-Users" (35.4%) had lower in-person connectedness and high levels of online attachment.

Compared with Socialites, Online-Abstainers were older (aOR=1.04, 95%CI:[1.02,1.06]), more likely to be bisexual (aOR=2.06, 95%CI:[1.12,3.82]), less likely to be single (aOR=0.50, 95%CI:[0.29,0.84]), had lower HIV/AIDS stigma scores (aOR=0.93, 95%CI:[0.87,0.99]), had fewer sexual partners (aOR=0.99, 95%CI:[0.98,1.00]), and were less likely to have recently tested for HIV (aOR=0.51, 95%CI:[0.32,0.80]); Online-Users were more likely to be "coming out" (vs. out, aOR=1.90, 95%CI:[1.07,3.36]), less likely to have heard about "Treatment as Prevention" from a community-based organization, if they were aware of it at all (aOR=0.41, 95%CI:[0.23,0.74]), and were more likely to report any sdCAS (aOR=1.46, 95%CI:[1.02,2.10]). Compared with other classes, Socialites were more likely to have an annual income ≥$30,000 (Online-Abstainers: aOR=0.47, 95%CI:[0.30,0.72], Online-Users: aOR=0.59, 95%CI:[0.41,0.85]).

Conclusions: Among online sex-seeking GBM, those with lower in-person attachment exhibited greater sdCAS than those who were highly connected. These findings suggest that in-person community attachments moderate the relationship between internet-use and sexual risk—highlighting the benefits of supporting inclusive community programs.

SSP12.02

"It's about having the open, authentic reality": Community-based research and recommendations for prison-based needle and syringe programs

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Conditions in Canada's federal prisons have significantly deteriorated in the past decade, with increases in the number of prisoners, double-bunking, and 'use of force' by correctional officers. Federal prisons are comprised disproportionately of racialized and low-income individuals, many of whom have mental health care needs and histories of problematic substance use prior to incarceration. Prisoners' high rates of drug use is often symptomatic of these underlying issues.

While correctional policy strictly prohibits drugs in prison, illegal drugs are commonly available. Access to harm reduction programming, however, is limited and prisoners who inject drugs are denied access to sterile injection equipment, leading to frequent equipment sharing. In turn, rates of HIV and HCV among federal prisoners are at least 10 and 25 times higher than the general public. Indigenous peoples, who are disproportionately incarcerated, experience a greater burden of this public health crisis.

Over two decades of empirical evidence has shown that prison-based needle and syringe programs (PNSPs), which have existed for over 20 years in a diversity of countries, are an important means of preventing HIV and HCV transmission in prison. While the Correctional Service of Canada has thus far resisted their implementation, a lawsuit initiated in 2012 could compel the prison service to make PNSPs available as a critical public health and human rights measure.

In light of this prospect, this study was conducted to ensure that the perspectives of former prisoners are central to the development of prison-based harm reduction measures. Drawing on primary data from a community-based study in Ontario with people who have been incarcerated in federal prisons and have experience with injection drug use, as well as community and medical professionals, this presentation will highlight the considerable evidence in support of PNSPs and six recommendations for PNSP implementation and HIV/HCV prevention in federal prisons.

SSP12.03

North-South Differences in the experiences of HIV-related stigma for women living with HIV in Canada

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Background: In Canada, individuals living in Northern regions report increased barriers to health care, significantly poorer health outcomes and increased mortality. These barriers may be exacerbated by experiences of HIV-related stigma. To further understand the impact of living in Northern regions on shaping social contexts of health and wellbeing among women living with HIV, we assessed geographic differences in HIV-related stigma experiences among women residing in Ontario and British Columbia

enrolled in the Canadian HIV Women's Sexual & Reproductive Health Cohort Study (CHIWOS) .

Methods: We used CHIWOS' baseline peer administered questionnaire data to compare HIV-related stigma among participants in Northern Canadian regions to participants in Southern regions. Northern regions were defined by healthcare delivery jurisdiction. The primary outcome was the shortened 10-item HIV Stigma Scale (sHSS) score (ranging from 0 to 40, higher scores indicating greater HIV-related stigma). Multivariable linear regression assessed the association between Northern region of residence and sHSS. Demographic characteristics were compared between Northern and Southern populations. Covariates that lead to a ≥10% change in the parameter estimate for Northern region were included in the multivariable model: years living with HIV, ethnicity, income, substance use and hepatitis C.

Results: Of 1043 women included in the analysis, 105 (10%) were from Northern regions and 938 (88%) were from Southern regions. Mean sHSS scores were high in Northern regions compared to Southern regions (25.4 vs. 23.4, p=0.014). In adjusted analyses, Northern region of residence was associated with a 1.97 point increase in sHHS score (95% confidence interval: 0.20, 3.73). Additional correlates of sHHS included annual household income <$20,000.

Conclusion: This study identified higher rates of perceived HIV-related stigma in Northern regions of Ontario and British Columbia in comparison to Southern regions. This, highlights the need for region-specific programs to support people living with HIV living in Northern communities.

SSP12.04

Realizing women's reproductive rights in the era of ART: The negative impact of having one's HIV status 'outed' on pregnancy decisions

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Background: While advances in antiretroviral therapy and 'prevention-of-mother-to child-transmission' have greatly supported women living with HIV's (WLWH's) reproductive choices, little is known about the influence of social factors on WLWH's pregnancy decisions. This study examined the effect of non-consensual HIV disclosure on WLWH's decision to become pregnant.

Methods: Analyses drew on baseline data (2015-present) from SHAWNA *(Sexual health and HIV/AIDS: Women's Longitudinal Needs Assessment),* a longitudinal community-based cohort with WLWH (trans inclusive), aged 14+ across Metro-Vancouver, Canada. Using community-recruitment strategies and referral by health providers, women are invited to participate and complete a semi-annual interviewer-administered questionnaire and HIV/STI monitoring. Multivariable logistic regression was used to model the effect of non-consensual HIV disclosure (having your HIV status 'outed') on WLWH's decision to become pregnant.

Results: Of the 216 cisgender women of reproductive age (at diagnosis) included in the analysis, 52.3% reported ever having their HIV status 'outed' and 25.0% had been discouraged from becoming pregnant due to their diagnosis. While only 11.6% had accessed formal preconception counseling, over half (50.5%) had accessed women-centred HIV care inclusive of sexual and reproductive health services. In multivariable analyses, women reporting non-consensual HIV sero-status disclosure had 3.47-fold increased odds being discouraged of becoming pregnant due to their HIV status (AOR: 3.47; 95%CI 1.60-7.52), independent of sexual and gender identity or previous HIV-related violence. Year of HIV diagnosis did not affect participants' pregnancy decisions.

Conclusions: Non-consensual HIV disclosure continues to undermine WLWH's ability to realize their reproductive rights. The low level of preconception counseling may reflect internalized stigma, which can prevent/delay women from disclosing pregnancy intentions to health providers or accessing SRH services. Supporting the reproductive rights of WLWH will require multi-level interventions, including efforts to better incorporate conception-focused discussions and address stigma in HIV clinical care interactions alongside increasing access to women-centred HIV care.

SSP12.05

Global Challenge, Local Responsibility: Implications for Canada of the UN Secretary-General's High-Level Panel on Access to Medicines

Richard Elliott, Nicholas Caivano

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In September 2016, a high-level body of eminent persons advising the UN released its controversial report recommending various measures to help remedy the evident "policy incoherence between the justifiable rights of inventors, international human rights law, trade rules and public health in the context of health technologies."

The High-Level Panel on Access to medicines was appointed by the Secretary-General in response to a recommendation by the Global Commission on HIV and the Law, which previously had issued a damning critique of the ongoing global inequality in access to medicines. The Commission laid the blame, in part, on international and domestic rules on patents and other aspects of intellectual property (IP) — including more restrictive rules being negotiated in successive international trade agreements (such as the Trans-Pacific Partnership) — that create and maintain barriers to more affordable medicines, contrary to

states' human rights obligations. These barriers are fuelling an ongoing public health and human rights crisis particularly in low- and middle-income countries, and increasingly posing unsustainable burdens on high-income countries.

In its Report, the High-Level Panel made recommendations regarding:

(1) intellectual property laws and policies to improve access to health technologies, including using and preserving "flexibilities" regarding IP rights and conditions that should attach to publicly-funded research;

(2) exploring new incentives and mechanisms for financing R&D that de-link costs of R&D from the price of the end product, including a new binding international convention of health R&D for public health needs; and

(3) various measures to improve domestic and national governance, accountability and transparency regarding negotiation of international rules affecting access to medicines, R&D costs, patent and registration status, and variability in pricing.

The presentation will examine the recommendations made by the High-Level Panel and how Canada can act on those recommendations to protect equitable access to affordable medicines for all.

SSP12.06

Social determinants of health among trans women with HIV in Canada: A cross-provincial comparison

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Background: Globally, transgender (trans) women are disproportionately affected by HIV, due in part to gendered and other intersecting forms of stigma and discrimination, poor social determinants of health (SDoH), and violence. Little is known about the experiences of trans women with HIV in Canada and how these experiences differ across provinces. Our study's purpose was to compare SDoH and mental health outcomes among trans women with HIV in British Columbia (BC), Ontario (ON), and Quebec (QC).

Methods: We analysed baseline survey data from the Canadian HIV Women's Sexual and Reproductive Health Study (CHIWOS), a multi-province (BC, ON, QC), community-based cohort study. We computed descriptive statistics and compared among trans women (n=53) in BC (n=10), ON (n=28), and QC (n=15) using chi-square or Fisher's exact test, and ANOVA.

Results: Trans women in CHIWOS reported a mean age of 41 years (SD=10). Many reported depression/PTSD (44.0%) and a household income <$20,000/year (92.3%). Significant cross-provincial differences were noted across several outcomes: proportion of refugees/permanent residents (BC: 0.0%, ON: 20.0%, QC: 53.3%, $p<0.001$); main source of income considered illegal (BC: 10.0%, ON: 7.4%, QC: 13.3%, $p<0.05$); ever incarcerated (BC: 80.0%, ON: 50.0%, QC: 26.7%, $p<0.001$); current housing instability (BC: 20.0%, ON: 39.3%, QC: 0.0%, $p<0.05$), history of injection drug use (BC : 80.0%, ON: 22.7%, QC: 6.7%, $p<0.001$); experienced violence in adulthood (BC: 100%, ON: 61.5%, QC: 100%, $p<0.001$); and delayed (≥ 3 months) access to HIV-related healthcare (BC: 60.0%, ON: 15.0%, QC: 35.7%, $p<0.05$).

Implications: These descriptive findings highlight social determinants that shape the health of trans women with HIV in Canada. These results suggest that such experiences may differ by province, indicating a need for further research to understand reasons for these differences in order to inform context-specific interventions to address the SDoH for trans women with HIV.

SSP12.07

Adapting the Asian MSM Resilience Dialogues for Asians Living with HIV/AIDS

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Background: To address the complex challenges related to racism, homophobia, and HIV stigma faced by Asian MSM, Asian Community AIDS Services (ACAS) in Toronto conducted a community-based research to identify resilience strategies to inform strength-based programming. Based on its findings, further literature search and stakeholder consultation, the research team developed an original group intervention: the MSM Resilience Dialogues (MSMRD). The intervention was piloted amongst Asian MSM with positive results and is now being adapted for scale-up for the Asian people living with HIV/AIDS through the Ontario Positive Asians Network (OPA).

Description: The MSMRD intervention consists of five 3-hour experiential learning sessions that engage participants in dialogues to foster critical self and group reflection, identity exploration, and values clarification. The intervention supports the participants to recognize individual and collective resilience; access strengths from their cultural identities and community connections; and apply transferrable resilience strategies across life challenges.To evaluate MSMRD, participants completed pre- and post-intervention questionnaires with scales that measured individual resilience, community engagement, social connection, safer sex self-efficacy, and mental wellness. They also completed anonymous online survey and a 3 month follow up focus group to reflect on longer term changes.

Results: Amongst the pilot participants (N=9), the pre- and post-intervention measures showed positive trends in most scales. The online survey showed that all participants felt that the intervention was effective in achieving all its stated objectives, and focus group discussion showed that many integrated behavioral challenges from new insights and skills learnt from the intervention.

Conclusions: Building on the promising results and feedback learnt from the MSMRD, ACAS developed partnership with OPA to adapt and scale up the intervention amongst Asian PHAs in spring of 2017. Evaluation results will be presented at CAHR to inform further scale up and adaptation for more diverse communities.

SSP12.08

Ideologies of Black Masculinity and HIV vulnerability among Self-Identified Heterosexual African, Caribbean and Black Canadian Youth Living in Ontario

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Background: In Ontario, HIV incidence attributed to the heterosexual/non-endemic and the heterosexual/endemic exposure categories were 16.7% and 19.5% respectively. Despite the fact that heterosexual transmission is the second mode of HIV exposure, the focus on heterosexual population has been minimal.

Purpose: We present preliminary findings of five focus group discussions in London, Ottawa, Toronto, and Windsor during phase one of weSpeak. weSpeak is a 5-year research program and related activities undertaken by a community-academic partnership in Ontario with a goal of reducing HIV vulnerabilities and promoting resilience through active engagement of self-identified heterosexual ACB men in programs, research, and policy.

Research Design: We organized 5 focus groups with self-identified heterosexual ACB youth (N=41) to explore how self-identified heterosexual ACB boys and men view, understand, and make sense of masculinity, heterosexuality and HIV vulnerability within the context of HIV prevention.Preliminary

Results: Data highlighted the power and burden of heteronormativity in the meaning and performance of being 'straight'. Data also opposed the stereotypes and marginalization of Black men while resisting and challenging the dominant discourses of Black masculinity as hyper- masculine and sexualized. Finally, youth constructed HIV vulnerability as a product of identity issues, unsafe sex practices, watered-down sex education, mental health challenges and lack of accessibility to inclusive HIV services; non-involvement and engagement of black men in HIV responses and outcome.

Implications: ACB youth understand how they may be vulnerable to HIV and made a number of recommendations including: raising awareness about HIV vulnerability, engaging young heterosexual Black men in critical dialogue about racist stereotypes and dominant discourses about Black heterosexual masculinities, introducing sex education in schools and communities, and to promote outreach- in groups. They further made a call on government to increase inclusive and accessible sexual health care, health promotion and HIV testing.

SSP12.09

Mapping Contextual Drivers of HIV Vulnerability: A study of African, Caribbean (ACB) youth in Windsor, Canada

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Participatory mapping and walking tours were used to inform the research and the intervention design of POWER, a project funded by CIHR to determine the contextual factors that increase the vulnerability and build the resilience of African, Caribbean and Black Canadian (ACB) youth in Windsor to HIV infection. We conducted a total of six mapping sessions, African, Caribbean, Black Canadian and mixed in which 16 to 27 years old youth physically identified on the map of Windsor, and discussed where to find ACB people, where they spend leisure time, places afraid to go, places to find casual partners, healthy and unhealthy places, where to find potential spouse, and secret places for secret things. Walking tours were conducted to further visualize the information and discussions in the mapping sessions. A total of 43 participants, made up of 24 males and 19 females in community mapping and eight participants in walking tours, participated in this data collection between May and November of 2013. We transcribed the tapes and notes verbatim into word documents and were analyzed using thematic content analysis and N6 qualitative software to identify the structural, social and environmental factors that expose youth to HIV infection. Results showed that ACB population mainly reside in downtown and west/Sandwich areas, with close proximity to bars, strip shops, recreational/sports places. Analyses also identified house parties as common places for social and sexual networking. Multidimensional factors including lack of entitlement due to marginalization, discrimination, poverty, drug and alcohol use, further complicated the exposure of AC youth to HIV/AIDS. The paper concludes that future HIV/AIDS program developers take into account individual, structural, environmental and socio-cultural factors in formulating HIV prevention strategies that are locality specific and sustainable.

SSP12.10

HIV And Housing Histories: Using Timelines to Trace Connections Between Housing and Health

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Background: *Positive Living, Positive Homes* (PLPH) is a community-based research (CBR) study examining the relationship between housing and health for adults living with HIV in British Columbia. In this paper we trace the connections between health and housing, and assess participants' awareness and perceptions of these connections.

Methods: PLPH is a longitudinal, qualitative CBR study taking place in three BC communities (Prince George, Kamloops, and Greater Vancouver). In each community, people living with HIV, service providers and other partners participate in study implementation, data analysis, and knowledge translation activities. As part of the baseline in-depth interviews for PLPH, HIV-positive participants were asked about their housing histories from the time of HIV diagnosis to the present, with a focus on the five years prior to interview. We transformed each response into a linear timeline on which significant points in housing history were noted. The timelines were compared to responses about health history. At one-year follow-up interviews, timelines will be revisited to update and further explore connections between health and housing.

Results: 99 adults living with HIV in a wide range of housing situations participated in baseline interviews. Age range was 25 to 71; 51% were female; 48% were Indigenous. Approximately 60% of participants reported illness episodes coinciding with periods of unstable housing and of those, approximately 20% said their lowest CD4 count came at a time of homelessness or precarious housing. The majority agreed that stable housing is critical to good health.

Conclusions: Timelines demonstrated that health and housing are closely linked. Many participants showed awareness of these links on a theoretical level, but often required prompting to discover meaning on a personal level. By providing simple visual representations of what were often very complex housing histories, the timelines proved a useful tool for collating and analyzing data.

SSP12.11

Housing Specialization located in Health Care

Sharon T. Pratt

McLaren Housing Society, Vancouver, BC

Founded in 1987 McLaren was the first HIV/AIDS housing provider in Canada. From a private residence offering accommodation to five people the organization has expanded to provide a variety of innovative affordable housing options to over 300 people in British Columbia.

McLaren Housing Society aims to provide housing and support services for individuals and families living with HIV/AIDS and to increase the opportunity for improved health, wellness, independent living and sense of community.

This 2 year-long project was envisioned by McLaren Housing Society (MHS) who identified a need to form a partnership with the Immuno Deficiency Clinic (IDC) St. Paul's Hospital Vancouver, BC which is aligned to the Centre for Excellence, Vancouver, BC. The IDC provides a multi-team approach for HIV care (Doctors: HIV Specialists: Psychiatrist; Psychologists; Nurses; Pharmacists; Social Workers; Dietician) & the housing specialist would address a range of housing concerns impacting patients. The proposal was to place a housing specialist within the healthcare system & support the social work team. Patients accessing the health system could then access the housing specialist who for the first time would link them into the very intricate social housing & market rental landscape and help them navigate the complexities of getting a roof over their heads. The MHS Housing Continuum was the assessment tool that was used to guide all the interventions.

Lessons Learned: A brief description of the results of the project. Since its inception, this project has seen over 200 patients. The most important lesson that we learnt was having a housing specialist on site made a huge difference in directing patients to various housing options that was a good fit for them. This meant that patients could now be better connected to their healthcare provider & other support services, which is key to their overall health outcomes.

SSP12.12

Self-compassion mediates the link between childhood trauma and syndemic HIV risk factor in gay and bisexual men

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Background: Depression is a syndemic factor shown to increase the risk of HIV in gay and bisexual men (GBM). Childhood emotional neglect (CEN) and childhood sexual abuse (CSA) are associated with depression in GBM. However, links between other forms of childhood trauma,

including emotional abuse (CEA) and physical abuse (CPA) and neglect (CPN), and depression have not been explored in this population. Self-compassion correlates with life satisfaction in gay men, subjective happiness in sexual minority adults, and with less depression in undergraduate students. The association between self-compassion and depression has not been explored among GBM, nor has the role of self-compassion in the relationship between childhood trauma and depression.

Methods: 470 HIV-negative sexually active GBM in Toronto completed a battery of questionnaires including the Childhood Trauma Questionnaire (CTQ), the Center for Epidemiologic Studies Depression Scale (CES-D), and the Self-Compassion Scale (SCS). Multiple mediation models were fit using MPlus 6.1 to examine direct and indirect effects of CEA, CEN, CPA, CPN, and CSA on depressive symptoms through the SCS and the SCS subscales.

Results: Most participants were White (59%) and gay (86%) and the mean age was 35 (SD=12). Each type of childhood trauma except CPN correlated with depression (r=.24~.39, p<.001) and negatively correlated with SCS subscore (r=-.10~-.25, p<.05). Depression was negatively associated with total SCS score and subscales (r=-.14~-.50, p<.01). Mediation analyses indicated that the sum of the indirect effects of self-compassion subscales attenuated the associations between depressive symptoms and CPA (β =.06, 95%CI:0.01-0.10), CEA (β =.11, 95%CI:0.07-0.16), and CEN (β =.08, 95%CI:0.03-0.13) but not CPN or CSA.

Conclusions: Self-compassion mediates the associations between CEA, CEN, and CPA and depression. Interventions aimed at increasing self-compassion should be explored in the prevention and treatment of adult depression among GBM who survived these types of trauma.

Substance Use, Transmission Networks and Local Contexts of HIV Risk

Toxicomanies, réseaux de transmission et contextes locaux du risque concernant le VIH

SSP13.01

Peel ACB Substance Use Project

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Roughly 75,500 people are living with HIV in Canada. In 2011, ACB communities accounted for 2.2% of the Canadian population, but comprised 16.9% of new HIV infections. Epidemiological data indicates that ACB migrants from endemic countries are 12.6 times more likely to contract HIV post-migration to Canada in comparison to their non-ACB counterparts. Heterosexual sex is reported to be the main mode of transmission among ACB people in Canada. However, given the social, economic and political exclusion of ACB communities, as well as the connection between low socio-economic status, substance use and HIV transmission, it is important to consider substance use in ACB communities. Toronto's gentrification over the last two decades and the "pushing out" of racialized bodies to surrounding areas such as Peel Region has left the region infrastructurally under-resourced and has left service providers such as the Peel HIV/AIDS Network with many questions about the specific needs of ACB communities.

This study explored the question: 'what are the service access needs of ACB substance users in Peel Region? Towards this end we used a key informant recruitment strategy to reach 25 community members who self-identified as ACB and who use substances; and 9 local service providers. We administered brief demographic surveys and conducted semi-structured interviews with each participant.

Preliminary results demonstrate that there is a growing number of ACB people who use substances. The vast majority reported using marijuana, many others reported using marijuana in conjunction with other drugs such as cocaine. Participants mainly used drugs as a form of escape from their everyday problems, which ranged from their involvement in sex work to coping with abuse, racialized poverty, and living with HIV. Service providers reported needing more resources, training and culturally appropriate supports to adequately address the local need of ACB substance users in Peel region.

SSP13.02

"Oh, and he's a drug user": the lived experience of inpatient hospital stays for people living with HIV/HCV who use substances

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Background: Hazardous drinking and illicit drug use (substance use) is associated with barriers to accessing and continuity in healthcare, sub-optimal medication adherence, negative health outcomes and poorer quality of and satisfaction with care. Little is known about the inpatient hospital care experiences of people living with HIV and/or HCV who use substances. Understanding the care experience is critical to inform interventions and quality improvement initiatives for those who use substances.

Methodology: We conducted a qualitative study involving semi-structured interviews with adults living with HIV and/or HCV who self-identified as using substances. Participants described their experiences accessing and receiving acute care, including management of their substance use, during overnight hospital stays. 24 adults (19 men, 5 women) from Ottawa and Toronto participated in the

study. Interviews were audio-recorded and transcribed. Data were analyzed inductively.

Results: Participants recounted diversity in the quality and timeliness of care while in hospital. Experiences of care varied across shifts, admissions, and hospitals often creating a sense of frustration. Most participants reported stigma and resulting difficulty accessing desired healthcare as a result of 'presumed' substance use. Open discussions between patients and clinicians about their drug use and related needs were infrequent. Inadequate pain management, withdrawal and boredom led to instances of leaving 'against medical advice', requesting drugs from visitors, and not prescribed psycho-active drug use during admission. Even when directly observed by staff, psycho-active drug use was rarely acknowledged by health care providers or discussed with patients.

Conclusion: People living with HIV/HCV perceived their substance use to be a barrier to seeking, accessing and continuing appropriate hospital-based care. Clinician-patient dialogue about substance use-related practices and needs rarely occur. Interventions to improve consistency of care, across shifts and admissions, decrease stigma, and provide adequate pain management are necessary to improve health care for those who use substances.

SSP13.03

"If I mix benzos with drugs, I don't give a f*ck about risk": Practices of Psychotropic Medication Use among Cocaine Users in Downtown Montreal

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Background: Cocaine abuse is a major public health concern due to its role in the HIV and hepatitis C virus (HCV) epidemics in Canada. A significant area of alarm among cocaine users who inject or smoke cocaine is their frequent misuse of psychotropic medication (PM), such as tranquilizers, sedatives, stimulants, and antipsychotics.

Objective: To describe and understand practices of PM use among cocaine users in Downtown Montreal.

Method: Ethnographic methods including participant observation and semi-structured interviews were used in an iterative manner. Participants were recruited using the snowball technique through outreach workers and study participants.

Results: Two thirds of participants (n=50) were male and range in age from 20 to 60. A significant proportion of them reported a polydrug use pattern that includes frequent concomitant opioid use (heroin and/or prescription opioids (PO)). Benzodiazepine-based tranquilizers and the atypical antipsychotic quetiapine were the most frequently used PM. We identified five main practices of PM use that take place in the context of polydrug consumption:

1) as "downers" from cocaine high (benzodiazepines and quetiapine),

2) as enhancers of the heroin/PO effects (benzodiazepines),

3) as reducers or suppressors of the heroin/PO withdrawal symptoms (benzodiazepines),

4) to enable a different type of "trip" (benzodiazepines) and

5) to treat mental and physical problems (benzodiazepines and quetiapine).

Conclusion: Practices of PM use showed several complementary functions that PM fulfill in the context of polydrug use. Both the soothing and stimulating effects of PM seemed to reinforce the patterns of drug use among participants, posing various risks including the one of HIV/HCV transmission. The results highlight the need for clinicians to assess clients' substance use patterns when prescribing PM and to question cocaine abusers about PM use. The findings also underline certain unmet service needs in relation to mental health and HIV/HCV prevention among cocaine users.

The Health of African, Caribbean and Black Communities

La santé des collectivités africaines, antillaises et noires

SSP14.01

Becoming Positive in Canada: The Social Drivers of HIV Acquisition Among Black Immigrants

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Background: HIV incidence in Canada is disproportionately high in persons emigrating from countries with generalized HIV epidemics. The MSAFIRI Study characterizes the social drivers of HIV acquisition in African, Caribbean and Black (ACB) immigrants in Ontario using mixed-methods. Quantitative analysis found that 33% of infections occurred post-arrival to Canada. We present the qualitative findings.

Methods: In-depth interviews with a purposive sample of ACB MSAFIRI Study participants were analyzed using

grounded theory to examine the social circumstances and sexual experiences underlying HIV acquisition in Canada. Participants were in HIV care, attributed HIV to sexual exposure and could identify their source partner/s.

Results: Participants included 20 women and 24 men (18 LGBQT) of median 41 years' age; 59% were from the Caribbean, 41% from Africa. The time to diagnosis post-migration ranged 2–38 years. Four crosscutting themes were identified: migrant and racial identity; cultural loss and social vulnerability; HIV risk perception; and relationship dynamic. Acculturation was an isolating and racialized process for many new immigrants, and around the time of infection most participants were detached from traditional social networks and families. Regardless of birthplace, nearly all participants believed HIV affected MSM, people of colour, and those living in their countries of origin but not "white Canadians". Men who had immigrated as young adults engaged in inter-racial relationships they had felt unable to access in their birthplace, and felt immune to HIV risk. MSM enjoyed multiple casual relationships, whereas heterosexual participants enjoyed serious monogamous relationships. Women became involved in relationships or encounters where they had limited power to enact sexual agency, even if realizing their risks.

Conclusion: HIV acquisition in ACB immigrants may reflect the perpetuation of a syndemic tied to risk misperceptions and inequities of race, gender, and social capital. This urges more targeted messaging and culturally competent prevention strategies for new immigrants.

SSP14.02

A qualitative exploration of stigma among African immigrants identified as HIV-positive during the Immigration Medical Examination

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Since 2000, there has been an increasing over-representation of immigrants from Africa living with HIV in Alberta, Canada (Alberta Health, 2012). There is a gap in our knowledge regarding the challenges faced by these immigrants and their families in coping with HIV illness, stigma, and settlement experiences. This multidisciplinary study involved researchers from both community and academic settings, and several collaborators who provided health and social services through AIDS Service Organizations (ASOs) and HIV clinics in Alberta. Using qualitative methods, we assessed HIV-related stigma among immigrants of African ancestry who experienced HIV testing through the Canadian Immigration Medical Examination (IME) process. The IME includes a mandatory HIV test; the test at times confirms prior knowledge of an HIV diagnosis, but at other times, is the initial diagnosis for immigrants, refugees, and temporary foreign workers. We collected interview data to explore and understand stigma related to the IME process. In addition to better understanding the complexity of stigma for this population, we also gained insights into the challenges of settlement when immigrants living with HIV moved between provinces and jurisdictions in Canada. A psychometric scale to explore and understand internalized, enacted, and anticipated stigma was also used. As part of this study we explored recruitment challenges with key stakeholders, who named HIV stigma and fear as a key barrier to participation. Finally, we discuss implications for future study and present recommendations for HIV community-based services and research among the African, Caribbean, and Black communities in Canada.

SSP14.03

Beyond "pacifier programs": engaging heterosexual Black men in community-based responses to HIV in Ontario

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Background: ACB people who acquired HIV through heterosexual relationships account for almost 20% of HIV-positive people in Ontario; yet, ACB people altogether make up less than 5% of the provincial population. Until recently, men outnumbered women among ACB people who acquired HIV through heterosexual contact, but men are less likely than ACB women to be tested and diagnosed, appear less likely than women to seek services.

Purpose: We present preliminary findings from phase one of weSpeak, comprising data from 26 focus groups in Ottawa, Toronto, London and Windsor. weSpeak is a 5-year program of research and related activities in Ontario with a goal of reducing HIV vulnerabilities and promoting resilience through active engagement of self-identified heterosexual ACB men in programs, research, and policy.

Methods: We organized 20 focus groups with self-identified heterosexual ACB men (N=145) to explore ideas and experiences related to the determinants of HIV vulnerabilities, resilience and engagement. Focus groups in Ottawa (5), Toronto (7), London (4) and Windsor (4) included youth aged 16-24 years, adult English-speaking and French-speaking men, and men who identified as living with HIV. Additionally, 6 focus groups were held with program and policy stakeholders (N=41) across the four cities to explore their perspectives on vulnerability and resilience in relation to heterosexual ACB men.

Results: The main determinants of interpersonal and structural vulnerability that have emerged include: lack of family discussion about sexuality; issues related to systemic racism; the absence of safe spaces where men may connect, learn together and support each other; and a lack

of programming that addresses issues related to heterosexuality and masculinity.

Implications: ACB men understand how they may be vulnerable to HIV but do not necessarily engage their vulnerabilities productively. There is a need for creative and context-specific approaches to engaging heterosexual ACB men in community-based responses to HIV.

SSP14.04

Community Response to HIV among Heterosexual Black Men in Ontario

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Background: ACB people make up about 2.5% and 4% of the Canadian and Ontario's population respectively. However, they account for nearly 20% of HIV infection in the province. Heterosexuality is the major mode of transmission of HIV among ACB. Sixty percent of the HIV infection among the ACB people in the province occurs among heterosexual ACB men due to the multifaceted challenges ACB men face coupled with other barriers to HIV testing. Ontario is one of the four Canadian provinces where HIV infection is concentrated.

Purpose: To reduce ACB men's vulnerability through engaging ACB men. This paper will discuss the preliminary findings from five community stakeholders and service providers' interactive focus group discussion (FGD) in the four cities.

Research Design: a team of researchers across the province developed a five years community-based program of research "weSpeak" which is being implemented in four cities of Ontario; Ottawa, Toronto, London and Windsor. We conducted five focus group discussions (FGDs) with various community stakeholders and service providers in four cities; Ottawa (1), Toronto (2), London (1) and Windsor (1). FGD participants were primarily various social and health service providers and community stakeholders. FDG were transcribed verbatim and thematic analysis was completed.

Preliminary Results: Major themes revealed were: Issues associated with vulnerability, access to health and social services, resilience among ACB men, and suggestions for moving forward.

Discussion and Implications: HIV research, programming and policy in Ontario have not been well aligned with the needs and interests of heterosexual ACB men. In order to effectively respond to the health and social service needs of ACB men, their involvement is needed at each level which previous efforts have not addressed well. This would be best achieved through collaborative partnership between sectors and community organizations serving the ACB men.

SSP14.05

"… helping people in the congregation view HIV/AIDS from a new perspective": Engaging Black Churches to Implement an HIV Stigma-Reduction Intervention in Ontario

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Background: HIV stigma impedes critical dialogue on HIV, and undermines community engagement in prevention and treatment. For Black communities, stigma-reduction efforts should be inclusive, culturally relevant, and promote empowerment and social justice. Black PRAISE emerged from stakeholders' concerns about the persistence of stigma, and their recommendation to engage community leaders in stigma-reduction.

Purpose: In various forums on the African and Caribbean Stigma Study (2004-2006), attendees prioritized engaging Black faith leaders in stigma-reduction efforts. In 2012, researchers, service providers, people living with HIV, community members and pastors convened a dialogue on stigma, and agreed to collaboratively develop and test a stigma-reduction intervention among Black congregations in Ontario.

Methods: Black PRAISE is a social network intervention where constituents facilitate development of the intervention, and change reverberates through intersecting networks. The stakeholders: developed the framework and content for the intervention and evaluation; recruited collaborating churches, and supported them to implement the intervention; and supported community stakeholders to implement the evaluation. The intervention addresses three domains of stigma: inappropriate fear of transmission, negative judgements about people living with HIV, and compound or layered stigma. Congregations participated in the following sequence of activities: distribution of a booklet promoting informed and critical understanding of HIV; a sermon on compassion and social justice; and a short video featuring community members' experiences of and responses to stigma. The evaluation includes surveys of the congregations (baseline, post-intervention, and 3-month follow-up), plus in-depth interviews with 2-3 congregants per church.

Results: Pastors and congregants expressed being more empathetic, viewed "HIV/AIDS from a new perspective", and increased their understanding of systemic issues. Black PRAISE strengthened trust, understanding and solidarity among the stakeholders.ImplicationsEngaging faith

institutions in stigma-reduction requires time, financial and other commitments to build trust, sustain infrastructures, and negotiate challenges. Black PRAISE is a model for implementing similar initiatives.

The Medico-Legal Borderland: Criminalization, Law, Policy and Resistance

La frontière médico-légale : Criminalisation, droit, politique et résistance

SSP15.01

Canadian Coalition to Reform HIV Criminalization: Supporting the engagement of people living with HIV who have survived criminal and public health laws

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This presentation will explore the emerging development of the Canadian Coalition to Reform HIV Criminalization. The coalition was formed in late 2016 and is comprised of people living with HIV - including people with lived experience of HIV criminalization, community workers, lawyers and academics from across the country working towards reforming discriminatory and unjust criminal and public health laws and practices that criminalize and regulate people living with HIV in relation to HIV exposure, transmission and non-disclosure. Canada has been known as a hot spot for the criminalization of HIV non-disclosure, exposure and transmission. But advocacy efforts to reform this situation have not sufficiently engaged those directly targeted by coercive laws – especially people with lived experience of HIV criminalization. This new coalition aims to centrally place the lived experience of people living with HIV directly impacted by the law in the development of advocacy and reform efforts. One of the main objectives of our work is to support people who have been criminally charged and build the capacity of people living with HIV in Canada to become advocates. Based on an analysis of our ongoing collaborative work, this presentation will elaborate our efforts to address unjust HIV criminalization in Canada and examine the practical complexities of realizing meaningful engagement of people living with HIV and provide support to those who have been criminalized. In our presentation we will explore our ongoing learning, including addressing critical reflections, complexities, and wise practices regarding how the coalition has practically worked to operationalize meaningful engagement. Finally, our presentation will also propose ways that organizations responding to HIV can better support people who have been criminally charged in relation to HIV and support the efforts of the coalition to reform HIV criminalization.

SSP15.02

HIV: The Affect of Assisted Dying Bill C-14

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Carter v. Canada was a turning point in Canadian law in February 2015, when the Supreme Court of Canada ruled that the section of The Criminal Code that restricted physician-assisted dying violated individuals right to life. Hospitals are currently generating protocols and guidelines, as Quebec has done, to better define the conditions in which patients meet the criteria for access to medical aid in dying (MAID). Meanwhile, in the face of so much uncertainty, it is unclear whether people living with HIV will be considered for euthanasia if all treatment options were exhausted.

The study will examine the Canadian model of MAID for people living with HIV. A review of the literature surrounding euthanasia and assisted suicide in Canada, and experience with MAID providers in Hamilton, Ontario, documents the paradigm shift in society's approach to care of terminally ill persons and the concept of health from a broad anthropological perspective. This study is part of a larger project that will conclude in 2017. The purpose of the project was two-fold: (a) assess the effectiveness and safety of the new medical assistance in dying legislation, and; (b) demonstrate how considerably more complex of a situation HIV is when applied to Bill C-14 criterion by comparison to other end-of-life conditions. Preliminary results indicate that patients still face barriers accessing MAID, including the mental health evaluation of competence to consent and development of an individualized plan of care. There are also concerns about change in quality of life after being diagnosed with HIV, and the interpretive conventions of Bill C-14 by a physician. Findings from this study inform the debate on the legalisation of assisted dying.

SSP15.03

Does training the police about HIV prevention and harm reduction goals help to build positive relationships with needle and syringe programs?

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Background: Training police on the HIV prevention benefits of needle and syringe programs (NSPs) and other harm reduction interventions is viewed as a best practice to facilitate more collaborative relationships between police and these programs. We assessed the relationship between offering training programs and self-reported relationships between NSPs and their local police departments.

Methods: Using an online survey, we asked NSP managers across Canada about their programs, the types of training offered to police, and the quality of their NSP-police relationships.

Results: Our survey response rate was 89%. Among NSP managers, 69% reported that their program had a "positive" or "mostly positive" relationship with the police. In-service training about topics such as needle-stick injury prevention and NSP effectiveness was provided by less than half of the programs surveyed. Over three-quarters reported no established protocols to resolve conflicts between NSP staff and police. Four variables, all related to in-service training, were significantly related to positive NSP-police relationships, including training about: NSP program goals (OR 7.7; 95% CI 2.0, 33.1); needle-stick injury prevention and basics of blood-borne virus transmission (OR 4.0; 95% CI 1.1, 15.34); the health and social concerns of people who use drugs (OR 3.9; 95% CI 1.1, 13.5); and evidence about the impact of injection equipment distribution (OR 3.9; 95% CI 1.1, 13.5).

Conclusions: Given the study design, we cannot discern if positive NSP-police relationships led to more opportunities to offer in-service training, if in-service training promotes the development of positive relationships, or if these relationships and in-service training are mutually reinforcing over time. Future longitudinal studies will help to better understand the association between inter-organizational relationships and in-service training, and how to promote delivery of harm reduction and HIV prevention knowledge to police.

Social Sciences: Other

Sciences sociales : Autre

SSP16.01

Evaluation of a Rapid Response Service focused on HIV/AIDS and other sexually transmitted and blood borne infections

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Background: The Ontario HIV Treatment Network's (OHTN) Rapid Response Service provides summaries of peer reviewed and grey literature on issues identified by community-based organizations, policy makers, and healthcare providers. These reports synthesize HIV research evidence to support programs, services and policies.

Methods: To assess the utility of the OHTN's Rapid Response Service, all reviews published since 2009 were analysed, examining characteristics including: populations and topics, requestor affiliations and number of downloads. Requestors of Rapid Responses between 2014 and 2015 were also interviewed to determine the impact of the reviews on programs and services.

Results: Of 111 Rapid Responses reviewed, the majority focused on the following populations: people living with HIV (n=41), men who have sex with men (n=25), people who use drugs (n=9), African-Caribbean and Black communities (n=6) and Indigenous people (n=2). They covered topics including HIV prevention (n=31), treatment (n=15), testing (n=12), epidemiology (n=8), linkage to care (n=1), and retention in care (n=1). Approximately one third of Rapid Responses (n=35) were on topics related to HIV-associated syndemics and co-morbidities. Most Rapid Responses were requested by AIDS service organizations (n=50). The average number of downloads per review was 1,015. Providing academically rigorous research in lay language and summarizing the most relevant evidence were identified as the most useful aspects of the service.

Conclusion: The OHTN's Rapid Response service is a highly demanded and widely accessed knowledge translation product. By summarizing HIV-related research evidence, community-based agencies and other stakeholders are able to inform their current and future programs, services and policies.

SSP16.02

Successfully Integrating HIV Point-of-Care Testing in Non-Traditional Settings: Results of an International Scoping Review of Provider Perspectives

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Background: Point-of-care HIV testing (HIV POCT) is believed to be an important tool to engage first-time testers, individuals at high risk, those living in remote communities, and to encourage more frequent testing. Introducing HIV POCT in non-traditional sites has the potential to increase the accessibility of HIV testing. However, this will often involve approaching providers who may have limited prior experience offering a rapid HIV test. This scoping review is of provider perspectives on offering HIV POCT in their practices.

Objectives:

- Explore lessons learned from HIV POCT pilot programs and compare the perceptions and levels of acceptability from different healthcare provider perspectives including physicians, nurses, dentists, pharmacists and social workers.

- Determine common barriers and facilitators to put forth a set of recommendations to increase the likelihood of successful program implementation.

Methods: Our team used a search strategy that combined controlled vocabulary and keyword searches for the terms "HIV/AIDS" and "Point-of-care testing". Databases searched included MEDLINE, EMBASE, EBM Reviews, PsychINFO and CINAHL. No language or date limiters were applied. Data extraction forms were tested by two team members, and study data was extracted by one member. Inclusion criteria for studies selected for this review included: empirical studies investigating HIV POCT programs, publication in English or French, and publications from OECD countries.

Results: Frequently cited barriers to HIV POCT included lack of training, time and financial constraints, concerns with confidentiality, lack of provider confidence, and staffing issues. Most commonly cited facilitators included the identification of testing as a priority, provider education, and supportive staff and administration.

Conclusions: This paper highlights the concerns and gaps in introducing HIV POCT as a routine practice for healthcare providers. Based on the literature, our recommendations for successful implementation of HIV POCT include: identifying an opinion leader, offering comprehensive training, and adaptation of standard operating procedures.

SSP16.03

Intersections of Access: HIV/AIDS Service Organizations & Disability Service Organizations

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Background: People with disabilities are at least as vulnerable to HIV as the general population (Groce, 2013) but are often missing from HIV prevention, care and treatment initiatives. People with HIV can experience their condition as an episodic disability (O'Brien et al, 2008)) but are also largely missing from disability community initiatives. People living with HIV and people with disabilities both face stigma and systemic barriers to employment, health, social services and community inclusion.

Methods: An environmental scan was conducted that examined the intersections between HIV/AIDS Service Organizations (ASOs) and Disability Service Organizations (DSOs) in the Greater Toronto Area. The websites of 13 ASOs and 16 DSOs were reviewed in order to determine preliminary access information that impacts people living with HIV and people who have disabilities. Keyword searches were conducted as well as more in-depth reviews of available organizations resources and policies.

Results: Of thirteen (13) ASO websites reviewed:

- 9 organizations' websites have no mention of disability or accessibility in any form
- 3 organizations have accessibility policies on their site
- 1 organization has specific programming for people with disabilities
- 1 organization specifies the accessibility/lack of accessibility of their physical location on their website

Of sixteen (16) DSO websites reviewed:

- 12 organizations' websites have no mention of HIV/AIDS
- 3 organizations have articles or resources that mention HIV/AIDS
- 1 organization mentions HIV specific programming

Conclusions: Within a UN policy context of UNAIDS' 90-90-90 Goals and the Sustainable Development Goals that call for the eradication of HIV by 2030, the clear gap between disability and HIV service organizations is cause for concern. People living with HIV can also be people with disabilities and people living with disabilities are also vulnerable to HIV. A lack of accessible HIV services may, in fact, contribute to a greater vulnerability for people living with disabilities.

SSP16.05

A training needs assessment to inform the design of an e-learning intervention supporting nursing practice related to antiretroviral treatment adherence

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Background: Supporting people living with HIV (PLWH) with their antiretroviral treatment (ART) adherence is a core nursing competency. Most interventions aimed at optimizing ART adherence target the development of self-management skills among PLWH. Few educational interventions target nurses to help them in developing, maintaining and strengthening their competencies to better support PLWH with their ART adherence. Electronic and mobile devices are increasingly used to support learning processes and educational programmes in nursing. This study utilizes a training needs assessment to inform the development of an e-learning intervention for nurses working with PLWH in Quebec.

Objective: To present the results of a training needs assessment as the initial phase of a wider implementation research/doctoral project.

Methods: The study design is qualitative, including a collaborative approach with HIV nurse specialists. Semi-structured interviews were conducted with seven nurses, complemented by one focus group with nine nurses. Interviews and meeting recordings were transcribed and subjected to thematic analysis. A competency-based framework supported the interpretive process of qualitative analysis.

Results: Nurses were from different professional backgrounds, had different levels of experience and worked as clinician, manager, public health nurse, research coordinator, researcher and/or professor. Three main themes emerged from qualitative analysis: 1) Challenges, complexity and facilitators surrounding ART adherence (e.g profiles of PLWH, characteristics of ART, nurse-patient relationship, access to ART); 2) Nurses' core competencies (e.g; applying motivational interviewing principles; managing emotional components of caring for PLWH; assessing and managing side effects); 3) Nurses' preferences regarding educational strategies.

Conclusion: This needs assessment provides critical insights to purposefully design an e-learning intervention informed by various ways of knowing, including nurses' experiential knowledge, with the ultimate goal of broadening their repertoire of competencies around ART and better support PLWH in self-managing and adhering with ART.

SSP16.06

Circle of Care for HIV positive Women

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Overview: It is all about a community "Circle of Care" for HIV+ Women

Introduction: Circle of Care is a collaborative approach to providing diverse, innovative and practical support services to women living with HIV in Toronto. It is a consortium of five AIDS Service Organizations including the AIDS Committee of Toronto (ACT), Black Coalition for AIDS Prevention (Black CAP), PASAN, Toronto People with AIDS Foundation (PWA) and The Teresa Group. The Peer Support program of Circle of Care recruits trains and supports HIV+ women to act as peers to support other women living with HIV. Circle of Care peers accompany HIV+ women to appointments and programs, provide interpretation, translation and service navigation support. Our peers also go to local community agencies to talk about their experiences living with HIV and services available to HIV+ women. The Peer Support program builds on value, impact and benefit that can be experienced by women living with HIV when they are able to receive support from other HIV positive women.

Most women living with HIV don't know where to go for physical, emotional and psycho-social support. Some of them have stigma issues and are afraid to show up for appointments. That is where we as Circle of Care come in to fill the gap and help our fellow women navigate the complex system and receive support.

The Women's nursing clinic happens every first and Third Wednesdays of every month. HIV positive women meet over lunch, always with different speakers and a nurse from Casey house.

Monthly meetings with Peers are held to discuss program updates, shift debrief as well as self-care tips. In 2017 we shall start home-based care to support clients more.

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